

UPPSALA UNIVERSITET

KBH 2017/13 Doss 1:3

# Department of Women's and Children's Health

Annual report 2016

## Introduction

The department is vital in education as well as in research. Our department runs research projects covering all kind of topics within our specialities. We have researchers with excellent knowledge in qualitative as well as in quantitative research methods. This knowledge forms a basis for fruitful collaboration within and between our research groups.

During 2016 the department has been located at two different sites; one at the Uppsala University Hospital and one at the University Campus, where the International Maternal and Child Health (IMCH) has had their research activities. In terms of research infrastructure, the research laboratories moved from the University hospital to Rudbeck and Munin as of December 2016. During 2017, the department will be scattered among five different locations (BMC, Uppsala University Hospital, IMCH and Munin and Rudbeck laboratories). However, in February 2018 the majority of department staff will move to a single location just outside the present hospital area (MTC building).

A new research group, Clinical Psychology in Health Care (U-CARE), has moved from the department of Public Health and Caring Sciences over to our department in January 2017. The group includes clinical psychology and implementation sciences. The new competences by U-care (project leader professor Louise von Essen) will be an excellent supplement to teaching and research in our department.

Our colleague Associate Professor Anna Sarkadi obtained a position as Professor in Social Medicine at the department of Public Health and Caring Sciences. The research group CHAP moved along, however some of the senior research groups members decided to stay and joined the Pediatric Inflammation research group at the department of Women's and Children's Health.

The Department of Women's and Children's Health has had extensive responsibilities in the teaching of nursing students in ground and advanced level, midwifery students, medical students, master of global health students, laboratory science and postgraduate students. The students generally give good evaluations on our educational programs. This would not have been possible without the extensive work of our teachers.

The overall research theme of the department has been covered by various dimensions of women's and children's health in low, middle, and high income countries. The research profiles cover various aspects of sexual and reproductive health in women and a wide spectrum of paediatric health issues. The research activities are organized in 13 research groups and many of the on-going projects are interdisciplinary and built on inter-professional collaboration. During the last year discussions on strategic issues have increased between the research group leaders in the sub-divisions, with the aim of improving our research and funding. The head of the department and the two new FOUU organizations (ObGyn and Ped) between the hospital and the university has helped to encourage strategic discussions. The number of PhD students are stable and around 110.

It is at present difficult to fully predict how the move of location will affect the ongoing research and the wide range of teaching programs. However, it is expected there will be a number of positive effects. For the very first time different professions and sub-units

will be integrated which hopefully will make them benefit from optimization of the administration capacity, use support interaction between research groups and will strengthen their research and teaching environment.

Despite the situation concerning workspace, the department of Women's and Children's Health will continue as a clinical research and educational institution and it is important that there is a good relation and mutual understanding with the OB GYN Department as well as the Children's Hospital of Uppsala. I am pleased to announce that this spirit in combination with a friendly atmosphere continues. Everybody is truly needed for a successful outcome.

A number of senior professors are having positions at the department. Ove Axelsson and Jan Gustafsson continue for another year, Ulf Högberg retired from his position as Professor in OB/Gyn and continues as senior professor. Tanja Tydén retired from her position as Professor in Caring Sciences at the department of Public Health and Caring Sciences and she also continues as senior professor but in our department. The two recruitment processes have been started to fill the vacancies of professors in OB/Gyn and Paediatrics.

To be the Head of the Department of Women's and Children's Health is an important and most often inspiring task. We have new exciting challenges to look forward to in the years to come. We are lucky to work within an important field with the aims to improve health for women and children around the world. The year 2016 was a successful year regarding both science and education. I want to thank all teachers, researchers, administrators and laboratory technicians for their outstanding work during the past year.

Agneta Skoog Svanberg Head of the Department of Women's and Children's Health

# List of Contents

INTRODUCTION	1
ADDRESS LIST	4
ORGANIZATION	8
RESEARCH GROUPS	10
SCIENTIFIC REPORTS OF RESEARCH GROUPS	11
Gynecological Endocrinology	12
Obstetrical Research	17
Reproductive Biology	33
Reproductive Health	38
International Child Health and Nutrition	47
International Maternal and Reproductive Health and Migration	66
International Sexual and Reproductive Health	78
Pediatric Endocrinology	91
Perinatal, Neonatal and Pediatric Cardiology Research	101
Pediatric Oncology and Neurology	109
Pediatric Surgery and Pediatric Urology	123
Pediatric Inflammation	133
Child Health and Parenting Research Group	142
UNDERGRADUATE TEACHING	148
RESEARCH EDUCATION	
AWARDS AND APPOINTMENTS	150

## Address List Department of Women's and Children's Health

### <u>www.kbh.uu.se</u>

Address: Uppsala University Hospital, SE- 751 85 Uppsala, Sweden Office: fax +46 (0)18 55 97 75

e-mail address: <u>firstname.lastname@kbh.uu.se</u>

Muzdalifat Muganyizi Abeid Beth Maina Ahlberg Fredrik Ahlsson Gunnar Ahlsten Tansim Akhter Ammar Al-Mashhadi Ann-Charlotte Almblad Kjell Alving Hanna Andersson Ola Andersson Gertrud Angsten Hashem Amini Riina Arnio Jonna Arousell Johan Arvidson Anna Arvidsson Kaime Wanjiku Atterhög Furaha August Pia Axemo Ove Axelsson Cathrine Axfors Nahar Baitun Elazar Tadelech Tadesse Balla Elin Bannbers Gillian Barker Johanna Belachew Eva Bergman Anna Berglund Lina Bergman Anna Bergström Hanna Berhane Lillemor Berntsson Magdalena Bjerneld Kathrine Bjersand Ingrid Blixt Ylva Thernström Blomqvist Maja Bodin Pär Bokström Marie Bolin Maria Borgestig Catrin Borneskog

Magnus Borres Vladimir Bourlev Katarina Strand Brodd Thomas Brodin Emma Bränn Ulrika Byrskog Ann-Sofie Båth Karin Cato Jenny Thorsell Cederberg Maria Cederblad Gianni Celsi Mickey Chopra Rolf Christofferson Iris Ciba Mariela Contreras Chris Cotter Fatimah Dabo Margareta Dahl Anton Dahlberg Ingrid Dahlbom Johan Danielson Elisabeth Darj Eva Davey Barbro Diderholm Tanya Doherty Felipe Donoso Sten Dreborg Duong Duc Patricia Eckerdal Orvar Eeg-Olofsson Greta Edelstam Agnes Edling Ann Edner Åsa Edvinsson Christoffer Ehrstedt Maria Ekelund Kristine Eklund Maria Ekstrand Eva-Charlotte Ekström **Evangelina Elenis** 

Hanna Eneroth Annika Englund Natalie Engsheden Gunn Engvall Leif Eriksson Olle Eriksson Annika Esscher Birgitta Essén Karin Eurenius Uwe Ewald Helena Fabian Inna Feldman Pauline Binder Finnema Peter Flacker Kristina Forsblad Anders Forslund Fanny Fredriksson Per Frisk Amy Lynn Frith **Britt-Marie Frost** Eva-Lotta Funkquist August Furaha Anna Fäldt Elisabet Fält Karin Fängström Mehari Gebre-Medhin Clary Georgantzi Malin Ghanem **Spyridon Gialamas** Malin Gingnell Geraldine Giraud Annika Grönberg William José Ugarte Guevara Johanna Gunnarsdottir Elisabet Gustafson Britt Gustafsson Jan Gustafsson Helen Haines Gunilla Hallberg Ulf Hanson **Tony Hansson** Sally Haroun Gunilla Hedén Lena Hedén Gun Heimer Dan Hellberg Charlotte Hellgren Lena Hellström-Westas Dorcus Kiwanuka Henriksson Hanna Henriksson **Ruth Hermansson** Susanne Hesselman Maria Heyman

Ingegerd Hildingsson Yngve Hofvander Annika Hollsing Kirsten Holmberg Waheedul Hoque Jan Holte Jenny Hultstrand Emma Håstad Hjördis Högberg Niclas Högberg Ulf Högberg Anette Höglund Berit Höglund Petrida Ijumba Stavros Iliadis Natalia Iliasova Juliana Inoue Natalja Jackmann Åke Jakobson Caroline Jansson Paridhi Jha Lana Salih Joelsson Emily White Johansson Jennifer Johnsson Inger Wahlström Jonsson Maria Jonsson Pysse Jonsson Anders Jonzon Malin Jordal Katja Junus Ashish KC Helena Kaihola Theodora Kunovac Kallak Tove Kamsvåg-Magnusson Malin Karlberg Victoria Karlsson Johan Kaarme Birgitta Karanikas Helena Karypidis Ann-Marie Kassa Ylva Fredriksson Kaul Islam Ashraful Khan Hussein Lesio Kidanto Eva Kimber Freddy Kitutu Marie Klingberg-Allvin Hans Kollberg Christina Krantz Åsa Kratz Jona Kristiansdottir Ingela Kristiansen Merit Kullinger Carina Källestål

Birgitta Larsson Margareta Larsson Camilla Larsson Elin Larsson Marita Larsson Helene Lidström Helene Engstrand Lilja Lena Liljeström Gunnar Liminga Solveig Nordén Lindeberg Nina Linder Hans Lindgren Karin Lindgren Gunilla Lindmark Annika Lindström Emma Lindström Linda Lindström Helena Litorp Gustaf Ljungman Staffan Lundberg Inger Wallin Lundell Helena Lundgren Maria Lundgren Cecilia Lundin Elisabet Lundmark Thomas Lundqvist Göran Läckgren Susanne Thorell Löberg Gudmar Lönnerholm Lena Lövkvist **Terese Magnusson** Marlene Makenzius Mari-Cristin Malm Laszlo Markasz Magdalena Mattebo Kokusiima Colomba Mbekenga Staffan Meurling Andrew Mgaya Christian Moberg Lena Moby Sibone Mocumbi Soheila Mohammadi Kajsa Åsling Monemi Cecilia Montgomery Rahman Syed Moshfiqur Projestine Muganyizi Ajlana Mulic-Lutvica Josanne Munsters Aimable Musafili Åsa Myrelid Mats Målqvist Andreas Mårtensson Tord Naessen

Nima Naseh Laleh Nayeb Maria Nelander Åsa Neuman Tryggve Nevéus Thu Nga Nguyen Maria Lindström Nilsson Barni Nor Sarah Nordqvist Lennart Nordvall Johanna Norenhag Erik Normann Britt-Inger Nyberg Kerstin Hedberg Nykvist Charlotte Nylander Camilla Nystrand Niklas Nyström Matts Olovsson Karl Wilhelm Olsson Pia Olsson Amal Omer-Salim Paola Oras Ulrika Wester Oxelgren Eunice Pallangyo Josefine Palle Anna Palm Maria Palm Ashish Pathak Mandira Paul Mattias Paulsson Christophe Pedroletti Gyula Pekar Andrea Pembe Kristina Persson Stefan Swartling Peterson Wilton Pérez Lars-Åke Persson Susan Pfeifer Inger Sundström Poromaa Lemm Proos Soorej Jose Puthoopparambil Jessica Påfs Anisur Rahman Nisha Rana Charlotte Heijkenskjöld Rentzhog Masoumeh Rezapour Inger Jönson Ring Christine Rubertsson Mattias Rööst Raziye Salari Raghad Samir Filipa Sampaio Petra Sandell

Anna Sandström Karin Sanner Anna Sarkadi Birgitta Segebladh Martin Selinus Katarina Ekholm Selling Fredrik Serenius Rubina Shaheen **Richard Sindelar** Josefin Sjömark Gunnar Sjörs Alkistis Skalkidou Ingridur Skirnisdottir Erik Sköldenberg Nazmul Sohel Sara Sohlberg Richard Ssegonja Johan Staaf Anneli Stavréus-Evers Arne Stenberg Anders Stenbäck Maria Halldin Stenlid Pia Kalm Stephens Margareta Strinnholm Bo Strömberg Karin Stålberg Kerstin Ståhlberg Maria Stålhammar Pernilla Svefors Liisa Svensson Ingemar Swenne Jörgen Syk Sara Sylvén Marie Säve Elisabet Söderberg Amare Tadesse Hanna Taylor Ellen Ternby Elin Ternström Jenny Thor Ylva Tindberg Linda Bratteby Tollerz Jill Trenholm Nikolaos Tsolakis Torsten Tuvemo Tania Tvdén Gerasimos Tzortzatos Antónia Tökés Karin Törnblom Helena Volgsten Åsa Wahlberg Anna Wahlberg Linda Wallström

Jan Wesström Maria Wickström Anna-Karin Wikström Ingrid Wikström Johan Wrammert Fatma Gulen Yaldir Shirin Ziaei Johan Ågren Annika Åhman Helena Åkerud, adjunct professor until June 2016 Anders. Öberg Mariella Öberg Anders Öman

e-mail address: <u>firstname.lastname@nck.uu.se</u>

Gun Heimer

e-mail address: firstname.lastname@akademiska.se

Christophe Pedroletti

## Organization

### Chairman

Agneta Skoog Svanberg

### **Deputy Chairman**

Matts Olovsson

### **Department board**

(from July 2015)

Skoog Svanberg	chairman
Essén	teacher representative
llström-Westas	teacher representative
ngvall	teacher representative
Källestål	teacher representative
Nevéus	teacher representative, deputy
lovsson	teacher representative, deputy
Selinus	representative for technical/adm. personnel
örnblom	representative for technical/adm. personnel, deputy
indström	graduate student representative
rammert	graduate student representative, deputy
dersson	student representative
öyttynen	student representative
	student representative, deputy
	Skoog Svanberg Essén Ilström-Westas ngvall Källestål Nevéus lovsson Jelinus örnblom ndström Yrammert dersson öyttynen

### Seniorprofessors

Ove Axelsson Jan Gustafsson Ulf Högberg Tanja Tydén

### **Professors emeriti**

Uwe Ewald Mehari Gebre-Medhin Yngve Hofvander Elof Johansson Gunilla Lindmark Gudmar Lönnerholm Lars-Åke Persson Claes Sundelin Torsten Tuvemo

### **Director of graduate studies**

Lena Hellström Westas

### Director of undergraduate studies

Tryggve Nevéus Inger Sundström Poromaa/Gunn Englund deputy

### Administration

Hanna Andersson Malin Ghanem Gunilla Hedén Susanne Thorell Löberg Terese Magnusson Martin Selinus Kerstin Ståhlberg Marie Säve Hanna Taylor Jenny Thor Karin Törnblom

### **Computers/IT**

Kristine Eklund Hans Lindgren

### Technicians

Eva Davey Lena Moby Elisabet Söderberg

### **Research Groups**

<u>Gynecological Endocrinology</u> Tord Naessén, MD, PhD, Professor

<u>Obstetrical Research</u> Alkistis Skalkidou, MD, PhD, Professor

<u>Reproductive Biology</u> Matts Olovsson, MD, PhD, Professor

<u>Reproductive Health</u> Inger Sundström Poromaa, MD, PhD, Professor

International Child Health and Nutrition Andreas Mårtensson, MD, PhD, Professor

International Maternal and Reproductive Health and Migration Birgitta Essén, MD, PhD, Professor, Senior lecturer

International Sexual and Reproductive Health Christine Rubertsson, PhD, Professor, Senior lecturer

<u>Pediatric Endocrinology</u> Ingemar Swenne, MD, PhD, Associate professor

Perinatal, Neonatal and Pediatric Cardiology Research Lena Hellström-Westas, MD, PhD, Professor

<u>Pediatric Oncology and Neurology</u> Gustaf Ljungman, MD, PhD, Associate Professor

<u>Pediatric Surgery and Pediatric Urology</u> Helena Engstrand Lilja, MD, PhD, Associate Professor

<u>Paediatric Inflammation</u> Kjell Alving, PhD, Professor

<u>Child Health and Parenting Research Group</u> Anna Sarkadi, MD, PhD, Associate professor, Adjunct senior lecture Scientific Reports

### **Gynecological Endocrinology**

### **Tord Naessen**

With extensive inter-disciplinary collaborations, our research group address; Effects of endogenous and exogenous steroid hormones with regard to the aging process in elderly, e.g. arterial aging, cardiovascular disease (CVD), cognition / brain volumes and survival. Possible effects of the sharp drop in menopausal hormone use, on certain age-related chronic diseases. Environmental pollutants and possible associations to age-related diseases in elderly; and whether these effects might be partly mediated via endogenous sex hormone levels. We also study premenstrual syndrome (PMS/PMDD), vascular effects of pre-eclampsia, recurrent depressions in adolescence and metabolic consequences later in life and the ovarian follicular fluid content of steroid hormones and proteins with regard outcome of in-vitro fertilization. We suggest and evaluate a new principle for non-invasive assessment of arterial aging/atherosclerosis, based on separate assessment of the artery wall layers by using non-invasive high-frequency ultrasound (20 - 50 MHz), which we apply in many of the conditions above.

### National Centre for Knowledge on Men's Violence against Women (NCK)

### **Gun Heimer**

NCK is a knowledge and resource centre at Uppsala University. NCK is positioned within Uppsala University as a centre for certain assignments, without faculty affiliation. NCK reports directly to the vice-chancellor and has its own Board. Website: <u>www.nck.uu.se</u>

### Members of the group during 2016

Tord Naessen, Professor Gun Heimer, Professor (NCK) Olle Eriksson, MD, PhD Gunilla Hallberg, MD, PhD Tansim Akhter, MD, PhD Mariella Öberg, MD, Doctoral student (NCK) Jona Kristiansdottir, MSc, Psychologist, Research student Marita Larsson, Research nurse

### Publications 2014-2016

### 2016

- 1. Al-Saqi SH, Jonasson AF, Naessen T, Uvnas-Moberg K. Oxytocin improves cytological and histological profiles of vaginal atrophy in postmenopausal women. *Post Reprod Health*. 2016;22(1):25-33.
- Berglund A och Heimer G. "Att ha varit utsatt för våld ökar risken för ohälsa senare i livet. Kunskap om våldets förekomst och konsekvenser behövs i hela vården – anamnesen bör innefatta fråga om våld" Särtryck ur Läkartidningen, volym 113, 2016.
- 3. Kushnir MM, Naessen T, Wanggren K, Hreinsson J, Rockwood AL, Meikle AW, et al. Exploratory study of the association of steroid profiles in stimulated ovarian follicular fluid with outcomes of IVF treatment. *J Steroid Biochem Mol Biol.* 2016;162:126-33.
- 4. Eriksson O, Wall A, Olsson U, Marteinsdottir I, Holstad M, Agren H, Hartvig P, Långström B, Naessén T. Women with Premenstrual Dysphoria Lack the Seemingly Normal Premenstrual Right-Sided Relative Dominance of 5-HTP-Derived Serotonergic

Activity in the Dorsolateral Prefrontal Cortices - A Possible Cause of Disabling Mood Symptoms. *PLoS One*. 2016;11(9):e0159538.

- 5. Bergman L, Akerud H, Wikstrom AK, Larsson M, Naessen T, Akhter T. Cerebral biomarkers in women with preeclampsia are still elevated 1 year postpartum. *Am J Hypertens*. 2016;29(12):1374-9. Sept 21, DOI: 10.1093/ajh/hpw097
- 6. Akhter T, Wikström A-K, Larsson M, Larsson A, Wikström G, Naessen T. Association between angiogenetic factors and signs of arterial aging in women with pre-eclampsia. *Ultrasound Obstet gynecol 2016*;10.1002/uog.15981
- Akhter T, Wikström A-K, Larsson M, Larsson A, Wikström G, Naessen T. Serum Pentraxin 3 is associated with signs of arterial alteration in women with preeclampsia. *Int J Cardiol* 2017;

### 2014

- Bergman L, Akhter T, Wikstrom AK, Wikstrom J, Naessen T, Akerud H. Plasma levels of S100B in preeclampsia and association with possible central nervous system effects. Am J Hypertens. 2014 Aug;27(8):1105-11.
- Akhter T, Larsson M, Wikstrom AK, Naessen T. Thicknesses of individual layers of artery wall indicate increased cardiovascular risk in severe pre-eclampsia. *Ultrasound Obstet Gynecol*. 2014 Jun;43(6):675-80.
- 3. Oberg M, Stenson K, Skalkidou A, Heimer G. Prevalence of intimate partner violence among women seeking termination of pregnancy compared to women seeking contraceptive counseling. *Acta Obstet Gynecol Scand* 2014:93:45-51.

### NCK-reports 2014 - 2016

### 2016

1. Våld mot äldre kvinnor – En forsknings- och kunskapsöversikt, ISSN 1654-7195, NCK-rapport 2016:1.

### 2015

1. Redovisning av regeringsuppdraget att *Utveckla den nationella stödtelefonen Kvinnofridslinjen* (U2011/3939/JÄM)", ISBN 978-91-978448-8-8, NCK-rapport 2015.

#### 2014

- 1. Heimer G, Andersson T, Lukas S. *Våld och hälsa en befolkningsundersökning om kvinnors och mäns våldsutsatthet*. Uppsala universitet, ISSN 1654-7195. NCK-rapport 2014:1.
- Violence and Health in Sweden A National Prevalence Study on Exposure to Violence among Women and Men and its Association to Health, ISSN 1654-7195, NCK-report 2015:1, (engelsk översättning av NCK-rapport 2014:1)
- 3. Heimer G, Björck A, Kunosson C. *Våldsutsatta kvinnor samhällets ansvar*. Tredje upplagan av NCK:s lärobok, ISBN 978-91-44–09444-1. Studentlitteratur 2014.

### Agencies that support the work

Selander's foundation, 300 000 SEK ALF 878,000 SEK

### Endogenous sex steroid concentrations in elderly in relations to prevalent age-related conditions (e.g. arterial aging, cardiovascular disease, brain volumes and cognition), as well as to prediction of CVD events/death and as potential mediators of health effects of environmental pollutants.

Endogenous steroids and precursors within the cholesterol pathway in samples from #1016, 70-year old men and women (in PIVUS), were analyzed using Liquid Chromatography Tandem Mass Spectrometry (LS-MS/MS), in collaboration with the Internal Medicine Department, Uppsala, and ARUP laboratories in Salt Lake City, Utah, USA. We have found increased endogenous estrogen levels in both men and women with prevalent cardiovascular disease (CVD) and significant associations to arterial aging, assessed by high-frequency ultrasound (20 - 50MHz). Both findings most likely represent an endogenous attempt of local estrogen synthesis to counteract ongoing inflammatory/atherosclerotic process.

Currently we evaluate potential effects of subtle differences in *endogenous* steroid hormone concentrations in elderly with regard to artery wall aging (ultrasound), prevalent CVD, coming risk of CVD/death, cognition/brain volumes and associations to environmental pollutants.

Results might elucidate effects of endogenous steroid hormones (esp. estrogens) on the aging process and guide in tailoring hormone therapy regimens in elderly, aiming to reduce/modify the expression of some age-related chronic diseases.

# Menopausal Hormone Therapy (MHT) – effects on the risk of certain age related diseases and whether the 80% drop in MHT prescriptions since 2002, have affected trends over time in incidence rates of these diseases.

In a National-based register study we investigate whether the sharp drop (>80%) in prescriptions on MHT since 2002, might have affected time trends in incidence rates for certain age-related diseases, e.g. osteoporotic fractures, myocardial infarction, ischemic stroke, colon cancer diabetes mellitus, thrombosis and breast cancer. Corresponding incidence rates in men might reflect general trends over time in these rates. In the material we also analyze relative risks in women w and w/o long-term MHT (>=5yrs), with regard to the above-mentioned diseases; and to possible effects of long-term so-called 'local' vaginal estrogens.

# New principle for non-invasive assessment of the artery wall with regard to arterial aging, based on very high-frequency ultrasound (22 – 50MHz), suggested and evaluated.

With increasing age and development of atherosclerosis the dimension of the intima layer of the artery wall increases, whereas that of the media layer decreases. These differential changes of the artery wall layers reduces the usefulness of the present 'gold-standard', the combined intima-media thickness, Common Carotid Artery – Intima media Thickness (CCA-IMT). We suggest separate assessment of the artery intima and media layers and use of the Intima/Media thickness ratio.

We have repeatedly found this principle preferable, compared to assessment of the total CCA-IMT, in imaging arterial effects of aging, menopausal hormone replacement, cardiovascular risk factors and prevalent CVD. Further, the suggested principle was preferable to CCA-IMT in imaging vascular effects of systemic lupus erythematosus, recurrent depressions in adolescents and artery wall changes during normal pregnancy and pre-eclampsia. We currently evaluate the strength of this principle to predict CVD events in elderly and to image effects of anti-estrogen therapy in women with breast cancer (and possible differences in effects between aromatase inhibitors and receptor blockers). We also study possible vascular effects of ultra-low local vaginal estrogens, pulmonary hypertension as well as obstructive sleep apnea. Preliminary analyses indicate that this principle for assessing arterial aging (but not CCA-IMT) can monitor effects of intervention against arterial aging

and correctly image beneficial vascular effects of menopausal hormone therapy initiated soon after menopause. The suggested principle might become an alternative to the present 'gold-standard, CCA-IMT, for non-invasive assessment of the artery wall with regard to arterial aging, stratification with regard to cardiovascular risk, prediction of CVD events and in monitoring effects of interventions against atherosclerosis/CVD.

### Pregnancy complications: signs of arterial aging during and after preeclampsia. Whether the preexisting vascular status of the mother might increase the risk of some complications in pregnancy.

Our recent data indicated that normal pregnancy is a 'stress' on the artery system, especially in women, who in early pregnancy are older, have a higher BMI or a higher blood pressure (all within normal ranges). High-frequency ultrasound of the separate arterial wall layers, but not CCA-IMT, clearly indicated the known increased risk of cardiovascular disease at diagnosis of preeclampsia, as well as one year and more than 10 years after delivery, compared to normal pregnancies. Currently we study whether a preexisting maternal vascular component at start of pregnancy, might increase the risk of pregnancy complications, e.g. pre-eclampsia, and intrauterine growth retardation.

The suggested method might become a mean to monitor vascular changes during risk pregnancies and to stratify women with regard to coming cardiovascular risk after e.g. pre-eclampsia.

### Premenstrual syndrome (PMS or PMDD).

The normal variations of sex steroids during the menstrual cycle are in some women associated with negative effects on mood and temper, with increased irritability and depressed mood. We have found increased sensitivity in PMS/PMDD women to estrogen provocation and very strong association between worsening of PMS symptoms over the menstrual cycle and lower 'serotonin' signal in pre-defined brain regions, as assessed by Positron Emission Tomography (PET). We have recently reported a lateralization of the serotoninergic activity in the frontal brain, in relation to PMS/PMDD symptoms.

The results might help to understand the relation between hormone changes and mental symptoms in PMS, a disorder affecting many women with consequences for the individual, her family- and professional life.

# Self-rated health in adolescents and recurrent depressions in the adolescence and metabolic consequences later in life.

Prevalence of self-rated health in adolescents with regard to sex and seasonality are studied. A large prospective population-based cohort of adolescents, with and without a history of recurrent depressive periods during adolescence was followed-up for 20 years. Pilot results indicated that women in their 30-ies, with a history of recurrent depression during adolescence, exhibit higher degree of arterial aging compared to control subject recruited in parallel with cases during adolescence. Currently we study associations to metabolic consequences, including inflammation markers and ultrasound imaging of arterial aging in about #200 subjects of both genders form this cohort.

# Steroid hormones and proteomics in ovarian follicular fluid during normal menstrual cycle, in polycystic ovary syndrome (PCOS) and after ovarian stimulation during in-vitro fertilization (IVF).

Steroid hormones and proteins were analyzed using Liquid Chromatography Tandem Mass Spectrometry (LS-MS/MS). In PCOS, we have found indications for a block in the aromatize enzyme function, which might be the background for the arrest in follicular development/anovulation in women with PCOS. Currently, we study steroid hormones and proteins in stimulated ovarian follicular fluid with regard to outcome of the IVF treatment.

The results might elucidate basic underlying causes of anovulation/infertility in PCOS. In IVF, we aim to develop methods that can help in choosing the ovum having optimal chances to succeed in fertilization, implantation and a resulting born baby. If proven useful, these methods might be applied more broadly when mass-spectrometry methods become easily available at university hospitals.

### Violence against women (NCK project), please see www.nck.uu.se

A Ph.D. project focused on violence against women, with special reference to sexual violence.

### **Obstetrical Research**

### Alkistis Skalkidou

The overall aim with our research is to improve health of both mothers and children, not only during the important perinatal period but also in the long term, a core theme being short- and long-term follow-up of children after different intrauterine and peripartum exposures. More specifically, we focus on human reproduction, from the conception until the postpartum period, improving the diagnostic and therapeutic procedures for various conditions as well as fetal monitoring during childbirth, while in parallel addressing perinatal mental health.

The research group consists of 11 senior researchers, 4 of whom are professors and 3 of whom are associate professors. We collaborate intensively within the group, other research groups in the Department and Faculty, as well as the Karolinska Institute and international centers. Our research methodology involves methods from laboratory work to clinical epidemiology, often in collaboration with other laboratory and radiological sciences. The group has 2 regular meetings per year, and organizes a 4-day research camp each winter, inviting participation from all OB/GYN research groups in the department.

Professor Alkistis Skalkidou, head of the research group, has a research profile in perinatal mental health and effects on the offspring. Professor Anna-Karin Wikström, appointed as professor at KI in 2016, has a research profile in clinical and reproductive epidemiology and experimental design. Associate professor Maria Jonsson's research profile of clinical obstetric epidemiology addresses fetal and maternal and complications such as asphyxia, metabolic acidosis and complications of abdominal delivery. Senior professor Ove Axelsson has a research profile in perinatal, obstetrical and clinical research. Senior professor Ulf Högberg's research profile is in clinical and reproductive epidemiology, integrating Swedish and low-income country research settings. Associate professor Ulf Hanson has a research profile in clinical and epidemiologic research.

### Members of the group during 2016

Alkistis Skalkidou, adjunct professor Anna-Karin Wikström, professor Maria Jonsson, associate professor Ulf Hanson, associate professor Solveig Nordén Lindeberg, associate professor Ove Axelsson, senior professor Ulf Högberg, senior professor

Hashem Amini, PhD Johanna Belachew, PhD Eva Bergman, PhD Anna Berglund, PhD Marie Bolin, PhD Agnes Edling, PhD Annika Esscher, PhD Karin Eurenius, PhD Spyridon Gialamas, PhD Stavros Iliadis, PhD Ajlana Mullic-Lutvica, PhD Sarah Nordqvist, PhD Maria Palm, PhD Anna Sandström, PhD Sara Sohlberg, PhD Sara Sylvén, PhD Gerasimos Tzortzatos, PhD

Cathrine Axfors, PhD-student, (50% Psychiatry) Lina Bergman, PhD-student Emma Bränn, PhD-student Patricia Eckerdal, PhD-student Johanna Gunnarsdottir, PhD-student Hanna Henriksson, PhD-student Jenny Hultstrand, PhD-student Susanne Hesselman, PhD-student Lana Salih Joelsson, PhD-student Merit Kullinger, PhD-student Lena Liljeström, PhD-student Linda Lindström, PhD-student Maria Nelander, PhD-student Sibone Mocumbi, PhD-student Anna Palm, PhD (student during 2016) Ellen Ternby, PhD-student Åsa Wahlberg, PhD-student

### Publications 2014-2016

#### 2016

- 1. Stephansson, A Sandström, G Petersson, AK Wikström, S Cnattingius. Prolonged second stage of labour, maternal infectious disease, urinary retention and other complications in the early postpartum period. *BJOG*. 2016 Mar;123(4):608-16
- Lisa A DeRoo, Rolv Skjaerven, Allen J Wilcox, Kari Klungsoyr, Anna-Karin Wikström, Nils-Halvdan Morken, Sven Cnattingius, Placental abruption and long-term cardiovascular disease mortality *European Journal of Epidemiology* 2016 May;31(5):501-58.
- Patricia Eckerdal, Natasa Kollia, Johanna Löfblad, Charlotte Hellgren, Linnea Karlsson, Ulf Högberg, Anna-Karin Wikström, Alkistis Skalkidou. Delineating the association between heavy postpartum haemorrhage and postpartum depression. *PLoS ONE*. 2016. DOI: 10.1371/journal.pone.0144274
- 4. Anna-Karin Wikström, Johanna Gunnarsdottir, Maria Nelander, Marija Simic, Olof Stephansson, Sven Cnattingius. Prehypertension in pregnancy and risks of small for gestational age infant and stillbirth. *Hypertension*. 2016; 67: 640-646.
- M. Nelander, S. Cnattingius, H. Åkerud, J. Wikström, N.L. Pedersen, A-K Wikström Pregnancy hypertensive disease and risk of dementia and cardiovascular disease in women 65 years or older: a cohort study. *BMJ Open* 2016; DOI:10.1136/bmjopen-2015-009880
- 6. A Lindam, O Stephansson, A-K Wikström, S Johansson, S Cnattingius. High maternal BMI in early pregnancy and risks of stillbirth and infant mortality a population-based sibling study in Sweden. *Am J Epidemiology*. 2016 Jul; 184(2): 98–105.
- Helen Elden, Henrik Hagberg..., Anna-Karin Wikström, Lars Ladfors, Ulla-Britt Wennerholm. Study protocol of SWEPIS a Swedish multicentre register based randomised controlled trial to compare induction of labour at 41 completed gestational weeks versus expectant management and induction at 42 completed gestational weeks. *BMC Pregnancy and Childbirth* 2016; 16:49 DOI 10.1186/s12884-016-0836-9
- 8. Sofia Dahlin, Anna Gunnerbeck, Anna-Karin Wikström, Sven Cnattingius, Anna-Karin Bonamy. Maternal tobacco habits and extremely premature birth a population-based cohort study. *BJOG*. 2016 123(12):1938-1946
- 9. Martina Persson, Anna-Karin Wikström, Sven Cnattingius, Stefan Johansson. Maternal

overweight and obesity and risk of preeclampsia in women with type 1 diabetes or type 2 diabetes. *Diabetologia* 2016; 59(10): 2099–210

- 10. Bergman L, Helena Åkerud, Wikström AK, Marita Larsson, Tord Naessen, Tansim Akhter. Cerebral Biomarkers in Women with Preeclampsia are Still Elevated One Year Postpartum. *American Journal of Hypertension*. 2016, 29 (12): 1374-1379.
- 11. Sven Cnattingius, Anna-Karin Wikström, Olof Stephansson, Kari Johansson. Are term preeclampsia with and without fetal growth restriction of different origin? A cohort study of successive pregnancies in Sweden. *Paediatric and Perinatal Epidemiology*.2016; 30:563-570
- 12. Millde Luthander C, Källen K, Nyström M, Högberg U, Håkansson S, Pukk Härenstam K, Grunewald C. <u>Results from the National Perinatal Patient Safety Program in Sweden: the challenge of evaluation</u>. AOGS. 2016 May;95(5):596-603. doi: 10.1111/aogs.12873. Epub 2016 Mar 20.
- Palm A, Danielsson I, Skalkidou A, Olofsson N, Högberg U. Violence victimisation-a watershed for young women's mental and physical health. Eur J Public Health. 2016 Jan 7. pii: ckv234. [Epub ahead of print] 2016 Oct;26(5):861-867.
- 14. Högberg G, Aspelin P, Högberg U, Colville-Ebeling B. Circularity bias in Abusive Head Trauma studies could be diminished with a new ranking scale. Egyptian Journal of Forensic Sciences, 2006;6(1):6-10 artikel <u>http://dx.doi.org/10.1016/j.ejfs.2015.12.001</u>
- Namatovu F, Olsson C, Lindkvist M, Myléus A, Högberg U, Ivarsson I, Sandström O. Maternal and perinatal conditions and celiac disease risk. BMC Pediatrics, 2016 Jun 8;16:77. doi: 10.1186/s12887-016-0613-y.
- Adolphson K, Axemo P, Högberg U. Midwives' experiences of working conditions, perceptions of professional role and attitudes towards mothers in Mozambique. Midwifery. 2016 Sep;40:95-101. doi: 10.1016/j.midw.2016.06.012. Epub 2016 Jun 15. DOI: 10.1016/j.midw.2016.06.012
- Millde Luthander C, Källen K, Nyström ME, Högberg U, Håkansson S, Härenstam KP, Grunewald C. <u>Results from the National Perinatal Patient Safety Program in Sweden: the</u> <u>challenge of evaluation</u>. Acta Obstet Gynecol Scand. 2016 May;95(5):596-603. doi: 10.1111/aogs.12873
- Blom H, Högberg U, Olofsson N, Danielsson I. <u>Multiple violence victimisation associated with</u> <u>sexual ill health and sexual risk behaviours in Swedish youth.</u> Eur J Contracept Reprod Health Care. 2016;21(1):49-56. doi: 10.3109/13625187.2015.1089227.
- 19. <u>Högberg U, Claeson C, Krebs L</u>, Skoog <u>Svanberg A</u>, Kidanto <u>H</u> Breech delivery at a University Hospital in Tanzania. <u>BMC Pregnancy Childbirth</u>. 2016 Nov 8;16(1):342.
- Palm A, Högberg U, Olofsson N, Skalkidou A, Danielsson I. <u>No Differences in Health</u> <u>Outcomes After Routine Inquiry About Violence Victimization in Young Women: A</u> <u>Randomized Controlled Study in Swedish Youth Health Centers.</u> J Interpers Violence. 2016 Nov 30. pii: 0886260516681878. [Epub ahead of print]
- Palm A, Olofsson N, Danielsson I, Skalkidou A, Wennberg P, Högberg U. <u>Motivational</u> interviewing does not affect risk drinking among young women: A randomised, controlled intervention study in Swedish youth health centres. Scand J Public Health. 2016 Aug;44(6):611-8. doi: 10.1177/1403494816654047
- Millde Luthander C, Källen K, Nyström ME, Högberg U, Håkansson S, Härenstam KP, Grunewald C. <u>Results from the National Perinatal Patient Safety Program in Sweden: the</u> <u>challenge of evaluation</u>. Acta Obstet Gynecol Scand. 2016 May;95(5):596-603. doi: 10.1111/aogs.12873
- Isaksson J, Högberg U, Valladares E, Lindblad F. <u>Associations between psychiatric symptoms</u> and cortisol levels in Nicaraguan young school-age children. Psychiatry Res. 2016 Jun 30;240:376-80. doi: 10.1016/j.psychres.2016.04.069.
- Wahlberg Å, Andreen Sachs M, Johannesson K, Hallberg G, Jonsson M, Skoog Svanberg A, Högberg U. <u>Post-traumatic stress symptoms in Swedish obstetricians and midwives after severe</u> <u>obstetric events: a cross-sectional retrospective survey.</u> BJOG. 2016 Aug 26. doi: 10.1111/1471-0528.14259. [Epub ahead of print]
- 25. Wahlberg Å, Andreen Sachs M, Bergh Johannesson K, Hallberg G, Jonsson M, Skoog Svanberg A, Högberg U. <u>Self-reported exposure to severe events on the labour ward among</u>

Swedish midwives and obstetricians: A cross-sectional retrospective study. Int J Nurs Stud. 2017 Jan;65:8-16. doi: 10.1016/j.ijnurstu.2016.10.009. Epub 2016 Oct 22

- 26. Wahlberg J, Ekman B, Nyström L. Hanson U, Persson B, Arnqvist HJ: Gestational Diabetes: Gly7cemic predictors of fetal macrosomia and maternal risk of future diabetes-Diabetes Res Clin pract- 2016 Apr;114:99-105doi:10.1016/j.diabres .Epub2016 Jan 12.
- Ronnberg A, Hanson U, Ostlund I, Nilsson K: Effects on postpartum weight retention after antenatal lifestyle intervention – a secondary analysis of of a ramdomised controlled trialk. Acta Obstet Gynecol scand. 2016 Sep;95(9).999-1007. Doi: 10.1111/aogs 12910. Epub 2016 May 13.
- Hilden K, Hanson U, Persson M, Fadl H: Overeight and obesity: a remaining problem in women treated for severe gestational diabetes. Diabet. Med. 2016 Aug. 33(8): 1045-51. Doi: 10 1111/dme.13156. Epub 2016 Jun 12.
- 29. Akhter T, Wikstrom AK, Larsson M, Larsson A, Wikstrom G, Naessen T. Association between angiogenic factors and signs of arterial aging in women with pre-eclampsia. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2016.
- Bergman L, Akerud H. Plasma Levels of the Cerebral Biomarker, Neuron-Specific Enolase, are Elevated During Pregnancy in Women Developing Preeclampsia. Reprod Sci. 2016;23(3):395-400.
- Cesta CE, Viktorin A, Olsson H, Johansson V, Sjolander A, Bergh C, Skalkidou A et al. Depression, anxiety, and antidepressant treatment in women: association with in vitro fertilization outcome. Fertility and sterility. 2016;105(6):1594-602.e3.
- Cnattingius S, Wikstrom AK, Stephansson O, Johansson K. The Impact of Small for Gestational Age Births in Early and Late Preeclamptic Pregnancies for Preeclampsia Recurrence: a Cohort Study of Successive Pregnancies in Sweden. Paediatr Perinat Epidemiol. 2016;30(6):563-70.
- 33. Comasco E, Gulinello M, Hellgren C, Skalkidou A, Sylven S, Sundström-Poromaa I. Sleep duration, depression, and oxytocinergic genotype influence prepulse inhibition of the startle reflex in postpartum women. Eur Neuropsychopharmacol. 2016;26(4):767-76.
- 34. Elenis E, Sydsjo G, Skalkidou A, Lampic C, Svanberg AS. Neonatal outcomes in pregnancies resulting from oocyte donation: a cohort study in Sweden. BMC pediatrics. 2016;16(1):170.
- Esscher A, Essen B, Innala E, Papadopoulos FC, Skalkidou A, Sundstrom-Poromaa I, et al. Suicides during pregnancy and 1 year postpartum in Sweden, 1980-2007. Br J Psychiatry. 2016;208(5):462-9.
- Fernbrant C, Essen B, Esscher A, Ostergren PO, Cantor-Graae E. Increased Risk of Mortality Due to Interpersonal Violence in Foreign-Born Women of Reproductive Age: A Swedish Register-Based Study. Violence against women. 2016;22(11):1287-304.
- Georgakis MK, Kalogirou EI, Diamantaras AA, Daskalopoulou SS, Munro CA, Lyketsos CG, Skalkidou et al. Age at menopause and duration of reproductive period in association with dementia and cognitive function: A systematic review and meta-analysis. Psychoneuroendocrinology. 2016;73:224-43.
- Georgakis MK, Skalkidou A, Petridou ET. Estrogen-Based Therapies and Depression in Women Who Naturally Enter Menopause Before Population Average-Reply. JAMA Psychiatry. 2016;73(8):874-5.
- Georgakis MK, Thomopoulos TP, Diamantaras AA, Kalogirou EI, Skalkidou A, Daskalopoulou SS, et al. Association of Age at Menopause and Duration of Reproductive Period With Depression After Menopause: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2016;73(2):139-49.
- 40. Hellgren C, Edvinsson Å, Olivier JD, Fornes R, Stener-Victorin E, Ubhayasekera SJKA, Skalkidou et al. Tandem mass spectrometry determined maternal cortisone to cortisol ratio and psychiatric morbidity during pregnancy-interaction with birth weight. Psychoneuroendocrinology. 2016;69:142-
- 41. Iliadis SI, Sylvén S, Hellgren C, Olivier JD, Schijven D, Comasco E, et al. MID-PREGNANCY CORTICOTROPIN-RELEASING HORMONE LEVELS IN ASSOCIATION

WITH POSTPARTUM DEPRESSIVE SYMPTOMS. Depression and Anxiety. 2016.

- 42. Joelsson LS, Berglund A, Wanggren K, Lood M, Rosenblad A, Tyden T. Do subfertile women adjust their habits when trying to conceive? Upsala journal of medical sciences. 2016;121(3):184-91.
- 43. Junus K, Wikstrom AK, Larsson A, Olovsson M. Early second-trimester plasma levels of NTproBNP in women who subsequently develop early-onset preeclampsia. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2016:1-3.
- 44. Kerstis B, Aarts C, Tillman C, Persson H, Engstrom G, Edlund B, Skalkidou et al. Association between parental depressive symptoms and impaired bonding with the infant. Arch Womens Ment Health. 2016;19(1):87-94.
- 45. Kullinger M, Haglund B, Kieler H, Skalkidou A. Effects of ultrasound pregnancy dating on neonatal morbidity in late preterm and early term male infants: a register-based cohort study. BMC Pregnancy Childbirth. 2016;16(1):335.
- 46. Marcotte EL, Thomopoulos TP, Infante-Rivard C, Clavel J, Petridou ET, Schuz J, Skalkidou A. et al. Caesarean delivery and risk of childhood leukaemia: a pooled analysis from the Childhood Leukemia International Consortium (CLIC). The Lancet Haematology. 2016;3(4):e176-85.
- 47. Skalkidou A, Bixo M, Skoldebrand Sparre AC, Strandell A, Linden Hirschberg A, Filipsson Nystrom H. [Hypothyroidism during pregnancy risks the child's neurocognitive development. New guidelines and remaining knowledge gaps]. Lakartidningen. 2016;113.
- 48. Sylvén SM, Thomopoulos TP, Kollia N, Jonsson M, Skalkidou A. Correlates of postpartum depression in first time mothers without previous psychiatric contact. Eur Psychiatry. 2016;40:4-12.
- 49. Ternby E, Axelsson O, Anneren G, Lindgren P, Ingvoldstad C. Why do pregnant women accept or decline prenatal diagnosis for Down syndrome? Journal of community genetics. 2016;7(3):237-42.
- 50. Thomopoulos TP, Skalkidou A, Dessypris N, Chrousos G, Karalexi MA, Karavasilis TG, et al. Prelabor cesarean delivery and early-onset acute childhood leukemia risk. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2016;25(2):155-61.
- 51. Yamamoto S, Nelander M. Ectopic pregnancy in simultaneous pancreas-kidney transplantation: A case report. International journal of surgery case reports. 2016;28:152-4.
- 52. Ternby E, Axelsson O, Annerén G, Lindgren P, Ingvoldstad C. Why do pregnant women accept or decline prenatal diagnosis for Down syndrome? J Community Genet 2016:7(3):237-42.

### 2015

- 1. Ahlsson F, Akerud H, Schijven D, Olivier J, Sundström Poromaa I. Gene Expression in Placentas From Nondiabetic Women Giving Birth to Large for Gestational Age Infants. Reproductive Sciences. 2015;22(10):1281-1288.
- Belachew J, Axelsson O, Eurenius K, Mulic-Lutvica A. Three-dimensional ultrasound does not improve diagnosis of retained placental tissue compared to two-dimensional ultrasound. Acta Obstet Gynecol Scand 2015:94(1):112-6.
- 3. Ternby E, Ingvoldstad C, Annerén G, Lindgren P, Axelsson O. Information and knowledge about Down syndrome among women and partners after first trimester combined testing. Acta Obstet Gynecol Scand 2015:94(3):329-32.
- 4. Sohlberg S, Mulic-Lutvica A, Olovsson M, Weis J, Axelsson O, Wikström J, Wikström AK. MRI estimated placental perfusion in fetal growth assessment. Ultrasound Obstet Gynecol 2015 [In Process Citation].

- 5. Dumitrescu B, Axelsson O, Strand R. [Sängläge vid tidig vattenavgång enligt evidens eller gammal vana?] Lakartidningen 2015:112
- 6. Ternby E, Ingvoldstad C, Annerén G, Axelsson O. Midwives and information on prenatal testing with focus on Down syndrome. Prenat Diagn. 2015
- Belachew J, Axelsson O, Eurenius K, Mulic-Lutvica A. Three-dimensional ultrasound does not improve diagnosis of retained placental tissue compared to two-dimensional ultrasound. Acta Obstetricia et Gynecologica Scandinavica. 2015;94(1):112-116.
- Bergman L, Åkerud H. Plasma Levels of the Cerebral Biomarker, Neuron-Specific Enolase, are Elevated During Pregnancy in Women Developing Preeclampsia. Reproductive Sciences. 2015 1-6. DOI: 10.1177/1933719115604732.
- 9. Dumitrescu B, Axelsson O, Strand R T. Sängläge vid tidig vattenavgång enligt evidens eller gammal vana?. Läkartidningen. 2015;(112)
- Esscher A, Essén B, Innala E, Papadopoulos F, Skalkidou A, Sundström-Poromaa I, Hogberg U. Suicides during pregnancy and one year postpartum in Sweden, 1980–2007. British Journal of Psychiatry. 2015;
- 11. Elenis E, Svanberg Skoog A, Lampic C, Skalkidou A, Åkerud H, Sydsjö G. Adverse obstetric outcomes in pregnancies resulting from oocyte donation : a retrospective cohort case study in Sweden. BMC Pregnancy and Childbirth. 2015;15:247.
- 12. Fadl H E, Gardefors S, Hjertberg R, Nord E, Persson B, Schwarcz E, Hanson U et al. Randomized controlled study in pregnancy on treatment of marked hyperglycemia that is short of overt diabetes. Acta Obstetricia et Gynecologica Scandinavica. 2015;94(11):1181-1187.
- Granfors M, Andersson M, Stinca S, Åkerud H, Skalkidou A, Sundström Poromaa I, et al. Iodine deficiency in a study population of pregnant women in Sweden. Acta Obstetricia et Gynecologica Scandinavica. 2015;94(11):1168-1174.
- 14. Hesselman S, Högberg U, Ekholm Selling K, Råssjö E, Jonsson M. The risk of uterine rupture is not increased with single- compared with double-layer closure : a Swedish cohort study. British Journal of Obstetrics and Gynecology. 2015;122(11):1535-1541.
- 15. Hogberg G, Hogberg U, Norlander K, Davidsson L. [Time for moderation and reflection regarding the AHT model]. Lakartidningen. 2015;112.
- 16. Isaksson J, Lindblad F, Valladares E, Högberg U. High maternal cortisol levels during pregnancy are associated with more psychiatric symptoms in offspring at age of nine : A prospective study from Nicaragua. Journal of Psychiatric Research. 2015;71:97-102.
- 17. Jonsson M, Ågren J, Nordén Lindeberg S, Ohlin A, Hanson U. Neonatal Encephalopathy and the Association to Asphyxia in Labor : EDITORIAL COMMENT. Obstetrical and Gynecological Survey. 2015;70(4):233-235.
- 18. Jonsson M. Induction of twin pregnancy and the risk of caesarean delivery : a cohort study. BMC Pregnancy and Childbirth. 2015;15:136.
- 19. Kaihola H, Olivier J D, Sundström Poromaa I, Åkerud H. The effect of antenatal depression and selective serotonin reuptake inhibitor treatment on nerve growth factor signaling in human placenta. PLoS ONE. 2015;10(1):e0116459.
- Kunovac Kallak T, Baumgart J, Nilsson K, Åkerud H, Sundström Poromaa I, Staverus-Evers A. Vaginal gene expression during treatment with aromatase inhibitors. Clinical Breast Cancer. 2015;15(6):527-535.
- 21. Nordqvist S, Kårehed K, Skoog Svanberg A, Menezes J, Åkerud H. Ovarian Response is Affected by a Specific Histidine-Rich Glycoprotein Polymorphism : a preliminary study. Reproductive Biomedicine Online. 2015;30(1):74-81.
- 22. Lovvik T S, Wikström A, Neovius M, Stephansson O, Roos N, Vanky E. Pregnancy and perinatal outcomes in women with polycystic ovary syndrome and twin births : a population-based cohort study. British Journal of Obstetrics and Gynecology. 2015;122(10):1295-1302.
- 23. Maghsoudlou S, Cnattingius S, Aarabi M, Montgomery S M, Semnani S, Stephansson O, Wikström A et al. Consanguineous marriage, prepregnancy maternal characteristics and stillbirth risk : a population-based case-control study. Acta Obstetricia et Gynecologica

Scandinavica. 2015;94(10):1095-1101.

- 24. Maliqueo M, Poromaa I S, Vanky E, Fornes R, Benrick A, Åkerud H, et al. Placental STAT3 signaling is activated in women with polycystic ovary syndrome. Human Reproduction. 2015;30(3):692-700.
- 25. Nordqvist S, Kårehed K, Skoog Svanberg A, Menezes J, Åkerud H. Ovarian Response is Affected by a Specific Histidine-Rich Glycoprotein Polymorphism : a preliminary study. Reproductive Biomedicine Online. 2015;30(1):74-81.
- 26. Olivier J D, Åkerud H, Skalkidou A, Kaihola H, Sundström-Poromaa I. The effects of antenatal depression and antidepressant treatment on placental gene expression. Frontiers in Cellular Neuroscience. 2015;8:465-.
- 27. Olivier J D, Akerud H, Sundström Poromaa I. Antenatal depression and antidepressants during pregnancy : Unraveling the complex interactions for the offspring. European Journal of Pharmacology. 2015;753:257-262.
- Olivier J D, Åkerud H, Skalkidou A, Kaihola H, Sundström-Poromaa I. The effects of antenatal depression and antidepressant treatment on placental gene expression. Frontiers in Cellular Neuroscience. 2015;8:465-.
- 29. Pettersson F D, Hellgren C, Nyberg F, Åkerud H, Sundström-Poromaa I. Depressed mood, anxiety, and the use of labor analgesia.. Archives of Women's Mental Health. 2015;
- Sandstrom A, Cnattingius S, Wikström A, Stephansson O, Iliadou A N. Does Use of Low-Molecular-Weight Heparin during Pregnancy Influence the Risk of Prolonged Labor : A Population-Based Cohort Study. PLoS ONE. 2015;10(10):e0140422.
- 31. Santosa A, Rocklov J, Högberg U, Byass P. Achieving a 25% reduction in premature noncommunicable disease mortality : the Swedish population as a cohort study. BMC Medicine. 2015;13:65.
- Skírnisdóttir I, Seidal T, Åkerud H. Differences in Clinical and Biological Features Between Type I and Type II Tumors in FIGO Stages I-II Epithelial Ovarian Carcinoma.. International Journal of Gynecological Cancer. 2015;25(7):1239-47.
- Sohlberg S, Mulic-Lutvica A, Olovsson M, Weis J, Axelsson O, Wikström J, et al. MRI estimated placental perfusion in fetal growth assessment. Ultrasound in Obstetrics and Gynecology. 2015;46(6):700-705.
- 34. Stenhammar C, Ehrsson Y T, Åkerud H, Larsson M, Tydén T. Sexual and contraceptive behavior among female university students in Sweden : repeated surveys over a 25-year period. Acta Obstetricia et Gynecologica Scandinavica. 2015;94(3):253-259.
- 35. Ternby E, Ingvoldstad C, Annerén G, Axelsson O. Midwives and information on prenatal testing with focus on Down syndrome. Prenatal Diagnosis. 2015;35(12):1202-1207.
- 36. Ternby E, Ingvoldstad C, Annerén G, Lindgren P, Axelsson O. Information and knowledge about Down syndrome among women and partners after first trimester combined testing. Acta Obstetricia et Gynecologica Scandinavica. 2015;94(3):329-32.
- 37. Tinglöf S, Högberg U, Wallin Lundell I, Skoog Svanberg A. Exposure to violence among women with unwanted pregnancies is associated with post-traumatic stress disorder, symptoms of anxiety and depression. Sexual & Reproductive HealthCare. 2015;6(2):50-53.
- 38. Tornell S, Ekeus C, Hultin M, Hakansson S, Thunberg J, Högberg U. Low Apgar score, neonatal encephalopathy and epidural analgesia during labour : a Swedish registry-based study. Acta Anaesthesiologica Scandinavica. 2015;59(4):486-495.
- 39. Wallin Lundell I, Ohman S G, Sundström-Poromaa I, Högberg U, Sydsjo G, Skoog Svanberg A. How women perceive abortion care : A study focusing on healthy women and those with mental and posttraumatic stress. European journal of contraception & reproductive health care. 2015;20(3):211-222.
- 40. Wikström A, Hagmar M, Ronquist G, Larsson A. Evaluation of a Plasma hCG Method for Point of Care Testing with the Aim of Shortening Test-Turnaround-Times. Open Journal of Obstetrics and Gynecology. 2015;5(6):341-343.
- 41. Wikstrom AK, Stephansson O. [Major challenge to inform about the risks of obesity in pregnancy. 38 percent of pregnant women in Sweden are overweight or obese]. Lakartidningen. 2015;112.

42. Wilbe M, Ekvall S, Eurenius K, Ericson K, Casar-Borota O, Klar J, et al. MuSK : a new target for lethal fetal akinesia deformation sequence (FADS).. Journal of Medical Genetics. 2015;52(3):195-202.

### 2014

- 1. Ahman A, Axelsson O, Maras G, Rubertsson C, Sarkadi A, Lindgren P. Ultrasonographic fetal soft markers in a low-risk population: prevalence, association with trisomies and invasive tests. Acta Obstet Gynecol Scand. 2014 Apr;93(4):367-73.
- 2. Akther T, Wikström A-K, Larsson M, Naessen T. Thicknesses of individual layers of artery wall indicate increased cardiovascular risk in severe pre-eclampsia. Ultrasound in Obstetrics and Gynecology. 2014 Jun;43(6):675-80.
- 3. Amark H, Millde-Luthander C, Ajne G, Hogberg U, Pettersson H, Wiklund I, et al. Single versus pairwise interpretation of cardiotochography, a comparative study from six Swedish delivery units. Sexual & reproductive healthcare : official journal of the Swedish Association of Midwives. 2014;5(4):195-8.
- 4. Baba S, Wikström A-K, Stephansson O, Cnattingius S. Changes in snuff and smoking habits in early pregnancy and risks of stillbirth and early neonatal mortality. Tobacco research. 2014. Jan 16 (1):78-83
- 5. Belachew J, Cnattingius S, Eurenius K, Lutvica A, Axelsson O, Wikström A-K. Risk of retained placenta in women previously delivered by caesarean section: a population-based cohort study. BJOG. 2014. Jan 121(2):224-9.
- Bergman L, Naessen T, Wikström A-K, Wikström J, Akther T, Åkerud H. Plasma Levels of S100B in Preeclampsia and Association with CNS affection. American Journal of Hypertension. 2014 Aug;27(8):1105-11
- Blom H, Högberg U, Olofsson N, Danielsson I. Strong association between earlier abuse and revictimization in youth. BMC Public Health. 2014 Jul 14;14:715. doi: 10.1186/1471-2458-14-715.
- Ekéus C, Högberg U, Norman M. Vacuum assisted birth and risk for cerebral complications in term newborn infants: a population-based cohort study. BMC Pregnancy and Childbirth 2014, 14:36 doi:10.1186/1471-2393-14-36
- Elenis E, Lindgren KE, Karypidis H, Skalkidou A, Hosseini F, Bremme K, Landgren BM, Skjöldebrand-Sparre L, Stavreus-Evers A, Sundström-Poromaa I, Åkerud H. The histidine-rich glycoprotein A1042G polymorphism and recurrent miscarriage: a pilot study. Reprod Biol Endocrinol. 2014 Jul 27;12:70.
- Endler M, Saltved S, Cnattingius S, Stephansson O, Wikström A-K. Retained placenta is associated with pre-eclampsia, stillbirth, giving birth to a small-for-gestational-age infant, and spontaneous preterm birth: a national register-based study. BJOG. 2014 Nov;121(12):1462– 1470
- 11. Eriksson PO, Aaltonen E, Petoral R, Jr., Lauritzson P, Miyazaki H, Pietras K, et al. Novel nanosized MR contrast agent mediates strong tumor contrast enhancement in an oncogene-driven breast cancer model. PLoS One. 2014;9(10):e107762.
- 12. Esscher A, Binder-Finnema P, Bødker B, Högberg U, Mulic-Lutvica A, Essén B. Suboptimal care and maternal mortality among foreign-born women in Sweden: maternal death audit with application of the 'migration three delays' model. BMC Pregnancy Childbirth. 2014 Apr 12;14:141. doi: 10.1186/1471-2393-14-141.
- Fadl H, Magnuson A, Östlund I, Montgomery S, Hanson U, Schwarcz E. <u>Gestational diabetes</u> <u>mellitus and later cardiovascular disease: a Swedish population based case-control study.</u> BJOG. 2014 Nov;121(12):1530-6. doi: 10.1111/1471-0528.12754. Epub 2014 Apr 25.
- 14. Fottrell E, Högberg U, Ronsmans C, Osrin D, Azad K, Nair N, Meda N, Ganaba R, Goufodji S, Byass P, Filippi V. A probabilistic method to estimate the burden of maternal morbidity in

resource-poor settings: preliminary development and evaluation. Emerg Themes Epidemiol. 2014 Mar 13;11(1):3. doi: 10.1186/1742-7622-11-3.

- 15. Granfors M, Åkerud H, Skogö J, Stridsberg M, Wikström A-K, Sundström-Poromaa I. Detection of thyroid dysfunction during pregnancy in clinical practice: Is targeted thyroid testing enough? Obstetrics & Gynecology. 2014 Jul;124(1):10-5
- Gunnarsdottir J, Åkerud H, Cnattingius S, Stephansson O, Wikström A-K. Risk of placental dysfunction disorders after prior miscarriages; a population based study. American Journal of Obstet & Gyn. 2014 Jul;211(1):34.e1-8.
- 17. Gunnerbeck A, Edstedt Bonamy A-K, Wikström A-K, Granath F, Wickström R, Cnattingius S. Maternal Snuff Use and Smoking and the Risk of Oral Cleft Malformations a population-based cohort study. PLoS ONE 9(1): e84715. doi:10.1371/journal.pone.0084715
- Haroun S, Altmäe S, Karypidis H, Kuningas M, Landgren BM, Akerud H, Skjöldebrand-Sparre L, Hosseini F, Bremme K, Sundström-Poromaa I, Stavreus-Evers A.Association between trefoil factor 3 gene variants and idiopathic recurrent spontaneous abortion. Reprod Biomed Online. 2014 Dec;29(6):737-44.
- Hellgren C, Åkerud H, Skalkidou A, Bäckström T, Sundström-Poromaa I. Low serum allopregnanolone is associated with symptoms of depression in late pregnancy. Neuropsychobiology. 2014;69(3):147-53
- 20. Hesselman S, Högberg U, Ekholm-Selling K, Råssjo<sup>••</sup> E-B, Jonsson M. The risk of uterine rupture is not increased with single compared with double-layer closure: a Swedish cohort study. BJOG 2014
- Hesselman S, Högberg U, Ekholm-Selling K, Råssjö E-B, Jonsson M. Single compared with double layer of closure does not increase the risk of uterine rupture: a Swedish cohort study. BJOG 2014 June 25 DOI: 10.1111/1471-0528.13015
- 22. Jonsson M, Agren J, Nordén-Lindeberg S, Ohlin A, Hanson U. Suboptimal care and metabolic acidemia is associated with neonatal encephalopathy but not with neonatal seizures alone: A population based clinical audit. Acta Obstet Gynecol Scand. 2014 Mar 19
- 23. Jonsson M, Ågren J, Norden-Lindeberg S, Ohlin A, Hanson U. Neonatal encephalopathy and the association to asphyxia in labor. Am J Obstet Gynecol 2014;211
- 24. Junus K, Wikström A-K, Larsson A, Olovsson M. Placental expression of NT-proBNP in earlyand late-onset preeclampsia. American Journal of hypertension. 2014 Sep;27(9):1225-30.
- 25. László K.D, Ananth C.V, Wikström A-K, Svensson T, Li J, Olsen J, Vestergaard M, Obel C, Cnattingius: <sup>S</sup>Loss of a close family member the year before or during pregnancy and the risk of placental abruption: A cohort study from Denmark and Sweden: Psycological Medicine. 2014 Jul;44(9):1855-66
- 26. Liljeström L, Wikström AK, Skalkidou A, Akerud H, Jonsson M. Experience of fetal scalp blood sampling during labor. Acta Obstet et Gynecol Scand. 2014;93:113–117
- Lundqvist A, Johansson I, Wennberg A, Hultdin J, Hogberg U, Hamberg K, et al. Reported dietary intake in early pregnant compared to non-pregnant women - a cross-sectional study. BMC Pregnancy Childbirth. 2014;14:373.
- 28. Nordqvist S, Kårehed K, Skoog Svanberg A, Menezes J, Åkerud Helena. Ovarian response is affected by a specific histidine-rich glycoprotein polymorphism: a preliminary study. Reprod Biomed Online. Doi10.1016/j.rbmo. 2014.09.016. Epub 2014 Oct 14.
- 29. Nordqvist S, Sydsjö G, Lampic C, Åkerud H, Elenis E, Skoog Svanberg A. Sexual orientation of women does not affect outcome of fertility treatment with donated sperm. Hum Reprod. 2014 Jan 15. PMID:24435777.
- Olivier J, Åkerud H, Skalkidou A, Kaihola H, Sundström-Poromaa I. The effects of antenatal depression and antidepressant treatment on placental gene expression. Front Cell Neurosci. 2015 Jan 13;8:465. doi: 10.3389/fncel.2014.00465. eCollection 2014
- 31. Olivier JD, Akerud H, Sundström Poromaa I. Antenatal depression and antidepressants during pregnancy: Unraveling the complex interactions for the offspring. Eur J Pharmacol. 2014 Aug

2.

- 32. Santosa A, Rocklöv J, Högberg U, Byass P. Socio-demographic predictors of mortality inequality among Swedish men and women: a longitudinal study. The European Journal of Public Health DOI: http://dx.doi.org/10.1093/eurpub/cku163.087 First published online: 31 October 2014
- Santosa A, Wall S, Fottrell E, Högberg U, Byass P. The development and experience of epidemiological transition theory over four decades: a systematic review. Glob Health Action. 2014 May 15;7:23574.
- Sohlberg S, Mulic-Lutvica A, Lindgren P, Axelsson O, Olovsson M, Wikström A-K, Wikström J. In vivo 31P-MR spectroscopy in normal pregnancy, early and late preeclampsia; a study of placental metabolism. Placenta. 2014 May;35(5):318-23
- 35. Sohlberg S, Mulic-Lutvica A, Lindgren P, Otriz-Nieto F, Wikström A-K, Wikström J. Placental perfusion in normal pregnancy and early and late preeclampsia; a magnetic resonance imaging study. Placenta 2014 Mar; 35(3):202-6.
- 36. Tinglöf S, Högberg U, Wallin Lundell I, Skoog Svanberg A. Exposure to violence among women with unwanted pregnancies is associated with posttraumatic stress disorder, symptoms of anxiety and depression. Sexual & Reproductive Healthcare. Available online 26 September 2014
- 37. Wahlberg A, Kallestal C, Lundgren A, Essen B. Causes of death among undocumented migrants in Sweden, 1997-2010. Global health action. 2014;7:24464.
- 38. Wallin Lundell I, Georgsson Öhman S, Högberg U, Sundström Poromaa I, Sydsjö G, Skoog Svanberg A. How do women perceive abortion care: A study focusing on healthy women and those with mental and posttraumatic stress. The European Journal of Contraception and Reproductive Health Care. doi:10.3109/13625187.2014.1002032
- 39. Wallstrom T, Hellgren C, Akerud H, Wiberg-Itzel E. Skin conductance activity in post-term pregnancies. J Matern Fetal Neonatal Med. 2014 Oct 30:1-5. [Epub ahead of print]
- 40. Wiberg-Itzel E, Pembe A, Wray S, Wihlbäck A-C, Darj E, Hoesli I, Åkerud H. Level of lactate in amniotic fluid and its relation to the use of oxytocin and adverse neonatal outcome. Acta Obstet Gynecol Scand. 2014 Jan;93(1):80-5.
- 41. Åmark H, Millde Luthander C, Pettersson HJ, Ajne G, Högberg U, Grunewald C. Single versus pair wise interpretation of cardiotochography, a comparative study from six Swedish delivery units. Sexual & Reproductive Healthcare 2014 Dec;5(4):195-8.

### **Dissertations 2016**

- Stavros Iliadis. Personality and the HPA axis in association with postpartum depression. 2016. Dept of Women's and Children's Health. Uppsala University. Alkistis Skalkidou was <u>main</u> supervisor
- 2. Evangelia Elenis. Genetic and epidemiological aspects of implantation defects Studies on recurrent miscarriage, preeclampsia and oocyte donation. 2016. Dept of Women's and Children's Health. Uppsala University. Alkistis Skalkidou was deputy supervisor
- 3. Margit Endler. Characterizing retained placenta: epidemiology and pathophysiology of a critical obstetric disorder. 2016. Dept of Clinical Science and Education, Södersjukhuset. KI. Anna-Karin Wikström was <u>deputy</u> supervisor
- 4. Siavash Maghsoudlou A population-based study of risk factors for adverse pregnancy outcomes in northern rural Iran: a follow-up from pre-pregnancy to delivery. Department of Medicine, Clinical Epidemiological Unit, KI. Anna-Karin Wikström was deputy supervisor
- Charlotte Millde Luthander. The National Perinatal Patient Safety Programme the Challenges of implementation and evaluation. Karolinska Institutet. Thesis for doctoral degree (Ph D), 2016. Ulf Högberg was <u>deputy</u> supervisor

### Agencies that support the work/Funding 2016 (with over 100.000 kr)

Vetenskapsrådet 1 950 000 Skalkidou Göran Gustafsson Stiftelse 750 000 Skalkidou RFR Uppsala-Örebro 450 000 Skalkidou Vetenskapsrådet 900 000 Wikström FoU Uppsala/Örebro 300 000 Wikström Vetenskapsrådet 600 000 Jonsson RFR Uppsala-Örebro 150 000 Jonsson

Together with two other research groups, Reproductive Biology and Reproductive Health, we are responsible for an ongoing collection of plasma and leucocyte samples from women pregnant at about 18 weeks (**UPPSALA BIOBANK FOR PREGNANT WOMEN**) since 2007. So far, blood samples from about 12 000 women have been collected and the collection of microbiome samples has also started. This unique biobank is a research source for several on-going research projects and will be source for future epigenetic studies.

In 2014, the research database **Uppsala Mother-Child Cohort** has been created. It is comprising 49 000 mother-child pairs (2000-2010), with clinical information from birth, neonatal and child health care linked to the national Swedish Health Registries. This database is presently up-dated until 2015. In 2015, data was collected on the follow up of mothers and their offspring who were part of the NICHD Scandinavian Successive Small-for-Gestational Age Births Study during the years 1986-88. The project, with Ulf Högberg as principal investigator, is performed in collaboration with Professor Geir Jacobsen and co-workers at NTNU, Trondheim. Responsible researchers at Uppsala University are Anna-Karin Wikström, Mia Ramklint, associate professor, children and adult psychiatrist.

The **BASIC study** (PI Alkistis Skalkidou) is on-going population-based longitudinal study aiming at enriching and expanding our knowledge on the pathophysiological processes underlying perinatal depression (PPD), pinpointing both epidemiological and biological predictors of the disease, in order to improve early detection. The BASIC project, funded mainly by the Swedish Research Council, aims to integrate information on environmental stressors and genetic predisposition with proteomic markers in shaping the risk for PPD. All women in Uppsala called for routine ultrasound examination in pregnancy week 16 -17 are invited to participate in this study since 2009. During pregnancy and after delivery, women are followed by web-based questionnaires (depression, anxiety and personality assessment tools, early life stress, sleep disorders, socioeconomic factors). Blood and tissue samples (placenta, umbilical cord) are collected from participants during childbirth, including cerebrospinal fluid samples from women undergoing elective cesarean deliveries. A sub-group of women are called to the clinic during pregnancy and postpartum for psychiatric interview, cognitive and metabolic testing. The study has so far included more than 4.900 women, at 5 assessment points and tissue samples are obtained in more than 80% of cases and stored in Uppsala Biobank.

The BASIC study data is also used in other projects, such as:

- to unravel the complex interplay between breastfeeding and PPD

- to assess the association between personality and attachment and PPD

- to assess the association between delivery complications and PPD

- to try to replicate UPPSAT findings on the <u>seasonality</u> of PPD in Sweden, and examine how the metabolom and inflammatory system are affected by seasons

- to assess if there are differences in <u>bio-impedance and heart variability</u> measurements between depressed and non-depressed women postpartum

- to assess differences in placental gene expression among SSRI-users, depressed and non-depressed pregnant women

to assess differences in <u>microbiome</u> composition among depressed and non-depressed women during and after pregnancy, and the assess the possible predictive role of the microbiome composition in mid-pregnancy for preterm delivery and postpartum depression
to identify the best <u>predictive</u> algorithm with data collected up to delivery for the risk for developing postpartum depression, for future application in clinical use

### U-BIRTH study (2012- ongoing)

### PI: A. Skalkidou

A <u>follow-up study</u> of the UPPSAT (children at 6 and 11 years of age) and BASIC studies (children at 18 months and 6 years) participants, with focus on maternal mental health and child development. The <u>aim</u> of the U-BIRTH study is to provide in-depth understanding of how exposure to factors, such as maternal depression during fetal and infant life, interact with psychosocial and genetic factors in shaping the clinical developmental phenotypes of children.

In this project, we have closely collaborated with researchers from the FinnBrain study in <u>Finland</u> since 2012. Both cohorts are planning to recruit about 5.000 mother-offspring pairs, use similar methods and aim to validate each other's results. We are also initiating contact with similar groups in Greece, Portugal and the Netherlands, in order to be able to seek funding from the <u>European</u> <u>Union</u> next year.

Approximately 60% of BASIC and 30% of UPPSAT mothers are included in follow-up, via webbased questionnaires, so we expect to include 2.800 mother-offspring pairs from the BASIC study and 800 pairs in the UPPSAT study. Thus far, about 50% these have already been recruited. An epigenome-wide association study (EWAS) among children with psycho-emotional problems and controls is planned and externally funded by the Göran Gustafsson Foundation, Hjärnfonden and the Swedish Medical Association (3.700.000 SEK).

### BASIC child study

### PI: K. Marcizco, Children- and Baby Lab, Uppsala University

An in-depth study initiated by Uppsala Children- and Baby Lab, Department of Psychology, studying child development in relation to maternal mood during and after pregnancy. Patients are recruited from the BASIC study and the children followed up with a series of psychological tests. Financed by Uppsala Children- and Baby Lab (Marianne and Marcus Wallenberg Foundation).

# Ultrasound Dating and perinatal morbidity and mortality PI: A. Skalkidou, PhD student Merit Kullinger

Swedish register-based studies on perinatal outcomes in relation to ultrasound dating.

Based on clinical observations and work in settings outside Sweden, a hypothesis formed around the precision of ultrasound dating in the second trimester. The introduction of ultrasound dating of pregnancy was shown to be associated with systematic bias in the estimate of the length of pregnancy. This proved to have consequences in terms of perinatal morbidity and mortality, in the form of e.g. increased risk of low Apgar, meconium aspiration and seizures in post-term born girls born after the introduction of ultrasound for pregnancy dating. The same was shown for prematurity related outcomes among early preterm-born boys. Work is now focusing on possible determinants of discrepancy between the various dating methods, as well as how large discrepancies associate with unfavorable outcomes. The project is financed by the Clinical Research Center, Västerås.

# EMBLA project- An Internet-based information platform for vulvodynia patients

### PI: A. Skalkidou

Vulvodynia is a very common, yet very under-diagnosed and under-treated gynecological disease that leads to great suffering for both women involved, but also their partners. It has also been associated with poor quality of life, which leads to depression and anxiety. Untreated, the condition can result in significant suffering with difficulties in intercourse, decreased desire, suffering gynecological diseases and childbirth. A cognitive behavioural therapy approach, together with psycho-educational self-help are evidence-based methods for the treatment of this condition. Internet-based interventions may result in increased availability of cost-effective care.

The study aims to evaluate the effectiveness of an intervention from a vulvodynia population of patients from clinics in Uppsala, Falun, Örebro and Gävle. Patients are recruited by treating physicians and get access to the web-based platform, where they fill out questionnaires during four different time points after randomization to control or intervention group. The intervention group also has access to several activities and information material in the web platform. Differences in the level of pain, quality of life and parameters of mental health will be assessed at the end of the study. If this intervention proves to be effective, it will be directly implemented into clinical practice in the region.

The project is financed through Regionala Forskningsrådet, Uppsala.

### SKDS study Svensk Studie för KönsDysphori

### PI: F. Papadopoulos, Psychiatry

The first nationwide study on Gender Dysphoria in Sweden.

The number of referrals for assessment of gender dysphoria patients has increased by six times during the last 7 years, not only in Sweden but internationally. This change warrants immediate attention and thorough investigation, both through a nation-wide clinical study (on-going, recruiting) but also using data from the Swedish Health Registries (ethical application sent).

### **Other projects:**

- Life-style factors and reproduction (Alkistis Skalkidou, Lana Salih Joelsson).
- Magnetic Resonance Tomography (MRT) and 3D-ultrasound for diagnosis of fetal malformations (Ajlana Mulic Lutvica och Ove Axelsson).
- Late pregnancy termination after fetal malformation diagnosis (Eva Bergman, Agnes Edling)
- Creation of new swedish intra-uterine growth curves (Eva Bergman, Linda Lindström).
- Information about fetal diagnostics (Ove Axelsson).
- Placenta dysfunction in miscarriage, growth restriction and preeclampsia (Anna-Karin Wikström).
- Prematurity, delivery complications and child outcomes (Ulf Högberg).
- Violence during pregnancy and among adolescents (Ulf Högberg).
- Cerebral complications in preeclampsia (Anna-Karin Wikström, Maria Nelander).
- Immunology and Epidemiology of preeclampsia (Anna-Karin Wikström).
- Markers that can predict the start of spontaneous delivery (Ove Axelsson).
- 3D-ultrasound among patients with previous caesarean section, as well as postpartum (Ajlana Mulic Lutvica).
- Delivery complications such as asphyxia in new-borns (Maria Jonsson).
- Pain disorders, caesarean section, and uterine complications (Maria Jonsson).

- Child development and long-term consequences of maternal mental illness or perinatal adverse for children born in Uppsala between 1986 and 2015 and in Ethiopia in 2001 (Ulf Högberg, Alkistis Skalkidou, Anna-Karin Wikström).
- Studies on maternal microbioma in relation to peripartum depression (Alkistis Skalkidou, Maria Jonsson).
- Pregnancy and delivery outcomes among mothers with ADHD (Annika Esscher, Ulf Högberg, Stavros Iliadis).
- Obstetric healthcare in Mozambique (Ulf Högberg).
- Delivery complications and healthcare professionals as a second victim (Ulf Högberg).
- Placenta complications after caesarean section (Ove Axelsson).
- Alternative diagnoses for shaken baby syndrome (Ulf Högberg).
- Web-based KBT intervention for patients with vulvodynia (Alkistis Skalkidou, Ulf Högberg, Susanne Hesselman).

### Senior researchers' activities

Alkistis Skalkidou, adjunct Professor and president of the Gynecological Endocrinology Workgroup of SFOG, is currently the main supervisor for 5 PhD students (Patricia Eckerdal, Merit Kullinger, Lana Salih Joelsson, Emma Bränn and Hanna Henriksson) and deputy supervisor for 6 PhD students (Karin Cato, Mariella Öberg, Caroline Cesta (KI), Theodoros Sergentanis (KI), Cathrine Axfors and Julia Breedh). She is also working with 4 post-docs (Stavros Iliadis, Theodora Kallak, Spyridon Gialamas and Emma Fransson). Her main research field is perinatal mental health, and in this context she is PI for the BASIC study (description ovan), the UPPSAT study (earlier cohort on perinatal depression), the U-BIRTH study (follow-up of the offspring in the BASIC and UPPSAT studies) and collaborator in the BASICchild study (a BASIC sub-study with focus on detailed psychological evaluation of the offspring, in collaboration with Uppsala Barn- and Baby-lab). In collaboration with Ulf Högberg, the project "EMBLA, an internet-based intervention as a supplement to clinical management for vulvodynia patients" was initiated as a randomized trial in 2015. Other research interests include ultrasound pregnancy dating, the risk for neoplasia among women treated with ovarian-stimulating drugs (Cochrane Review) and the association between mode of delivery and child morbidity. Alkistis is an Associate Editor in Acta Obstetricia et Gynecologica Scandinavica and a member of the board of "Födelsefonden".

Anna-Karin Wikström focuses her research on placental dysfunctional disorders, with preeclampsia as the main focus. Anna-Karin is a Professor at Clinical Sciences at Karolinska Institutet (KI) Danderyds sjukhus and affiliated Professor at the Clinical Epidemiology Unit KI. Anna-Karin still has the major part of her research at Uppsala University. She is main supervisor for three PhD students: Epidemiological studies of preeclampsia (PhD-student Johanna Gunnarsdottir); half-time seminar 2016. Planned dissertation June 2017), Maria Nelander Preeclampsia and the brain. Half time seminar 2016; planned dissertation April 2018), and Linda Lindström (Intrauterine Growth. Planned half-time seminar 2017). Anna-Karin Wikström is also deputy supervisor of Lena Liljeström (Fetal hypoxia), Katja Junus (Pro-BNP in preeclampsia), Patricia Eckerdahl (Pregnancy complications). She was deputy supervisor of a PhD student at KI who defended his thesis in 2016 and is at present deputy supervisor of two PhD students at KI. Anna-Karin is in the steering committee for several the national RCT and for the Pregnancy Register.

Maria Jonsson is main supervisor for Lena Liljeström and Susanne Hesselman (planned dissertations 2018) and Jenny Hulstrand and deputy supervisor for Åsa Wahlberg. She is also the principal

investigator for three clinical multicenter RCTs that are conducted at the delivery ward, Akademiska hospital, two national and one international trial.

Eva Bergman, Senior Consultant and PhD, is a deputy supervisor of the PhD student Linda Lindström in the project Aspects of Intrauterine Growth Restriction. She is also supervisor for the resident doctor Agnes Edling in a descriptive project of: Second trimester abortions due to fetal anomalies. She is involved in several collaborations concerning fetal growth; The ULSCHED study including excessive fetal growth. The TRUFFLE2 study which is a European multicentre study on intrauterine growth restrictions in late pregnancies. A study on fetal growth in IVF pregnancies.is under planning. She is also involved in a Nordic multicentre study on women's choice in fetal prenatal screening involving non-invasive prenatal testing (NIPT).

Ajlana Mulic-Lutvica, Senior Consultant and PhD, was deputy supervisor of two PhD students who defended their thesis, Johanna Belachew (principal supervisor Prof Ove Axelsson) and Sara Sohlberg (main supervisor prof Anna-Karin Wikström). She collaborated with prof Birgitta Essén (IMCH) concerning prof Essén's two PhD students Annika Esscher who worked on research project about Maternal Mortality in Sweden och Soheila Mohamadi on maternal near miss in Iran. She was also co-investigator in PROGNOSIS study: Prediction of short-term outcome in pregnant women with suspected preeclampsia study – an international multi-center, non-interventional double-blind study. The principal investigator for Uppsala was Prof Matts Olovsson. Together with professor Ove Axelsson and prof Johan Wikström she is deputy supervisor for a planned PhD student, Rober Råman, on a project concerning fetal anomalies, comparative study of 2D Ultrasound versus 3D Ultrasound versus MR and a comparative study concerning fetal anomaly screening among morbid obese women -first trimester vaginal ultrasound versus routine ultrasound. She is now collaborating with professor Inger Sundström-Poromaa (Reproductive Health, KBH) and Anna-Karin Wikström on a new project on obesity and pregnancy complications and also with professor Alkistis Skalkidou on a project on hyperemesis and perinatal depression.

Annika Esscher, Senior Consultant and PhD is the principal investigator in an upcoming study on the association between ADHD diagnoses in the mother and several obstetrical and neonatal outcomes.

Senior professor Ove Axelsson is main supervisor for PhD student Ellen Ternby, whose research project deals with knowledge of Down syndrome among pregnant women, partners and professionals within antenatal care. Ellen Ternby has passed her half time control and is now embarking on a qualitative study where pregnant women are to asked about how they wish to be informed on fetal diagnostics. Ove Axelsson is also a cooperator in Tommy Carlsson's thesis project where web-sites concerning fetal anomalies are evaluated. Tommy Carlsson will defend his thesis in the autumn of 2017. Finally, together with professor Johan Wikström, Ove Axelsson continues to assess pictorial magnetic resonance imaging for diagnosis of fetal anomalies.

Senior Professor Ulf Högberg is the main supervisor for Åsa Walberg and Sibone Mocumbi, with deputy supervisors Anna Bergström, research Group International Child Health and Nutrition, and associate professor Claudia Hanson, KI. Högberg is deputy supervisor for Susanne Hesselman and Charlotta Millde Luthander, department of Clinical Science and Education, Unit of Obstetrics and Gynecology, KI who defended her thesis defence in 2016. Ulf Högberg is principal investigator in the project started in 2015 "Shaken baby syndrome/abusive head trauma in Sweden - Diagnosis, occurrence, risk factors, societal consequences and perspectives."

Associate professor Ulf Hanson has been continuing his studies on diabetes during pregnancy in collaboration with KI and Örebro university: 1) the effect of overweight and obesitas in the outcome of GDM women; 2) national register studies of outcome of pregnancies complicated by type-1-diabetes, type-2-diabetes and Gestational Diabetes Mellitus; 3) addressing the issue of, different screening criteria for OGTT in relation to different diagnostic levels for hyperglycemia during

pregnancy by using 3500 consecutive OGTT during pregnancy. He is deputy supervisor for Ann-Kristin Rönnberg, department of Obsterics and gynecology, Örebro University, who defended her thesis in 2016. He and associate professor Solveig Norden Lindeberg has ongoing register studies regarding preeclampsia and malformations.

### **Reproductive Biology**

### Matts Olovsson

### Members of the group during 2016

Olovsson, Matts, Professor Bourlev, Vladimir, Professor Stavréus-Evers, Anneli, Professor Edelstam, Greta, Associate professor Rezapour, Masoumeh, Associate professor Skirnisdottir, Ingridur, Associate professor

Holte, Jan, MD, PhD Wikström, Ingrid, MD, PhD Lindström, Annika, MD, PhD Brodin, Thomas, MD, PhD Karypidis, Helena, MD, PhD Sanner, Karin, MD, PhD Moberg, Christian, MD, PhD Lövkvist, Lena, PhD Kunovac Kallak, Theodora, PhD

Junus, Katja, PhD-student Jansson, Caroline, PhD-student Arnio, Riina, PhD-student Norenhag, Johanna, PhD-student

Hermansson, Ruth, Research student Iliasova, Natalia, Research student Karlberg, Malin, Research student Haroun, Sally, Research student Sandell, Petra, Research student Yaldir, Fatma Gulen, Research student

Davey, Eva, Biomedical laboratory scientist Båth, Ann-Sofie, Study nurse

### Publications 2014-2016

### 2016

 Mizuuchi M, Cindrova-Davies T, Olovsson M, Charnock-Jones DS, Burton GJ, Yung HW. Placental endoplasmic reticulum stress negatively regulates transcription of placental growth factor via ATF4 and ATF6β: implications for the pathophysiology of human pregnancy complications. J Pathol. 2016 Mar;238(4):550-61.

- Junus K, Wikström AK, Larsson A, Olovsson M. Early second-trimester plasma levels of NTproBNP in women who subsequently develop early-onset preeclampsia. J Matern Fetal Neonatal Med. 2016 Oct 19:1-3.
- 3. Lövkvist L, Boström P, Edlund M, Olovsson M. Age-Related Differences in Quality of Life in Swedish Women with Endometriosis. J Womens Health (Larchmt). 2016 Jun;25(6):646-53.
- 4. Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, Olovsson M, Brennecke SP, Stepan H, Allegranza D, Dinkel C, Schoedl M, Dilba P, Hund M, Verlohren S. Soluble fms-Like Tyrosine Kinase-1-to-Placental Growth Factor Ratio and Time to Delivery in Women With Suspected Preeclampsia. Obstet Gynecol. 2016 Aug;128(2):261-9.
- Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, Olovsson M, Brennecke SP, Stepan H, Allegranza D, Dilba P, Schoedl M, Hund M, Verlohren S. Predictive Value of the sFlt-1 : PIGF Ratio in Women With Suspected Preeclampsia EDITORIAL COMMENT. Obstetrical and Gynecological Survey. 2016 71(5):273–4.
- Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, Olovsson M, Brennecke SP, Stepan H, Allegranza D, Dilba P, Schoedl M, Hund M, Verlohren S. Predictive Value of the sFlt-1:PIGF Ratio in Women with Suspected Preeclampsia. N Engl J Med. 2016 Jan 7;374(1):13-22.
- Altmäe S, Tamm-Rosenstein K, Esteban FJ, Simm J, Kolberg L, Peterson H, Metsis M, Haldre K, Horcajadas JA, Salumets A, Stavreus-Evers A. Endometrial transcriptome analysis indicates superiority of natural over artificial cycles in recurrent implantation failure patients undergoing frozen embryo transfer. Reprod Biomed Online. 2016 Jun;32(6):597-613.
- Aghajanova L, Altmäe S, Kasvandik S, Salumets A, Stavreus-Evers A, Giudice LC. Stanniocalcin-1 expression in normal human endometrium and dysregulation in endometriosis. Fertil Steril. 2016 Sep 1;106(3):681-691.
- Skirnisdottir I, Seidal T, Åkerud H. The relationship of the angiogenesis regulators VEGF-A, VEGF-R1 and VEGF-R2 to p53 status and prognostic factors in epithelial ovarian carcinoma in FIGO-stages I-II. Int J Oncol. 2016 Mar;48(3):998-1006.
- 10. Lindgren KE, Hreinsson J, Helmestam M, Wånggren K, Poromaa IS, Kårehed K, Åkerud H. Histidine-rich glycoprotein derived peptides affect endometrial angiogenesis in vitro but has no effect on embryo development. Syst Biol Reprod Med. 2016 Jun;62(3):192-200.
- 11. Kushnir MM, Naessén T, Wanggren K, Hreinsson J, Rockwood AL, Meikle AW, Bergquist J. Exploratory study of the association of steroid profiles in stimulated ovarian follicular fluid with outcomes of IVF treatment. J Steroid Biochem Mol Biol. 2016 Sep;162:126-33.

### 2015

- 1. Sanner K, Wikström I, Gustavsson I, Wilander E, Lindberg JH, Gyllensten U, Olovsson M. Daily self-sampling for high-risk human papillomavirus (HR-HPV) testing. J Clin Virol. 2015 Dec;73:1-7.
- Sohlberg S, Mulic-Lutvica A, Olovsson M, Weis J, Axelsson O, Wikström J, Wikström AK. Magnetic resonance imaging-estimated placental perfusion in fetal growth assessment. Ultrasound Obstet Gynecol. 2015 Dec;46(6):700-5.
- 3. Zieba A, Sjöstedt E, Olovsson M, Fagerberg L, Hallström BM, Oskarsson L, Edlund K, Tolf A, Uhlen M, Ponten F. The Human Endometrium-Specific Proteome Defined by Transcriptomics and Antibody-Based Profiling. OMICS. 2015 Nov;19(11):659-68.
- 4. Brodin T, Hadziosmanovic N, Berglund L, Olovsson M, Holte J. Comparing four ovarian reserve markers--associations with ovarian response and live births after assisted reproduction. Acta Obstet Gynecol Scand. 2015 Oct;94(10):1056-63.
- 5. Saha R, Pettersson HJ, Svedberg P, Olovsson M, Bergqvist A, Marions L, Tornvall P, Kuja-Halkola R. Heritability of endometriosis. Fertil Steril. 2015 Oct;104(4):947-52.
- 6. Moberg C, Bourlev V, Ilyasova N, Olovsson M. Endometrial expression of LIF and its receptor and peritoneal fluid levels of IL-1 $\alpha$  and IL-6 in women with endometriosis are associated with the probability of pregnancy. Arch Gynecol Obstet. 2015 Aug;292(2):429-37.

- 7. Moberg C, Bourlev V, Ilyasova N, Olovsson M. Levels of oestrogen receptor, progesterone receptor and αB-crystallin in eutopic endometrium in relation to pregnancy in women with endometriosis. Hum Fertil (Camb). 2015 Mar;18(1):30-7.
- Rhenman A, Berglund L, Brodin T, Olovsson M, Milton K, Hadziosmanovic N, Holte J. Which set of embryo variables is most predictive for live birth? A prospective study in 6252 single embryo transfers to construct an embryo score for the ranking and selection of embryos. Hum Reprod. 2015 Jan;30(1):28-36.
- Kallak TK, Baumgart J, Nilsson K, Åkerud H, Poromaa IS, Stavreus-Evers A. Vaginal Gene Expression During Treatment With Aromatase Inhibitors. Clin Breast Cancer. 2015 Dec;15(6):527-535.e2.
- Pärn T, Grau Ruiz R, Kunovac Kallak T, Ruiz JR, Davey E, Hreinsson J, Wånggren K, Salumets A, Sjöström M, Stavreus-Evers A, Ortega FB, Altmäe S. Physical activity, fatness, educational level and snuff consumption as determinants of semen quality: findings of the ActiART study. Reprod Biomed Online. 2015 Jul;31(1):108-19.
- 11. Aghajanova L, Mahadevan S, Altmäe S, Stavreus-Evers A, Regan L, Sebire N, Dixon P, Fisher RA, Van den Veyver IB. No evidence for mutations in NLRP7, NLRP2 or KHDC3L in women with unexplained recurrent pregnancy loss or infertility. Hum Reprod. 2015 Jan;30(1):232-8.
- Murto T, Kallak TK, Hoas A, Altmäe S, Salumets A, Nilsson TK, Skoog Svanberg A, Wånggren K, Yngve A, Stavreus-Evers A. Folic acid supplementation and methylenetetrahydrofolate reductase (MTHFR) gene variations in relation to in vitro fertilization pregnancy outcome. Acta Obstet Gynecol Scand. 2015 Jan;94(1):65-71.
- 13. Skirnisdottir I, Seidal T, Åkerud H. Differences in Clinical and Biological Features Between Type I and Type II Tumors in FIGO Stages I-II Epithelial Ovarian Carcinoma. Int J Gynecol Cancer. 2015 Sep;25(7):1239-47.
- Häggström M, Spira J, Edelstam G. Transducer hygiene: comparison of procedures for decontamination of ultrasound transducers and their use in clinical practice. J Clin Ultrasound. 2015 Feb;43(2):81-8.

### 2014

- 1. Helmestam M, Lindgren KE, Stavreus-Evers A, Olovsson M. Mifepristone-exposured human endometrial endothelial cells in vitro. Reprod Sci. 2014 Mar;21(3):408-14.
- Junus K, Wikström AK, Larsson A, Olovsson M. Placental Expression of proBNP/NT-proBNP and Plasma Levels of NT-proBNP in Early- and Late-Onset Preeclampsia. Am J Hypertens. 2014 Sep;27(9):1225-30.
- 3. Sohlberg S, Wikström AK, Olovsson M, Lindgren P, Axelsson O, Mulic-Lutvica A, Weis J, Wikström J. In vivo(31)P-MR spectroscopy in normal pregnancy, early and late preeclampsia: A study of placental metabolism. Placenta. 2014 May;35(5):318-23.
- 4. Helmestam M, Davey E, Stavreus-Evers A, Olovsson M. Bisphenol A affects human endometrial endothelial cell angiogenic activity in vitro. Reprod Toxicol. 2014 Jul;46:69-76.
- 5. Yung HW, Atkinson D, Campion-Smith T, Olovsson M, Charnock-Jones DS, Burton GJ. Differential activation of placental unfolded protein response pathways implies heterogeneity in causation of early- and late-onset pre-eclampsia. J Pathol. 2014 Oct;234(2):262-76.
- Haroun S, Altmäe S, Karypidis H, Kuningas M, Landgren BM, Akerud H, Skjöldebrand-Sparre L, Hosseini F, Bremme K, Sundström-Poromaa I, Stavreus-Evers A. Association between trefoil factor 3 gene variants and idiopathic recurrent spontaneous abortion. Reprod Biomed Online. 2014 Dec;29(6):737-44
- Elenis E, Lindgren KE, Karypidis H, Skalkidou A, Hosseini F, Bremme K, Landgren BM, Skjöldebrand-Sparre L, Stavreus-Evers A, Sundström-Poromaa I, Åkerud H. The histidine-rich glycoprotein A1042G polymorphism and recurrent miscarriage: a pilot study. Reprod Biol Endocrinol. 2014 Jul 27;12:70
- 8. Murto T, Skoog Svanberg A, Yngve A, Nilsson TK, Altmäe S, Wånggren K, Salumets A, Stavreus-Evers A. Folic acid supplementation and IVF pregnancy outcome in women with unexplained infertility. Reprod Biomed Online. 2014 Jun;28(6):766-72
- 9. Wånggren K, Baban M, Svanberg AS. Attitudes toward embryo donation among staff at in vitro fertilization clinics. Acta Obstet Gynecol Scand. 2014 Aug;93(8):765-70.
- Kallak TK, Baumgart J, Göransson E, Nilsson K, Poromaa IS, Stavreus-Evers A. Aromatase inhibitors affect vaginal proliferation and steroid hormone receptors. Menopause. 2014 Apr;21(4):383-90.

#### Reviews 2014-2016

 Altmäe S, Esteban FJ, Stavreus-Evers A, Simón C, Giudice L, Lessey BA, Horcajadas JA, Macklon NS, D'Hooghe T, Campoy C, Fauser BC, Salamonsen LA, Salumets A. Guidelines for the design, analysis and interpretation of 'omics' data: focus on human endometrium. Hum Reprod Update. 2014 Jan-Feb;20(1):12-28.

#### **Dissertations 2016**

Christian Moberg, 160330.

#### Agencies that support the work/Funding

ALF, 1 704 000 SEK Vinnova/Eurostar 350 000 SEK Lions cancerforskningsfond, 300 000 SEK The Swedish Research Council, 700 000 SEK

#### Endometrial receptivity

For a successful implantation and pregnancy it is important that the endometrial development is normal. We can now show that failure in endometrial development could offer an explanation of both of unexplained infertility and recurrent pregnancy loss.

Experience of miscarriage, including recurrent pregnancy loss, is associated with reduced mental health. For future improvement of care for miscarriage patients, we have now validated a new instrument, included in Caroline Jansson's thesis work.

We are also studying genetic, hormonal and health factors in associated with endometrial receptivity, specifically in relation to unexplained infertility and recurrent pregnancy loss. Furthermore, the role of prostasomes, exosomes from the prostate gland, for endometrial receptivity is studied.

Anneli Stavreus-Evers is coordinating these studies.

**Preeclampsia**, a project aiming at a better understanding of the pathogenesis of PE and how to diagnose, predict and treat the disease. Within the PE-projects we have cooperation with Professor Graham Burton in Cambridge (UK) on placental/trophoblast metabolism. In cooperation with Professor Gernot Desoye in Graz (Austria) we are currently studying the possible involvement of NT-proBNP in the pathogenesis of PE. Matts Olovsson is coordinating these studies.

**Endometriosis**, we have recently published data from a study on quality of life (QoL) where we for the first time can show that the QoL is worse among younger women with endometriosis. From the same study we will publish data on cost of illness. We can show that women with symptomatic endometriosis cost about 90 000 SEK/year compared with about 20 000 SEK/year in a age and gender matched background population.

We have evaluated the Swedish version of the questionnaire Endometriosis Health Profile -30. We are currently performing several studies on new medications for the treatment of endometriosis associated pain as well as new markers to diagnose endometriosis. We are performing studies on endometriosis associated pain. There are also studies of endometrial factors associated with endometriosis related infertility. Our endometriosis research is done at our National Endometriosis Centre. Matts Olovsson is coordinating these studies.

**Cervical cancer** is the second most frequent cancer among women worldwide and caused by persistent infection by oncogenic types of human papillomavirus (HR-HPV). We are studying self-sampling for the analysis of HR-HPV. We are currently compiling data from a large population-based study where we compare conventional cytology with self-sampling for HPV-testing. A first manuscript showing superiority of self-sampling combined with HPV-testing has been submitted. We have recently finalized a large randomized study where we compare self-sampling wits sampling by a midwife, both for the analysis of HR-HPV. We have also recently finalized two studies on the prevalence of HR-HPV in women aged 60-75 years, one based on sampling by a gynaecologist and the other on self-sampling. Both these studies show a prevalence of HPV just above 4% and among them that also were positive in a second test four months later a large proportion actually had H-SIL. We are currently performing a questionnaire study to find out why women do not take part in the screening program and what would make do.

The studies are coordinated by a steering group consisting of Matts Olovsson, Ulf Gyllensten, Erik Wilander, Annika Lindström, Ingrid Wikström, Karin Sanner and Riina Aarnio.

We have studied **prognostic factors in assisted reproduction techniques**. Currently we are studying which of several embryo scoring variables that have independent predictive power for pregnancy and live birth following embryo transfer. These studies are coordinated by Jan Holte, Thomas Brodin and Matts Olovsson.

**Ovarian cancer**, prognostic factors for epithelial ovarian cancer are studied. These studies are coordinated by Ingridur Skirnisdottir.

# Obstetrik och gynekologi

#### **Reproductive Health**

#### Inger Sundström Poromaa

The Reproductive Health research group focuses on all aspects of reproductive health, with an aim of improving mental and sexual well-being of women at all ages. The studies range from investigator-initiated clinical trials, to neuroimaging, and laboratory analyses of human tissue. Women throughout the entire reproductive span are included in these studies, from young women requesting contraception, to pregnant and newly delivered women, and finally also postmenopausal women.

#### Members of the group during 2016

Inger Sundström Poromaa, professor Helena Åkerud, adjunct professor until June 2016 Dan Hellberg, adjunct professor Charlotte Hellgren, post doc Elin Bannbers, PhD Catrin Borneskog, PhD Fatimah Dabo, PhD Malin Gingnell, PhD Annika Lindström, PhD Helena Lundgren, PhD Karin Stålberg, PhD Birgitta Segebladh, PhD Jan Wesström, PhD Inger Wallin Lundell, PhD Helena Kaihola, PhD Theodora Kunovac Kallak, PhD Raghad Samir, PhD Evangelina Elenis, PhD student Karin Lindgren, PhD Josefin Sjömark, PhD studen Emma Håstad, PhD student Kathrine Bjersand, PhD student Åsa Edvinsson, PhD student Cecilia Lundin, PhD student Paridhi Jha, PhD student Gyula Pekar, PhD student Lena Moby, research nurse

#### Publications 2014-2016

#### 2016

1. Wahlberg A, Andreen Sachs M, Johannesson K, Hallberg G, Jonsson M, Skoog Svanberg A, et al. Post-traumatic stress symptoms in Swedish obstetricians and midwives after severe obstetric events: a cross-sectional retrospective survey. BJOG : an international journal of obstetrics and gynaecology. 2016.

- 2. Tiblom Ehrsson Y, Stenhammar C, Rosenblad A, Akerud H, Larsson M, Tyden T. Selfreported sexually transmitted infections among female university students. Upsala journal of medical sciences. 2016;121(1):45-9.
- 3. Svanberg AS, Sydsjo G, Bladh M, Lampic C. Attitudes about donor information differ greatly between IVF couples using their own gametes and those receiving or donating oocytes or sperm. Journal of assisted reproduction and genetics. 2016;33(6):703-10.
- 4. Sundstrom Poromaa I, Mellembakken JR, Papunen LM, Piltonen T, Puurunen J, Tapanainen JS, et al. Should we individualize lipid profiling in women with polycystic ovary syndrome? Human reproduction (Oxford, England). 2016;31(12):2791-5.
- 5. Stalberg K, Crona J, Razmara M, Taslica D, Skogseid B, Stalberg P. An Integrative Genomic Analysis of Formalin Fixed Paraffin-Embedded Archived Serous Ovarian Carcinoma Comparing Long-term and Short-term Survivors. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2016;26(6):1027-32.
- 6. Pettersson FD, Hellgren C, Nyberg F, Akerud H, Sundstrom-Poromaa I. Depressed mood, anxiety, and the use of labor analgesia. Archives of women's mental health. 2016;19(1):11-6.
- Lundin C, Danielsson KG, Bixo M, Moby L, Bengtsdotter H, Jawad I, et al. Combined oral contraceptive use is associated with both improvement and worsening of mood in the different phases of the treatment cycle-A double-blind, placebo-controlled randomized trial. Psychoneuroendocrinology. 2016;76:135-43.
- 8. Lindgren KE, Nordqvist S, Karehed K, Sundstrom-Poromaa I, Akerud H. The effect of a specific histidine-rich glycoprotein polymorphism on male infertility and semen parameters. Reproductive biomedicine online. 2016;33(2):180-8.
- 9. Lindgren KE, Hreinsson J, Helmestam M, Wanggren K, Poromaa IS, Karehed K, et al. Histidine-rich glycoprotein derived peptides affect endometrial angiogenesis in vitro but has no effect on embryo development. Systems biology in reproductive medicine. 2016:1-9.
- 10. Kaihola H, Yaldir FG, Hreinsson J, Hornaeus K, Bergquist J, Olivier JD, et al. Effects of Fluoxetine on Human Embryo Development. Frontiers in cellular neuroscience. 2016;10:160.
- 11. Isaksson S, Skoog-Svanberg A, Sydsjo G, Linell L, Lampic C. It takes two to tango: information-sharing with offspring among heterosexual parents following identity-release sperm donation. Human reproduction (Oxford, England). 2016;31(1):125-32.
- 12. Iliadis SI, Sylven S, Hellgren C, Olivier JD, Schijven D, Comasco E, et al. MID-PREGNANCY CORTICOTROPIN-RELEASING HORMONE LEVELS IN ASSOCIATION WITH POSTPARTUM DEPRESSIVE SYMPTOMS. Depression and anxiety. 2016.
- 13. Hogberg U, Claeson C, Krebs L, Svanberg AS, Kidanto H. Breech delivery at a University Hospital in Tanzania. BMC pregnancy and childbirth. 2016;16(1):342.
- Hellgren C, Edvinsson A, Olivier JD, Fornes R, Stener-Victorin E, Ubhayasekera SJ, et al. Tandem mass spectrometry determined maternal cortisone to cortisol ratio and psychiatric morbidity during pregnancy-interaction with birth weight. Psychoneuroendocrinology. 2016;69:142-9.
- 15. Gingnell M, Bannbers E, Engman J, Frick A, Moby L, Wikstrom J, et al. The effect of combined hormonal contraceptives use on brain reactivity during response inhibition. The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception. 2016;21(2):150-7.
- 16. Esscher A, Essen B, Innala E, Papadopoulos FC, Skalkidou A, Sundstrom-Poromaa I, et al. Suicides during pregnancy and 1 year postpartum in Sweden, 1980-2007. The British journal of psychiatry : the journal of mental science. 2016;208(5):462-9.
- 17. Elenis E, Sydsjo G, Skalkidou A, Lampic C, Svanberg AS. Neonatal outcomes in pregnancies resulting from oocyte donation: a cohort study in Sweden. BMC pediatrics. 2016;16(1):170.
- Comasco E, Gulinello M, Hellgren C, Skalkidou A, Sylven S, Sundstrom-Poromaa I. Sleep duration, depression, and oxytocinergic genotype influence prepulse inhibition of the startle reflex in postpartum women. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology. 2016;26(4):767-76.

 Bergman L, Akerud H. Plasma Levels of the Cerebral Biomarker, Neuron-Specific Enolase, are Elevated During Pregnancy in Women Developing Preeclampsia. Reproductive sciences (Thousand Oaks, Calif). 2016;23(3):395-400.

#### 2015

- Witjes H, Creinin MD, Sundstrom-Poromaa I, Martin Nguyen A, Korver T. Comparative analysis of the effects of nomegestrol acetate/17 beta-estradiol and drospirenone/ethinylestradiol on premenstrual and menstrual symptoms and dysmenorrhea. The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception. 2015;20(4):296-307.
- 2. Wallstrom T, Hellgren C, Akerud H, Wiberg-Itzel E. Skin conductance activity in post-term pregnancies. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2015;28(16):1912-6.
- 3. Wallin Lundell I, Ohman SG, Sundstrom Poromaa I, Hogberg U, Sydsjo G, Skoog Svanberg A. How women perceive abortion care: A study focusing on healthy women and those with mental and posttraumatic stress. The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception. 2015;20(3):211-22.
- 4. Tinglof S, Hogberg U, Lundell IW, Svanberg AS. Exposure to violence among women with unwanted pregnancies and the association with post-traumatic stress disorder, symptoms of anxiety and depression. Sexual & reproductive healthcare : official journal of the Swedish Association of Midwives. 2015;6(2):50-3.
- 5. Sydsjo G, Vikstrom J, Bladh M, Jablonowska B, Skoog Svanberg A. Men report good mental health 20 to 23 years after in vitro fertilisation treatment. BMC public health. 2015;15:1175.
- 6. Stenson D, Wallstrom T, Sjostrand M, Akerud H, Gemzell-Danielsson K, Wiberg-Itzel E. Induction of labor in women with a uterine scar. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2015:1-6.
- 7. Stenhammar C, Ehrsson YT, Akerud H, Larsson M, Tyden T. Sexual and contraceptive behavior among female university students in Sweden repeated surveys over a 25-year period. Acta obstetricia et gynecologica Scandinavica. 2015;94(3):253-9.
- Skirnisdottir I, Seidal T, Akerud H. Differences in Clinical and Biological Features Between Type I and Type II Tumors in FIGO Stages I-II Epithelial Ovarian Carcinoma. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2015;25(7):1239-47.
- 9. Sergentanis TN, Thomopoulos TP, Gialamas SP, Karalexi MA, Biniaris-Georgallis SI, Kontogeorgi E, et al. Risk for childhood leukemia associated with maternal and paternal age. European journal of epidemiology. 2015;30(12):1229-61.
- Pinola P, Piltonen TT, Puurunen J, Vanky E, Sundstrom-Poromaa I, Stener-Victorin E, et al. Androgen Profile Through Life in Women With Polycystic Ovary Syndrome: A Nordic Multicenter Collaboration Study. The Journal of clinical endocrinology and metabolism. 2015;100(9):3400-7.
- 11. Petridou ET, Sergentanis TN, Skalkidou A, Antonopoulos CN, Dessypris N, Svensson T, et al. Maternal and birth anthropometric characteristics in relation to the risk of childhood lymphomas: a Swedish nationwide cohort study. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2015;24(6):535-41.
- 12. Petridou ET, Sergentanis TN, Perlepe C, Papathoma P, Tsilimidos G, Kontogeorgi E, et al. Socioeconomic disparities in survival from childhood leukemia in the United States and globally: a meta-analysis. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2015;26(3):589-97.
- 13. Olivier JD, Akerud H, Sundstrom Poromaa I. Antenatal depression and antidepressants during pregnancy: unraveling the complex interactions for the offspring. European journal of pharmacology. 2015;753:257-62.

- Nordqvist S, Karehed K, Skoog Svanberg A, Menezes J, Akerud H. Ovarian response is affected by a specific histidine-rich glycoprotein polymorphism: a preliminary study. Reproductive biomedicine online. 2015;30(1):74-81.
- Murto T, Kallak TK, Hoas A, Altmae S, Salumets A, Nilsson TK, et al. Folic acid supplementation and methylenetetrahydrofolate reductase (MTHFR) gene variations in relation to in vitro fertilization pregnancy outcome. Acta obstetricia et gynecologica Scandinavica. 2015;94(1):65-71.
- 16. Maliqueo M, Sundstrom Poromaa I, Vanky E, Fornes R, Benrick A, Akerud H, et al. Placental STAT3 signaling is activated in women with polycystic ovary syndrome. Human reproduction (Oxford, England). 2015;30(3):692-700.
- Karalexi MA, Skalkidou A, Thomopoulos TP, Belechri M, Biniaris-Georgallis SI, Bouka E, et al. History of Maternal Fetal Loss and Childhood Leukaemia Risk in Subsequent Offspring: Differentials by Miscarriage or Stillbirth History and Disease Subtype. Paediatric and perinatal epidemiology. 2015;29(5):453-61.
- Kallak TK, Baumgart J, Nilsson K, Akerud H, Poromaa IS, Stavreus-Evers A. Vaginal Gene Expression During Treatment With Aromatase Inhibitors. Clinical breast cancer. 2015;15(6):527-35.e2.
- 19. Kaihola H, Olivier J, Poromaa IS, Akerud H. The effect of antenatal depression and selective serotonin reuptake inhibitor treatment on nerve growth factor signaling in human placenta. PloS one. 2015;10(1):e0116459.
- Iliadis SI, Koulouris P, Gingnell M, Sylven SM, Sundstrom-Poromaa I, Ekselius L, et al. Personality and risk for postpartum depressive symptoms. Archives of women's mental health. 2015;18(3):539-46.
- 21. Iliadis SI, Comasco E, Sylven S, Hellgren C, Sundstrom Poromaa I, Skalkidou A. Prenatal and Postpartum Evening Salivary Cortisol Levels in Association with Peripartum Depressive Symptoms. PloS one. 2015;10(8):e0135471.
- 22. Iliadis S, Sylven S, Jocelien O, Hellgren C, Hannefors AK, Elfstrom D, et al. Corticotropinreleasing hormone and postpartum depression: A longitudinal study. Psychoneuroendocrinology. 2015;61:61.
- 23. Hannerfors AK, Hellgren C, Schijven D, Iliadis SI, Comasco E, Skalkidou A, et al. Treatment with serotonin reuptake inhibitors during pregnancy is associated with elevated corticotropin-releasing hormone levels. Psychoneuroendocrinology. 2015;58:104-13.
- 24. Granfors M, Andersson M, Stinca S, Akerud H, Skalkidou A, Poromaa IS, et al. Iodine deficiency in a study population of pregnant women in Sweden. Acta obstetricia et gynecologica Scandinavica. 2015;94(11):1168-74.
- 25. Gingnell M, Bannbers E, Moes H, Engman J, Sylven S, Skalkidou A, et al. Emotion Reactivity Is Increased 4-6 Weeks Postpartum in Healthy Women: A Longitudinal fMRI Study. PloS one. 2015;10(6):e0128964.
- 26. Gingnell M, Bannbers E, Engman J, Frick A, Moby L, Wikstrom J, et al. The effect of combined hormonal contraceptives use on brain reactivity during response inhibition. The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception. 2015:1-8.
- 27. Esscher A, Essen B, Innala E, Papadopoulos FC, Skalkidou A, Sundstrom-Poromaa I, et al. Suicides during pregnancy and 1 year postpartum in Sweden, 1980-2007. The British journal of psychiatry : the journal of mental science. 2015.
- 28. Elenis E, Svanberg AS, Lampic C, Skalkidou A, Akerud H, Sydsjo G. Adverse obstetric outcomes in pregnancies resulting from oocyte donation: a retrospective cohort case study in Sweden. BMC pregnancy and childbirth. 2015;15:247.
- 29. Comasco E, Sundstrom-Poromaa I. Neuroimaging the Menstrual Cycle and Premenstrual Dysphoric Disorder. Current psychiatry reports. 2015;17(10):77.
- 30. Comasco E, Hellgren C, Olivier J, Skalkidou A, Sundstrom Poromaa I. Supraphysiological hormonal status, anxiety disorders, and COMT Val/Val genotype are associated with reduced sensorimotor gating in women. Psychoneuroendocrinology. 2015;60:217-23.

- 31. Bjersand K, Mahteme H, Sundstrom Poromaa I, Andreasson H, Graf W, Larsson R, et al. Drug Sensitivity Testing in Cytoreductive Surgery and Intraperitoneal Chemotherapy of Pseudomyxoma Peritonei. Annals of surgical oncology. 2015;22 Suppl 3:S810-6.
- Bhandage AK, Hellgren C, Jin Z, Olafsson EB, Sundstrom-Poromaa I, Birnir B. Expression of GABA receptors subunits in peripheral blood mononuclear cells is gender dependent, altered in pregnancy and modified by mental health. Acta physiologica (Oxford, England). 2015;213(3):575-85.
- Ahlsson F, Akerud H, Schijven D, Olivier J, Sundstrom-Poromaa I. Gene Expression in Placentas From Nondiabetic Women Giving Birth to Large for Gestational Age Infants. Reproductive sciences (Thousand Oaks, Calif). 2015;22(10):1281-8.

#### 2014

- 1. Wiberg-Itzel E, Pembe AB, Wray S, Wihlback AC, Darj E, Hoesli I, et al. Level of lactate in amniotic fluid and its relation to the use of oxytocin and adverse neonatal outcome. Acta obstetricia et gynecologica Scandinavica. 2014;93(1):80-5.
- 2. Wesstrom J, Ulfberg J, Sundstrom-Poromaa I, Lindberg E. Periodic limb movements are associated with vasomotor symptoms. J Clin Sleep Med. 2014;10(1):15-20.
- Wesstrom J, Skalkidou A, Manconi M, Fulda S, Sundstrom-Poromaa I. Pre-pregnancy restless legs syndrome (Willis-Ekbom Disease) is associated with perinatal depression. J Clin Sleep Med. 2014;10(5):527-33.
- 4. Wanggren K, Baban M, Svanberg AS. Attitudes toward embryo donation among staff at in vitro fertilization clinics. Acta obstetricia et gynecologica Scandinavica. 2014;93(8):765-70.
- 5. Toffoletto S, Lanzenberger R, Gingnell M, Sundstrom-Poromaa I, Comasco E. Emotional and cognitive functional imaging of estrogen and progesterone effects in the female human brain: a systematic review. Psychoneuroendocrinology. 2014;50:28-52.
- 6. Sydsjo G, Svanberg AS, Bladh M, Lampic C. Relationships in couples treated with sperm donation a national prospective follow-up study. Reprod Health. 2014;11:62.
- Sydsjo G, Lampic C, Bladh M, Svanberg AS. Oocyte and sperm donors' opinions on the acceptable number of offspring. Acta obstetricia et gynecologica Scandinavica. 2014;93(7):634-9.
- 8. Sydsjo G, Lampic C, Bladh M, Skoog Svanberg A. Relationships in oocyte recipient couples a Swedish national prospective follow-up study. Reprod Health. 2014;11:38.
- 9. Sundstrom Poromaa I, Gingnell M. Menstrual cycle influence on cognitive function and emotion processing-from a reproductive perspective. Front Neurosci. 2014;8:380.
- 10. Stalberg K, Svensson T, Lonn S, Kieler H. The influence of comorbidity on mortality in ovarian cancer patients. Gynecologic oncology. 2014;133(2):298-303.
- 11. Sergentanis TN, Diamantaras AA, Perlepe C, Kanavidis P, Skalkidou A, Petridou ET. IVF and breast cancer: a systematic review and meta-analysis. Hum Reprod Update. 2014;20(1):106-23.
- 12. Ridefelt P, Hellberg D, Aldrimer M, Gustafsson J. Estimating reliable paediatric reference intervals in clinical chemistry and haematology. Acta Paediatr. 2014;103(1):10-5.
- 13. Ridefelt P, Gustafsson J, Aldrimer M, Hellberg D. Alkaline phosphatase in healthy children: reference intervals and prevalence of elevated levels. Horm Res Paediatr. 2014;82(6):399-404.
- 14. Poromaa IS. Physiological Correlates of Premenstrual Dysphoric Disorder (PMDD). Curr Top Behav Neurosci. 2014;21:229-43.
- 15. Pekar G, Gere M, Tarjan M, Hellberg D, Tot T. Molecular phenotype of the foci in multifocal invasive breast carcinomas: intertumoral heterogeneity is related to shorter survival and may influence the choice of therapy. Cancer. 2014;120(1):26-34.
- 16. Olivier JD, Akerud H, Sundstrom Poromaa I. Antenatal depression and antidepressants during pregnancy: Unraveling the complex interactions for the offspring. European journal of pharmacology. 2014.
- 17. Olivier JD, Akerud H, Skalkidou A, Kaihola H, Sundstrom-Poromaa I. The effects of antenatal depression and antidepressant treatment on placental gene expression. Frontiers in cellular neuroscience. 2014;8:465.

- Oberg M, Stenson K, Skalkidou A, Heimer G. Prevalence of intimate partner violence among women seeking termination of pregnancy compared to women seeking contraceptive counseling. Acta obstetricia et gynecologica Scandinavica. 2014;93(1):45-51.
- 19. Nordqvist S, Sydsjo G, Lampic C, Akerud H, Elenis E, Skoog Svanberg A. Sexual orientation of women does not affect outcome of fertility treatment with donated sperm. Human reproduction (Oxford, England). 2014;29(4):704-11.
- 20. Murto T, Skoog Svanberg A, Yngve A, Nilsson TK, Altmae S, Wanggren K, et al. Folic acid supplementation and IVF pregnancy outcome in women with unexplained infertility. Reproductive biomedicine online. 2014;28(6):766-72.
- 21. Lindstrom AK, Hellberg D. Immunohistochemical LRIG3 expression in cervical intraepithelial neoplasia and invasive squamous cell cervical cancer: association with expression of tumor markers, hormones, high-risk HPV-infection, smoking and patient outcome. Eur J Histochem. 2014;58(2):2227.
- 22. Liljestrom L, Wikstrom AK, Skalkidou A, Akerud H, Jonsson M. Experience of fetal scalp blood sampling during labor. Acta obstetricia et gynecologica Scandinavica. 2014;93(1):113-7.
- 23. Lampic C, Skoog Svanberg A, Sydsjo G. Attitudes towards disclosure and relationship to donor offspring among a national cohort of identity-release oocyte and sperm donors. Human reproduction (Oxford, England). 2014;29(9):1978-86.
- 24. Karamanis G, Skalkidou A, Tsakonas G, Brandt L, Ekbom A, Ekselius L, et al. Cancer incidence and mortality patterns in women with anorexia nervosa. International journal of cancer. 2014;134(7):1751-7.
- Kallak TK, Baumgart J, Goransson E, Nilsson K, Poromaa IS, Stavreus-Evers A. Aromatase inhibitors affect vaginal proliferation and steroid hormone receptors. Menopause. 2014;21(4):383-90.
- 26. Isaksson S, Sydsjo G, Skoog Svanberg A, Lampic C. Preferences and needs regarding future contact with donation offspring among identity-release gamete donors: results from the Swedish Study on Gamete Donation. Fertility and sterility. 2014;102(4):1160-6.
- 27. Iliadis SI, Koulouris P, Gingnell M, Sylven SM, Sundstrom-Poromaa I, Ekselius L, et al. Personality and risk for postpartum depressive symptoms. Archives of women's mental health. 2014.
- Hellgren C, Akerud H, Skalkidou A, Backstrom T, Sundstrom-Poromaa I. Low serum allopregnanolone is associated with symptoms of depression in late pregnancy. Neuropsychobiology. 2014;69(3):147-53.
- 29. Hellberg D, Tot T. Tumor Marker Score for Prognostication of Early-stage Squamous Cell Cervical Cancer. Anticancer Res. 2014;34(2):887-92.
- 30. Haroun S, Altmae S, Karypidis H, Kuningas M, Landgren BM, Akerud H, et al. Association between trefoil factor 3 gene variants and idiopathic recurrent spontaneous abortion. Reproductive biomedicine online. 2014;29(6):737-44.
- 31. Gunnarsdottir J, Stephansson O, Cnattingius S, Akerud H, Wikstrom AK. Risk of placental dysfunction disorders after prior miscarriages: a population-based study. American journal of obstetrics and gynecology. 2014;211(1):34.e1-8.
- 32. Gremel G, Bergman J, Djureinovic D, Edqvist PH, Maindad V, Bharambe BM, et al. A systematic analysis of commonly used antibodies in cancer diagnostics. Histopathology. 2014;64(2):293-305.
- Granfors M, Akerud H, Skogo J, Stridsberg M, Wikstrom AK, Sundstrom-Poromaa I. Targeted thyroid testing during pregnancy in clinical practice. Obstetrics and gynecology. 2014;124(1):10-5.
- Gingnell M, Ahlstedt V, Bannbers E, Wikstrom J, Sundstrom-Poromaa I, Fredrikson M. Social stimulation and corticolimbic reactivity in premenstrual dysphoric disorder: a preliminary study. Biol Mood Anxiety Disord. 2014;4(1):3.
- 35. Elenis E, Lindgren KE, Karypidis H, Skalkidou A, Hosseini F, Bremme K, et al. The histidinerich glycoprotein A1042G polymorphism and recurrent miscarriage: a pilot study. Reprod Biol Endocrinol. 2014;12:70.

- 36. Comasco E, Hahn A, Ganger S, Gingnell M, Bannbers E, Oreland L, et al. Emotional frontocingulate cortex activation and brain derived neurotrophic factor polymorphism in premenstrual dysphoric disorder. Hum Brain Mapp. 2014;35(9):4450-8.
- 37. Comasco E, Frokjaer VG, Sundstrom-Poromaa I. Functional and molecular neuroimaging of menopause and hormone replacement therapy. Front Neurosci. 2014;8:388.
- 38. Cato K, Sylven SM, Skalkidou A, Rubertsson C. Experience of the first breastfeeding session in association with the use of the hands-on approach by healthcare professionals: a population-based Swedish study. Breastfeed Med. 2014;9(6):294-300.
- 39. Borneskog C, Lampic C, Sydsjo G, Bladh M, Skoog Svanberg A. How do lesbian couples compare with heterosexual in vitro fertilization and spontaneously pregnant couples when it comes to parenting stress? Acta Paediatr. 2014;103(5):537-45.
- 40. Bergman L, Akhter T, Wikstrom AK, Wikstrom J, Naessen T, Akerud H. Plasma levels of S100B in preeclampsia and association with possible central nervous system effects. American journal of hypertension. 2014;27(8):1105-11.

#### Reviews 2014-2016

#### 2016

1. Sundstrom Poromaa I, Comasco E, Georgakis MK, Skalkidou A (2017) Sex differences in depression during pregnancy and the postpartum period. J Neurosci Res 95: 719-730.

#### 2015

1. Comasco E, Sundstrom-Poromaa I. Neuroimaging the Menstrual Cycle and Premenstrual Dysphoric Disorder. Current psychiatry reports. 2015;17(10):77.

#### 2014

- 1 Poromaa IS. Physiological Correlates of Premenstrual Dysphoric Disorder (PMDD). Curr Top Behav Neurosci. 2014; 21:229-43.
- 2. Toffoletto S, Lanzenberger R, Gingnell M, Sundstrom-Poromaa I, Comasco E. Emotional and cognitive functional imaging of estrogen and progesterone effects in the female human brain: a systematic review. Psychoneuroendocrinology. 2014; 50:28-52.
- 3. Sundstrom Poromaa I, Gingnell M. Menstrual cycle influence on cognitive function and emotion processing-from a reproductive perspective. Front Neurosci. 2014; 8:380.
- 4. Olivier JD, Akerud H, Sundstrom Poromaa I. Antenatal depression and antidepressants during pregnancy: Unraveling the complex interactions for the offspring. Eur J Pharmacol. 2014.
- 5. Comasco E, Frokjaer VG, Sundstrom-Poromaa I. Functional and molecular neuroimaging of menopause and hormone replacement therapy. Front Neurosci. 2014; 8:388.

#### **Dissertations 2016**

- 1. Karin Lindgren
- 2. Evangelina Eleni

#### Agencies that support the work/Funding

The Swedish Research Council 700 000 SEK (ISP) The Swedish Research Council 1100 000 SEK (ISP) ALF, 2 900 000 SEK (ISP, ASS)

# The Swedish multicenter study on gamete donation

#### Agneta Skoog Svanberg, Gunilla Sydsjö, Evangelina Elenis, Claudia Lampic

To improve the readiness of the general population to act as gamete donors, more research on the psychosocial consequences for donors and recipients is needed. The aims of the study are to study short- and long-term psychosocial consequences of oocyte and sperm donation for the donors as well as the recipients. The multi-center study includes all infertility clinics performing gamete donation in Sweden. Donors, recipients, and control subject individually completed questionnaires: at the start of treatment, 2 months after treatment, and 3 and 7 years after treatment. Twenty-two papers from the study have thus far been published where some of the publications were included in two theses at Uppsala University at 2013 and 2015. At present three PhD students (Uppsala University, Linköpings University and Karolinska Institutet) and two postdocs (both Linköping University) are working within the project.

# The JUNO study: Internet-based psychological support following negative or traumatic experiences at delivery

#### Agneta Skoog Svanberg, Josefin Sjömark, Margareta Larsson, Thomas Parling

In Sweden, approximately 100 000 women give birth every year. Obstetric interventions, obstetric complications, a sense of losing control during delivery and inadequate information may contribute to traumatic experiences and subsequent stress symptoms in laboring women. This projects is a longitudinal, randomized controlled trial on internet-based support to women with stress symptoms (anxiety, depression and posttraumatic stress symptoms) following delivery. Endpoints include propensity to request Caesarean section at next pregnancy. The first 200 women have been included in the trial which aims at a final study population of 500.

#### Obstetric care in India

#### Agneta Skoog Svanberg, Paridhi Jha, Margareta Larsson, Kyllike Christensson

Through a number of national programs, and with the aim of fulfilling the Millennium Development Goals, India has over the past years promoted institutionalized deliveries. By these measures, maternal mortality has been significantly reduced and 80 % of deliveries now take place in the clinic. Together with Indian collaborators this study evaluates quality of obstetric care in India, and women's satisfaction with given care. Qualitative and quantitative data will be collected from public delivery clinics in specific parts of Indian.

#### Adverse mood effects on combined oral contraceptives

#### Inger Sundström Poromaa, Cecilia Lundin, Lena Moby

Adverse mood symptom and sexual dysfunction are common complaints in oral contraceptive users, but no placebo-controlled trials have been performed in this area to establish drug-related causality. This multi-center, placebo-controlled oral contraceptive trial was started in 2013, and finalized in 2015. Participating sites include Uppsala, Stockholm, Linköping, Örebro, Göteborg and Umeå. Preliminary data suggest that oral contraceptive use is associated with significant worsening of a number of mood symptoms and sexual dysfunction. The first manuscript is being drafted.

# U-CAN Gynecologic cancer.

#### Karin Stålberg, Inger Sundström Poromaa, Kathrine Bjersand

The U-CAN project in Uppsala has continued to include gynecologic cancers, i.e. cervical, endometrial and ovarian cancer, with excellent coverage. Samples include tumor tissues at surgery and blood samples. Tissue samples are biobanked at the pathology unit according to U-CAN routines. Clinical data and patient information is stored as quality registry forms (both gynecologic and pathologic), together with information on family history, general and reproductive health. Karin Stålberg is chairman of the U-CAN gynecology research team. Thus far, the UCAN-Gyn has included more than 560 cases of gynecologic cancer, and the first research projects on this important scientific resource is underway.

# **Obesity in pregnancy**

# Inger Sundström Poromaa, Anna-Karin Wikström, Karin Eurenius, Ajlana Lutvica, Birgitta Segebladh, Eva Bergman.

The incidence of obesity is increasing at an alarming rate and this epidemic has also reached the pregnant population of developed countries. Today, obesity is, by far, the greatest challenge of obstetricians. The challenge for clinicians within the obstetric field is three-fold; first, obesity is associated with a number of *obstetric risks* that may have fatal or long-term consequences for both mother and offspring such as preeclampsia, preterm birth, intrauterine death, and congenital malformations. Secondly, while the risk of having an obstetric or perinatal complication due to obesity is as high as 30%, the majority of obese women will have uncomplicated, normal pregnancies and deliveries. Hence, maternity health care needs to improve the general risk assessment in order to identify those in need of surveillance and intervention. In this project we will develop risk scores for any obesity-related adverse outcome that may have repercussions for the short- and long-term morbidity of the mother and her infant. In doing so, we will adhere to the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity joint 2009 criteria for the metabolic syndrome. In short, we will make use of the well-recognized relationship of obesity to cardiovascular disease in the general population, and adopt the strategies for cardiovascular research to the obstetric field.

The research program is divided into four aims: 1/ Defining risk scores for obesity-related adverse outcomes based on information already collected in maternal health care. 2/ Defining risk scores for obesity-related adverse outcomes based on the addition of a waist circumference measurement at first antenatal booking. 3/ Defining risk scores for obesity-related adverse outcomes based on direct measures of subcutaneous and visceral fat at routine ultrasound assessment. 4/ Defining risk scores for obesity-related adverse outcomes by the addition of biochemical markers reflecting adipose tissue inflammation and endothelial dysfunction.

The project was started in January 2015, and data collection is expected to continue until 2017.

# International Child Health and Nutrition

#### Andreas Mårtensson

The research group International Child Health and Nutrition focuses on interventions for reduced neonatal mortality, global nutrition, improved childhood fever and malaria case management, health systems research, and implementation research, i.e. optimizing strategies to translate knowledge into sustainable clinical practice.

#### Members of the group during 2016

Almblad, Ann-Charlotte, Doctoral student Andersson, Ola, Researcher Balla, Elazar Tadelech Tadesse, Doctoral student Bergström, Anna, Researcher Berhane Hanna, Doctoral student Chopra, Mickey, Researcher Contreras, Mariela, Researcher Doherty, Tanya, Professor Duc, Duong, Doctoral student Cotter, Chris, Doctoral student KC, Ashish, Doctoral student Ekström, Eva-Charlotte, Professor Eneroth, Hanna, PhD, Nutritionist Eriksson, Leif, Lecturer Ewald, Uwe, Professor emeritus Henriksson, Dorcus Kiwanuka, Doctoral student Hofvander, Yngve, Professor emeritus Hoque, Waheedul, Doctoral student Inoue, Juliana, Post-doc researcher Ijumba, Petrida, Researcher Johansson, Emily White, Doctoral student Khan, Islam Ashraful, Researcher Kitutu Freddy, Doctoral student Källestål, Carina, Researcher, associate professor Linder, Nina, Researcher Lindström, Emma, Researcher Lynn Frith Amy, Guest researcher Moshfiqur Rahman Syed, Researcher Musafili, Aimable, Post doc researcher Målqvist, Mats, Researcher, associate professor Mårtensson, Andreas, Professor, Research group leader Nahar, Baitun, Doctoral student Nguyen Thu Nga, Researcher Pathak Ashish, Post doc researcher Pérez, Wilton, Researcher Pernilla Svefors, Doctoral student Persson, Lars-Åke, Senior Professor Peterson, Stefan Swartling, Professor Rahman, Anisur, Researcher Rana Nisha, Research assistant Selling, Katarina Ekholm, Researcher, associate professor Shaheen, Rubina, Doctoral student Sohel, Nazmul, Researcher Tadesse, Amare, Doctoral student Wrammert, Johan, Doctoral student Ziaei, Shirin, Doctoral student Åsling Monemi, Kajsa, Physician

#### Publications 2014-2016

## 2016

- Almblad, A., Målqvist, M., Engvall, G. Caring for the Acutely, Severely Ill Child-A Multifaceted Situation with Paradoxical Elements: Swedish Healthcare Professionals' Experiences. Journal of Pediatric Nursing 2016 Oct vol. 31; 31 (4): ss. E293-E300 <u>http://www.sciencedirect.com/science/article/pii/S0882596316300471</u>
- Andersson O. The transition to extra-uterine life by extremely preterm infants-handle with care. Acta Paediatrica. 2016 Apr 1;105(4):337-8. <u>http://onlinelibrary.wiley.com/doi/10.1111/apa.13261/full</u>
- Andersson O, Hellström-Westas L, Domellöf M. Elective caesarean: does delay in cord clamping for 30 s ensure sufficient iron stores at 4 months of age? A historical cohort control study. BMJ open. 2016 Nov 1;6(11):e012995. http://bmjopen.bmj.com/content/6/11/e012995.short
- Bergman M, Nygren-Brunell O, Vilakati D, Målqvist M. Prolonged Exclusive Breastfeeding Through Peer Support: A Cohort Study From a Community Outreach Project in Swaziland. Journal of community health. 2016 Oct 1;41(5):932-8. http://link.springer.com/article/10.1007/s10900-016-0173-y
- Bich TH, Hoa DT, Ha NT, Vui LT, Nghia DT, Målqvist M. Father's involvement and its effect on early breastfeeding practices in Viet Nam. Maternal & child nutrition. 2015 Aug 1. <u>http://onlinelibrary.wiley.com/doi/10.1111/mcn.12207/pdf</u>
- Blacklock C, Bradley DC, Mickan S, Willcox M, Roberts N, Bergström A, Mant D. Impact of contextual factors on the effect of interventions to improve health worker performance in sub-Saharan Africa: review of randomised clinical trials. PloS one. 2016 Jan 5;11(1):e0145206. <u>http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0145206</u>
- Contreras M, Zelaya Blandón E, Persson LÅ, Ekström EC. Consumption of highly processed snacks, sugar-sweetened beverages and child feeding practices in a rural area of Nicaragua. Maternal & child nutrition. 2016 Jan 1;12(1):164-76. <u>http://onlinelibrary.wiley.com/doi/10.1111/mcn.12144/full</u>
- Duc DM, Bergström A, Eriksson L, Selling K, Ha BT, Wallin L. Response process and testretest reliability of the Context Assessment for Community Health tool in Vietnam. Global health action. 2016;9. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4904068/</u>
- Ekström EC, Lindström E, Raqib R, El Arifeen S, Basu S, Brismar K, Selling K, Persson LÅ. Effects of prenatal micronutrient and early food supplementation on metabolic status of the offspring at 4.5 years of age. The MINIMat randomized trial in rural Bangladesh. International Journal of Epidemiology. 2016 Sep 30:dyw199. <u>https://academic.oup.com/ije/article/45/5/1656/2450931/Effects-of-prenatal-micronutrient-and-</u>

early-food

- Elfving K, Shakely D, Andersson M, Baltzell K, Ali AS, Bachelard M, Falk KI, Ljung A, Msellem MI, Omar RS, Parola P. Acute Uncomplicated Febrile Illness in Children Aged 2-59 months in Zanzibar–Aetiologies, Antibiotic Treatment and Outcome. PloS one. 2016 Jan 28;11(1):e0146054. <u>http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0146054</u>
- Eriksson L, Huy TQ, Duc DM, Selling KE, Hoa DP, Thuy NT, Nga NT, Persson LÅ, Wallin L. Process evaluation of a knowledge translation intervention using facilitation of local stakeholder groups to improve neonatal survival in the Quang Ninh province, Vietnam. Trials. 2016 Jan 13;17(1):23. <u>http://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-1141-z</u>
- 12. Johansson EW. Beyond 'test and treat'-malaria diagnosis for improved pediatric fever management in sub-Saharan Africa. Global Health Action. 2016;9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5165056/
- 13. Johansson EW, Kitutu FE, Mayora C, Awor P, Peterson SS, Wamani H, Hildenwall H. It could be viral but you don't know, you have not diagnosed it: health worker challenges in managing non-malaria paediatric fevers in the low transmission area of Mbarara District, Uganda. Malaria journal. 2016 Apr 11;15(1):197.

https://malariajournal.biomedcentral.com/articles/10.1186/s12936-016-1257-y

- Johansson EW, Selling KE, Nsona H, Mappin B, Gething PW, Petzold M, Peterson SS, Hildenwall H. Integrated paediatric fever management and antibiotic over-treatment in Malawi health facilities: data mining a national facility census. Malaria Journal. 2016 Aug 4;15(1):396. <u>https://malariajournal.biomedcentral.com/articles/10.1186/s12936-016-1439-7</u>
- 15. Juliano JJ, Parobek CM, Brazeau NF, Ngasala B, Randrianarivelojosia M, Lon C, Mwandagalirwa K, Tshefu A, Dhar R, Das BK, Hoffman I. Pooled amplicon deep sequencing of candidate *Plasmodium falciparum* transmission-blocking vaccine antigens. The American journal of tropical medicine and hygiene. 2016 Jan 6;94(1):143-6. <u>http://www.ajtmh.org/content/journals/10.4269/ajtmh.15-0571</u>
- Kaime-Atterhög W, Persson LÅ, Ahlberg BM. "With an open heart we receive the children": Caregivers' strategies for reaching and caring for street children in Kenya. Journal of Social Work. 2012:1468017316651989.

http://journals.sagepub.com/doi/abs/10.1177/1468017316651989

- Ashish KC, Målqvist M, Rana N, Ranneberg LJ, Andersson O. Effect of timing of umbilical cord clamping on anaemia at 8 and 12 months and later neurodevelopment in late pre-term and term infants; a facility-based, randomized-controlled trial in Nepal. BMC pediatrics. 2016 Mar 10;16(1):35. <u>https://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-016-0576-z</u>
- Ashish KC, Wrammert J, Clark RB, Ewald U, Målqvist M. Inadequate fetal heart rate monitoring and poor use of partogram associated with intrapartum stillbirth: a case-referent study in Nepal. BMC Pregnancy and Childbirth. 2016 Aug 19;16(1):233. https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-016-1034-5
- Ashish KC, Wrammert J, Clark RB, Ewald U, Vitrakoti R, Chaudhary P, Pun A, Raaijmakers H, Målqvist M. Reducing perinatal mortality in Nepal using Helping Babies Breathe. Pediatrics. 2016 May 25:e20150117.

http://pediatrics.aappublications.org/content/early/2016/05/23/peds.2015-0117

 Ashish KC, Wrammert J, Ewald U, Clark RB, Gautam J, Baral G, Baral KP, Målqvist M. Incidence of intrapartum stillbirth and associated risk factors in tertiary care setting of Nepal: a case-control study. Reproductive Health. 2016 Aug 31;13(1):103. <u>https://reproductive-health-journal.biomedcentral.com/articles/10.1186/s12978-016-0226-9</u>

- Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, Flenady V, Frøen JF, Qureshi ZU, Calderwood C, Shiekh S. Stillbirths: rates, risk factors, and acceleration towards 2030. The Lancet. 2016 Feb 12;387(10018):587-603. http://www.sciencedirect.com/science/article/pii/S0140673615008375
- 22. Lindstrand A, Kalyango J, Alfvén T, Darenberg J, Kadobera D, Bwanga F, Peterson S, Henriques-Normark B, Källander K. Pneumococcal Carriage in Children under Five Years in Uganda-Will Present Pneumococcal Conjugate Vaccines Be Appropriate?. PloS one. 2016 Nov 9;11(11):e0166018. <u>http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0166018</u>
- 23. Mideo N, Bailey JA, Hathaway NJ, Ngasala B, Saunders DL, Lon C, Kharabora O, Jamnik A, Balasubramanian S, Björkman A, Mårtensson A. A deep sequencing tool for partitioning clearance rates following antimalarial treatment in polyclonal infections. Evolution, medicine, and public health. 2016 Jan 1;2016(1):21-36. https://academic.oup.com/emph/article/2016/1/21/2802531/A-deep-sequencing-tool-for-partitioning-clearance
- 24. Mohammadi S, Essén B, Fallahian M, Taheripanah R, Saleh Gargari S, Källestål C. Maternal near-miss at university hospitals with cesarean overuse: an incident case-control study. Acta obstetricia et gynecologica Scandinavica. 2016 Jul 1;95(7):777-86. http://onlinelibrary.wiley.com/doi/10.1111/aogs.12881/full
- 25. Mwaiswelo R, Ngasala BE, Jovel I, Gosling R, Premji Z, Poirot E, Mmbando BP, Björkman A, Mårtensson A. Safety of a single low-dose of primaquine in addition to standard artemetherlumefantrine regimen for treatment of acute uncomplicated *Plasmodium falciparum* malaria in Tanzania. Malaria journal. 2016 Jun 10;15(1):316.

https://malariajournal.biomedcentral.com/articles/10.1186/s12936-016-1341-3

- 26. Mwaiswelo R, Ngasala B, Jovel I, Aydin-Schmidt B, Gosling R, Premji Z, Mmbando B, Björkman A, Mårtensson A. Adding a single low-dose of primaquine (0.25 mg/kg) to artemether-lumefantrine did not compromise treatment outcome of uncomplicated *Plasmodium falciparum* malaria in Tanzania: a randomized, single-blinded clinical trial. Malaria Journal. 2016 Aug 26;15(1):435. <u>https://malariajournal.biomedcentral.com/articles/10.1186/s12936-016-1430-3</u>
- 27. Målqvist M. Time to step up commitments to child survival and poverty reduction. Scandinavian Journal of Public Health 2016 Oct. 733-733. <u>http://journals.sagepub.com/doi/abs/10.1177/1403494816675713</u>
- Målqvist M, Clarke K, Matsebula T, Bergman M, Tomlinson M. Screening for Antepartum Depression Through Community Health Outreach in Swaziland. Journal of community health. 2016 Oct 1;41(5):946-52. <u>http://link.springer.com/article/10.1007/s10900-016-0175-9</u>
- 29. Nonyane BA, Ashish KC, Callaghan-Koru JA, Guenther T, Sitrin D, Syed U, Pradhan YV, Khadka N, Shah R, Baqui AH. Equity improvements in maternal and newborn care indicators: results from the Bardiya district of Nepal. Health policy and planning. 2015 Aug 24:czv077. <u>https://academic.oup.com/heapol/article/31/4/405/2363043/Equity-improvements-in-maternaland-newborn-care</u>
- Odaga J, Henriksson DK, Nkolo C, Tibeihaho H, Musabe R, Katusiime M, Sinabulya Z, Mucunguzi S, Mbonye AK, Valadez JJ. Empowering districts to target priorities for improving child health service in Uganda using change management and rapid assessment methods. Global health action. 2016;9. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4880621/</u>
- 31. Saulnier DD, Persson LÅ, Streatfield PK, Faruque AS, Rahman A. Using health and demographic surveillance for the early detection of cholera outbreaks: analysis of community-

and hospital-based data from Matlab, Bangladesh. Global health action. 2016;9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4871895/

- 32. Svefors P, Rahman A, Ekström EC, Khan AI, Lindström E, Persson LÅ, Selling KE. Stunted at 10 Years. Linear Growth Trajectories and Stunting from Birth to Pre-Adolescence in a Rural Bangladeshi Cohort. PloS one. 2016 Mar 2;11(3):e0149700. <u>http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0149700</u>
- 33. Tabernero P, Parker M, Ravinetto R, Phanouvong S, Yeung S, Kitutu FE, Cheah PY, Mayxay M, Guerin PJ, Newton PN. Ethical challenges in designing and conducting medicine quality surveys. Tropical medicine & international health. 2016 Jun 1;21(6):799-806. <u>http://onlinelibrary.wiley.com/doi/10.1111/tmi.12707/full</u>
- 34. Tadesse E, Ekström EC, Berhane Y. Challenges in implementing the integrated communitybased outpatient therapeutic program for severely malnourished children in rural southern Ethiopia. Nutrients. 2016 Apr 27;8(5):251. http://www.mdpi.com/2072-6643/8/5/251/html
- 35. Waiswa P, O'Connell T, Bagenda D, Mullachery P, Mpanga F, Henriksson DK, Katahoire AR, Ssegujja E, Mbonye AK, Peterson SS. Community and District Empowerment for Scale-up (CODES): a complex district-level management intervention to improve child survival in Uganda: study protocol for a randomized controlled trial. Trials. 2016 Mar 11;17(1):135. https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-016-1241-4
- 36. Ziaei S, Frith AL, Ekström EC, Naved RT. Experiencing lifetime domestic violence: associations with mental health and stress among pregnant women in rural Bangladesh: the MINIMat Randomized Trial. PLoS one. 2016 Dec 19;11(12):e0168103. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0168103
- 37. Ziaei S, Rahman A, Raqib R, Lönnerdal B, Ekström EC. A Prenatal Multiple Micronutrient Supplement Produces Higher Maternal Vitamin B-12 Concentrations and Similar Folate, Ferritin, and Zinc Concentrations as the Standard 60-mg Iron Plus 400-μg Folic Acid Supplement in Rural Bangladeshi Women. The Journal of Nutrition. 2016 Oct 19:jn235994. <u>http://jn.nutrition.org/content/early/2016/10/19/jn.116.235994.abstract</u>

#### 2015

- 1. Abdulla, S., Ashley, E., Bassat, Q., Bethell, D., Bjorkman, A. et al.(2015).Baseline data of parasite clearance in patients with falciparum malaria treated with an artemisinin derivative: an individual patient data meta-analysis. Malaria Journal, vol. 14.
- Adjuik, M., Allan, R., Anvikar, A., Ashley, E., Ba, M. et al.(2015). The effect of dosing strategies on the therapeutic efficacy of artesunate-amodiaquine for uncomplicated malaria: a meta-analysis of individual patient data. BMC Medicine, vol. 13
- 3. Awor, P., Wamani, H., Tylleskar, T., Peterson, S.(2015).Drug seller adherence to clinical protocols with integrated management of malaria, pneumonia and diarrhoea at drug shops in Uganda.Malaria Journal, vol. 14
- Baker, U., Peterson, S., Marchant, T., Mbaruku, G., Temu, S. et al.(2015).Identifying implementation bottlenecks for maternal and newborn health interventions in rural districts of the United Republic of Tanzania.Bulletin of the World Health Organization, vol. 93, ss. 380-389
- Bergström A, Skeens S, Duc DM, Blandon EZ, Estabrooks C, Gustavsson P, Hoa DT, Källestål C, Målqvist M, Nga NT, Persson LÅ, Pervin J, Peterson S, Rahman A, Selling K, Squires JE, Tomlinson M, Waiswa P, Wallin L. Health system context and implementation of evidencebased practices – development and validation of the Context Assessment for Community Health (COACH) tool for low- and middle-income settings. Implement Sci 2015 Aug 15;10:120. doi: 10.1186/s13012-015-0305-2.

- 6. Binder-Finnema, P., Lien, P., Hoa, D., Målqvist, M.(2015).Determinants of marginalization and inequitable maternal health care in North-Central Vietnam: a framework analysis.Global health action, vol. 8
- Contreras M., Blandón E.Z., Persson L-Å, Hjern A, Ekström E-C. Socio-economic resources, young child feeding practices, consumption of highly processed snacks and sugar-sweetened beverages: a population-based survey in rural northwestern Nicaragua. BMC Public Health (2015) 15:25. <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4308884/</u>
- 8. Duong, D., Bergström, A., Wallin, L., Bui, H., Eriksson, L. et al.(2015).Exploring the influence of context in a community-based facilitation intervention focusing on neonatal health and survival in Vietnam: a qualitative study.BMC Public Health, vol. 15
- 9. Eriksson, L., Wallin, L.(2015).Using facilitation to improve neonatal health and survival in Vietnam.I Gill Harvey, Alison Kitson (red.) Implementing Evidence-Based Practice in Healthcare, USA: Routledge. ss. 151-168
- 10. Forsén, E., Tadesse, E., Berhane, Y., Ekström, E.(2015).Predicted implications of using percentage weight gain as single discharge criterion in management of acute malnutrition in rural southern Ethiopia.Maternal and Child Nutrition, vol. 11, ss. 962-972
- 11. Frith, A., Naved, R., Persson, L., Frongillo, E.(2015).Early prenatal food supplementation ameliorates the negative association of maternal stress with birth size in a randomised trial.Maternal and Child Nutrition, vol. 11, ss. 537-549
- 12. Hesselman, S., Högberg, U., Ekholm Selling, K., Råssjö, E., Jonsson, M.(2015). The risk of uterine rupture is not increased with single- compared with double-layer closure: a Swedish cohort study. British Journal of Obstetrics and Gynecology, vol. 122, ss. 1535-1541
- 13. Ivarsson, A., Kinsman, J., Johansson, K., Mohamud, K., Weinehall, L. et al.(2015). Healing the health system after civil unrest. Global health action, vol. 8
- 14. Johansson, E., Gething, P., Hildenwall, H., Mappin, B., Petzold, M. et al.(2015).Effect of diagnostic testing on medicines used by febrile children less than five years in 12 malaria-endemic African countries: a mixed-methods study.Malaria Journal, vol. 14
- 15. Juliano JJ, Parobek CM, Brazeau NF, Ngasala B, Randrianarivelojosia M, Lon C, Mwandagalirwa K, Tshefu A, Dhar R, Das BK, Hoffman I, Martinson F, Mårtensson A, Saunders DL, Kumar N, Meshnick SR: Pooled Amplicon Deep Sequencing of Candidate Plasmodium falciparum Transmission-Blocking Vaccine Antigens. http://www.ncbi.nlm.nih.gov/pubmed/26503281
- 16. Katahoire Anne Ruhweza, Dorcus Kiwanuka Henriksson, corresponding author Eric Ssegujja, Peter Waiswa, Florence Ayebare, Danstan Bagenda, Anthony K. Mbonye, and Stefan Swartling Peterson: Improving child survival through a district management strengthening and community empowerment intervention: early implementation experiences from Uganda. <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4545317/</u>
- 17. KC Ashish, Johan Wrammert, Viktoria Nelin, Uwe Ewald, Robert Clark and Mats Målqvist: Level of mortality risk for babies born preterm or with a small weight for gestation in a tertiary hospital of Nepal. <u>http://www.biomedcentral.com/1471-2458/15/877</u>
- 18. KC, A., Nelin, V., Vitrakoti, R., Aryal, S., Målqvist, M.(2015). Validation of the foot length measure as an alternative tool to identify low birth weight and preterm babies in a low-resource setting like Nepal: a cross-sectional study.BMC Pediatrics, vol. 15
- 19. K.C, A., Nelin, V., Wrammert, J., Ewald, U., Vitrakoti, R. et al.(2015). Risk factors for antepartum stillbirth: a case-control study in Nepal.BMC Pregnancy and Childbirth, vol. 15
- Khan, A., Kabir, I., Hawkesworth, S., Ekström, E., Arifeen, S. et al. (2015). Early invitation to food and/or multiple micronutrient supplementation in pregnancy does not affect body composition in offspring at 54 months: follow-up of the MINIMat randomized trial, Bangladesh. Maternal and Child Nutrition, vol. 11, ss. 385-397
- Kiguli, J., Namusoko, S., Kerber, K., Peterson, S., Waiswa, P.(2015).Weeping in silence: community experiences of stillbirths in rural eastern Uganda.Global health action, vol. 8, ss. 24011-
- 22. Kozuki Naoko, Tanya Guenther, Lara Vaz, Allisyn Moran, Sajid B. Soofi, Christine Nalwadda Kayemba, Stefan S. Peterson, Zulfiqar A. Bhutta, Sudhir Khanal, James M. Tielsch, Tanya

Doherty, Duduzile Nsibande, Joy E. Lawn and Stephen Wall: A systematic review of community-to-facility neonatal referral completion rates in Africa and Asia. http://www.biomedcentral.com/1471-2458/15/989

- Leufvén M, Vitrakoti R, Bergström A, Ashish KC, Målqvist M. Dimensions of Learning Organizations Questionnaire (DLOQ) in a low-resource health care setting in Nepal. Health Research Policy and Systems 2015; 13:6 doi:10.1186/1478-4505-13-6. http://www.ncbi.nlm.nih.gov/pubmed/25608765
- Ljumba P, Doherty T, Jackson D, Tomlinson M, Sanders D, Swanevelder S, Persson L-Å. Effect of an integrated community-based package for maternal and newborn care on feeding patterns during the first 12 weeks of life: a cluster-randomized trial in a South African township. Public Health Nutrition. http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=9547966&fileId

http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=9547966&fileId=S 1368980015000099

- Lubega, M., Tumwesigye, N., Kadobera, D., Marrone, G., Wabwire-Mangen, F. et al.(2015).Effect of Community Support Agents on Retention of People Living With HIV in Pre-antiretroviral Care: A Randomized Controlled Trial in Eastern Uganda.Journal of Acquired Immune Deficiency Syndromes, vol. 70, ss. E36-E43
- 26. Contreras, Mariela. Child nutrition in rural Nicaragua: Population-based studies in a transitional society, 2015
- 27. Målqvist M. Abolishing inequity, a necessity for poverty reduction and the realization of child mortality targets. Arch Dis Child 2015;100(Suppl 1):s5-s9. http://www.ncbi.nlm.nih.gov/pubmed/25613969
- 28. Malqvist M. Linking Community with Primary Health Care through Peer Support in Swaziland. Primary Health Care 5:176 <u>http://dx.doi.org/10.4172/2167-1079.1000176</u>
- Målqvist Mats, Dinh Phuong Thi Hoa, Lars-Åke Persson, Katarina Ekholm Selling: Effect of Facilitation of Local Stakeholder Groups on Equity in Neonatal Survival; Results from the NeoKIP Trial in Northern Vietnam. PLoS One. 2015 Dec 29;10(12):e0145510. doi: 10.1371/journal.pone.0145510.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0145510

- Musafili A, Essén B, Baribwira C, Binagwaho A, Persson LÅ, Selling K. Trends and social differentials in child mortality in Rwanda 1990-2010: results from three demographic and health surveys. J Epidemiol Community Health 2015 Sep;69(9):834-40. doi: 10.1136/jech-2014-204657.
- 31. Musafili A, Essén B, Baribwira C, Selling KE, Persson LÅ. Social equity in perinatal survival: a case-control study at hospitals in Kigali, Rwanda. Acta Paediatr 2015 Dec;104(12):1233-40. doi: 10.1111/apa.12951.
- 32. Nahar, B., Hossain, I., Hamadani, J., Ahmed, T., Grantham-McGregor, S. et al.(2015).Effect of a food supplementation and psychosocial stimulation trial for severely malnourished children on the level of maternal depressive symptoms in Bangladesh.Child Care Health and Development, vol. 41, ss. 483-493
- 33. Nalwadda, C., Waiswa, P., Guwatudde, D., Kerber, K., Peterson, S. et al.(2015).'As soon as the umbilical cord gets off, the child ceases to be called a newborn': sociocultural beliefs and newborn referral in rural Uganda.Global health action, vol. 8, ss. 24386-
- Namazzi, G., Waiswa, P., Nakakeeto, M., Nakibuuka, V., Namutamba, S. et al.(2015).Strengthening health facilities for maternal and newborn care: experiences from rural eastern Uganda.Global health action, vol. 8, ss. 24271-
- 35. Nonyane B, Kc A, Callaghan-Koru JA, Guenther T, Sitrin D, Syed U, Pradhan YV, Khadka N, Shah R, Baqui AH: Equity improvements in maternal and newborn care indicators: results from the Bardiya district of Nepal. http://www.pabi.plm.pib.gov/pubmed/2term=Equity\_improvements\_in\_maternal\_and\_newbor

 $\label{eq:http://www.ncbi.nlm.nih.gov/pubmed/?term=Equity+improvements+in+maternal+and+newborn+care+indicators%3A+results+from+the+Bardiya+district+of+Nepal}$ 

 Omer-Salim, Amal. Mothers' Agency in Managing Breastfeeding and Other Work in Dar es Salaam, Tanzania and New Delhi, India, 2015

- Omer-Salim, A., Suri, S., Dadhich, J., Faridi, M., Olsson, P.(2015). 'Negotiating the tensions of having to attach and detach concurrently': A qualitative study on combining breastfeeding and employment in public education and health sectors in New Delhi, India.Midwifery, vol. 31, ss. 473-481
- Persson, L.(2015).Numbering the uncounted, focusing the unseen.Acta Paediatrica, vol. 104, ss. 1206-1207
- Pervin J, Gustafsson FE, Moran AC, Roy S, Persson LÅ, Rahman A. Implementing Kangaroo mother care in a resource-limited setting in rural Bangladesh. Acta Paediatr 2015 May;104(5):458-65. doi: 10.1111/apa.12929.
- 40. Puthoopparambil, S., Bjerneld, M., Källestål, C.(2015).Quality of life among immigrants in Swedish immigration detention centres: a cross-sectional questionnaire study.Global health action, vol. 8
- 41. Rutebemberwa E1, Mpeka B, Pariyo G, Peterson S, Mworozi E, Bwanga F, KäLlander K.: High prevalence of antibiotic resistance in nasopharyngeal bacterial isolates from healthy children in rural Uganda: A cross-sectional study. <u>http://www.ncbi.nlm.nih.gov/pubmed/26305429</u>
- 42. Rutebemberwa Elizeus, Betty Mpeka, George Pariyoc, Stefan Peterson, Edison Mworozi, Freddie Bwanga & Karin Källander: High prevalence of antibiotic resistance in nasopharyngeal bacterial isolates from healthy children in rural Uganda: A cross-sectional study. http://www.tandfonline.com/doi/full/10.3109/03009734.2015.1072606
- 43. Sewankambo N, Tumwine J, Tomson G, Obua C, Bwanga F, Waiswa P, Katabira E, Akuffo H, Persson K, Peterson S. Enabling Dynamic Partnerships through Joint Degrees between Lowand High-Income Countries for Capacity Development in Global Health Research: Experience from the Karolinska Institutet/Makerere University Partnership. PLOS Medicine http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001784
- 44. Shaheen R, Persson LÅ, Ahmend S, Streatfield PK, Lindholm L. Cost-effectiveness of invitation to food supplementation early in pregnancy combined with multiple micronutrients on infant survival: analysis of data from MINIMat randomized trial, Bangladesh. BMC Pregnancy Childbirth 2015 May 28;15:125. doi: 10.1186/s12884-015-0551-y.
- Skröder HM, Hamadani JD, Tofail F, Persson LÅ, Vahter ME, Kippler MJ. Selenium status in pregnancy influences children's cognitive function at 1.5 years of age. Clin Nutr 2015 Oct;34(5):923-30. doi: 10.1016/j.clnu.2014.09.020.
- 46. Tadesse, E., Berhane, Y., Hjern, A., Olsson, P., Ekström, E.(2015).Perceptions of usage and unintended consequences of provision of ready-to-use therapeutic food for management of severe acute child malnutrition: A qualitative study in Southern Ethiopia.Health Policy and Planning
- 47. Waiswa, P., Akuze, J., Peterson, S., Kerber, K., Tetui, M. et al.(2015).Differences in essential newborn care at birth between private and public health facilities in eastern Uganda.Global health action, vol. 8, ss. 24251-
- 48. Waiswa, P., Namazzi, G., Kerber, K., Peterson, S.(2015).Designing for action: adapting and implementing a community-based newborn care package to affect national change in Uganda.Global health action, vol. 8, ss. 24250-
- 49. Waiswa, P., Pariyo, G., Kallander, K., Akuze, J., Namazzi, G. et al.(2015).Effect of the Uganda Newborn Study on care-seeking and care practices: a cluster-randomised controlled trial.Global health action, vol. 8, ss. 24584-
- 50. Ziaei S, Contreras M, Selaya Blandón E, Persson LÅ, Hjern A, Ekström EC. Women's autonomy and social support and their associations with infant and young child feeding and nutritional status: community-based survey in rural Nicaragua. Public Health Nutr 2015 Aug;18(11):1979-90. doi: 10.1017/S1368980014002468.

#### 2014

1. Awor P, Miller J, Peterson S. Systematic literature review of integrated community case management and the private sector in Africa: Relevant experiences and potential next step. Journal of global health 2014; Vol 4, No. 2.

- 2. Ziaei S., Contreras M., Zelaya Blandón E., Persson L-Å, Hjern A., Ekström E-C. Women's autonomy and social support and their associations with infant and young child feeding and nutritional status: community-based survey in rural Nicaragua. Public Health Nutrition 2014, Nov 20:1-12 <u>http://www.ncbi.nlm.nih.gov/pubmed/25409706?report=abstract</u>
- Hawlander M., Ma E., Noguchi E., Itoh M, Arifeen S, Persson L-Å, Moore S, Raquib R, Wagatsuma Y. Ascaris lumbricoids Infection as a Risk Factor for Asthma ans Atopy in Rural Bangladeshi Children. Topical Medicine and Health Vol 42, No. 2, 2014, 77-85
- 4. Tancred T, Manu R, Hanson C, Okuyga M, Manzi F, Peterson S, Schellenberg J, Waiswa P, Marchant T and the EQUIP Study Team. How people-centred health systems can reach the grassroots: experiences implementing community-level quality improvement in rural Tanzania and Uganda. Health Policy and Planning 2014;1-13.
- 5. Hamadani J, Nahar B, Nazmul Huda S and Tofail F. Integrating early child development programs into health and nutrition services in Bangladesh: benefits and challenges. Ann. N.Y. Acad. Sci 1308 (2014) 192-203.
- 6. Wazny K, Sadruddin S, Zipursky A, Davidson H, Jacobs T, Kallander K, Pagnoni F, Peterson S, Qazi S, Raharison S, Ross K, Young M and Marsh D. Setting global research priorities for integrated community case management (iCCM): Results from a CHNRI (Child Health and Nutrition Research Initiative) exercise. Journal of Global Health 2014:Vol 4, No 2
- Sahoo KC, Sahoo S, Marrone G, Pathak A, Lundborg CS, Tamhankar Aj. Climatic Factors and Community – Associated Methicillin-Resistant Staphylococcus aureus Skin and Soft-Tissue Infections - A Time-Series Analysis Study. Int J Environ Res Public Health 2014, 11, 8966-9007. doi:<u>10.3390/ijerph110908996</u>
- Pathak A, Mårtensson A. Gawariker S, Mandliya J, Sharma A, Diwan V, Ursing J. Characterization of drug resistance associated genetic polymorphisms among Plasmodium falciparum field isolates in Ujjain, Madhya Oradesh, India. Malaria Journal 2014, 13:182. http://www.malariajournal.com/content/pdf/1475-2875-13-182.pdf
- Shakya O, Barrett P, Diwan V, Marothi Y, Shah H, Chhari N, Tamhankar AJ, Pathak A, Lundborg CS. Antibiotic resistance among Escherichia coli isolates from stool samples of children aged 3 to 14 years from Ujjain, India. BMC Infectious Deseases 2013, 13:477 http://www.biomedcentral.com/content/pdf/1471-2334-13-477.pdf
- 10. Pathak A, Saliba EA, Sharma S, Mahadik VK, Shah H, Lundberg CS. Incidence and factors associated with surgical site infections in a teaching hospital in Ujjain, American Journal of Infection Control 2014 42, e11-e15. <u>http://dx.doi.org/10.1016/j.ajic.2013.06.013</u>
- 11. Rathi M, Rathi SK, Purohit M, Pathak A. Couvelaire uterus. BMJ Case Rep 2014.
- Yuan B, Målqvist M, Trygg N, Qian X, Ng N, Thomsen S. What interventions are effective on reducing inequalities in maternal and child health in low- and middle-income settings? A systematic review. BMC Public Health 2014, 14:634. http://www.biomedcentral.com/content/pdf/1471-2458-14-634.pdf
- Lindbäck C, KC A, Wrammert J, Vitrakoti R, Ewald U, Målqvist M. Poor adherence to neonatal resuscitation guidelines exposed; an observational study using camera surveillance at a tertiary hospital in Nepal. BMC Pediatrics 2014, 14:233. http://www.biomedcentral.com/content/pdf/1471-2431-14-233.pdf
- Kitutu F, Mayora C, Awor P, Forsberg B, Peterson S, Wamani H. Inclusion of private sector in district health systems; case study of private drug shops iomplementing modified Integrated Community Case Management (iCCM) strategy in Rural Uganda. Poster Presentation, BMC Health Services Research 2014, 14 (suppl 2):P65.
- Nalwadda CK, Peterson S, Tomson G, Guwatudde D, Kiguli J, Namazzi G, Namutamba S, Namugaya F, Nambuya H, Tagoola A, Waiswa P. Health system preparedness for newborn care: a health facility assessment in rural Uganda. Poster Presentation, BMC Health Services Research 2014, 14(Suppl 2):P63.
- 16. Marchant T, Schellenberg J, Peterson S, Manzi F, Waiswa P, Hanson C, Temu S, Darious K, Sedekia Y, Akuze J, Rowe A. The use of continuous surveys to generate and continuously report high quality timely maternal and newborn health data at the district level in Tanzania and Uganda. Implementation Science 2014, 9:112 doi:10.1186/s13012-014.0112-1.

- 17. Hesselman S, Högberg U, Ekholm-Selling K, Råssjö E-B, Jonsson M. The risk of uterine rupture is not increased with single- compared with double-layer closure: a Swedish cohort study. <u>BJOG</u>. 2014 Aug 4. doi: 10.1111/1471-0528.13015. [Epub ahead of print].
- Doherty T, Jackson D, Swanevelder S, Lombard C, Engebretsen IMS, Tylleskär T, Goga A, Ekström E-C, Sanders D. Severe events in the first 6 months of life in a cohort of HIVunexposed infants from South Africa: effects of low birthweight and breastfeeding status. Trop Med Int Health. 2014 Jul 23. doi: 10.1111/tmi.12355. [Epub ahead of print].
- Engebretsen IMS, Jackson D, Fadnes LT, Nankabirwa V, Diallo AH, Doherty T, Lombard C, Swanvelder S, Nankunda J, Ramokolo V, Sanders D, Wamani H, Meda N, Tumwine JK, Ekström E-C, Van de Perre P, Kankassa C, Sommerfelt H, Tylleskär T. Growth effects of exclusive breastfeeding promotion by peer counsellors in sub-Saharan Africa: the clusterrandomised PROMISE EBF trial. BMC Public Health 2014, 14:633. http://www.biomedcentral.com/content/pdf/1471-2458-14-633.pdf
- 20. Rydbeck F, Rahman A, Grandér M, Ekström E-C, Vahter M, Kippler M. Maternal Urinary Iodine Concentration up to 1.0 mg/L Is Positively Associated with Birth Weight, Length, and Head Circumference of Male Offspring.
- Nahar B, Hossain I, Hamadani JD, Ahmed T, Grantham-McGregor S, Persson L\_A. Effect of a food supplementation and psychosocial stimulation trial for severely malnourished children on the level of maternal depressive symptoms in Bangladesh. <u>Child Care Health Dev.</u> 2014 Jul 4. doi: 10.1111/cch.12176. [Epub ahead of print].
- 22. Contreras M, Zelaya BE, Persson L-Å, Ekström E-C. Consumption of highly processed snacks, sugar-sweetened beverages and child feeding practices in a rural area of Nicaragua. <u>Matern</u> <u>Child Nutr.</u> 2014 Aug 19. doi: 10.1111/mcn.12144. [Epub ahead of print]
- 23. Yan B, Målqvist M, Trygg N, Qian X, Ng N, Thomsen S. What interventions are effective on reducing inequalities in maternal and child health in low- and middle-income settings? A systematic review. BMC Public Health 2014;14:634.
- 24. Eriksson, Leif. Strategi för förbättrad vård av nyfödda barn i Vietnam (in Swedish). Chapter 11 in the book "Implementering av evidensbaserad praktik". Glerup Utbildning AB, 2014, Per Nilsen (red.) ISBN 978-91-40-68447-9
- 25. Hanson C, Waiswa P, Marchant T, Marx M, Manzi F, Mbaruku G, Rowe A, Tomson G, Schellenberg J, Peterson S, Jaribu J, Sedekia Y, Arafumin P, Temu S, Okuga M, Kajjo D, Manu R, Akuze J, Balidawa H, Baker U, Tancred T. Expanded Quality Management Using Information Power (EQUIP): protocol for a quasi-experimental study to improve maternal and newborn health in Tanzania and Uganda (E-pub ahead of print).
- 26. Heyman G, Cares O, Bejarano MT, Peterson S. Access, excess, and ethics towards a sustainable distribution model for antibiotics. Ups J Med Sci 2014; Early Online.
- 27. Storberg V. ESBL-producing *Enterobacteriaceae* in Africa a non-systematic literature review of research published 2008-2012. Infect Ecol Epidemiol 2014, 4: 20342 http://dx.doi.org/10.3402/iee.v4.20342
- Moore SE, Fulford AJC, Wagatsuma Y, Persson LÅ, Arifeen SE, Prentice AM. Thymus development and infant and child mortality in Rural Bangladesh. Int J Epidemiol 2014;43:216-223. <u>http://ije.oxfordjournals.org/content/43/1/216.full.pdf+html</u>
- 29. Tomlinson M, Doherty T, Ijumba P, Jackson D. Lawn J, Persson LÅ, Lombard C, Sanders D, Daviaud E, Nkonki L, Goga A, Rohde S, Sitrin D, Colvin M, Chopra M. Goodstart: a cluster randomised effectiveness trial of an integrated, community-based package for maternal and newborn care, with prevention of mother-to-child transmission of HIV in a South African township. Trop Med Int Health 2014 Jan 17. (Epub ahead of print). http://onlinelibrary.wiley.com/doi/10.1111/tmi.12257/pdf
- Bengtsson N, Peterson S, Sävje F. Revisiting the Educational Effects of Fetal Iodine Deficiency. Working Papers, Uppsala Center for Labor Studies 2013:13. <u>http://www.ucls.nek.uu.se/digitalAssets/199/199882\_201313.pdf</u>
- 31. Mayega RW, Guwatudde D, Makumbi FE, Nakwagala FN, Peterson S, Tomson G, Östenson CG. Comparison of fasting plasma glucose and haemoglobin A1c point-of-care tests in screening for diabetes and abnormal glucose regulation in a rural low income setting. Diabetes

Res Clin Pract. 2014 Jan 3. pii: S0168-8227(13)00464-6. doi: 10.1016/j.diabres.2013.12.030. (Epub ahead of print). <u>http://www.sciencedirect.com/science/article/pii/S0168822713004646#</u>

- 32. Perez W, Eriksson L, Zelaya EB, Persson LÅ, Källestål C, Peña R. Comparing progress toward the millennium development goal for under-five mortality in Leon and Cuatro Santos, Nicaragua, 1990-2008. BMC Pediatr. 2014 Jan 15;14(1):9 <u>http://www.biomedcentral.com/content/pdf/1471-2431-14-9.pdf</u>
- 33. Shaheen R, Streatfield PK, Naved RT, Lindholm L, Persson LÅ. Equity in adherence to and effect of prenatal food and micronutrient supplementation on child mortality: results from the MINIMat randomized trial, Bangladesh. BMC Public Health. 2014 Jan 7;14(1):5. (Epub ahead of print). <u>http://www.biomedcentral.com/content/pdf/1471-2458-14-5.pdf</u>
- 34. Johansson EW, Gething PW, Hildenwall H, Mapping B, Petzold M, Peterson SS, Selling KE. Diagnostic Testing of Pediatric Fevers: Meta-Analysis of 13 National Surveys Assessing Influences of Malaria Endemicity and Source of Care on Test Uptake for Febrile Children under Five Years. PLoS One 2014 Apr 18;9(4):e95483.

#### **Dissertations 2016**

- 1. Ashish KC: Neonatal Resuscitation: Understanding challenges and identifying a strategy for implementation in Nepal.
- 2. Elazar Tadesse: Integrated community-based management of severe acute child malnutrition: Studies from rural Southern Ethiopia.
- 3. Emily White Johansson: Beyond "test and treat": Malaria diagnosis for improved pediatric fever management in sub-Saharan Africa.
- Shirin Ziaei: Women's status and child nutrition: Findings from community studies in Bangladesh and Nicaragua.

#### Agencies that support the work/Funding

ALF 2 323 663 VR 3 876 708 Formas 2 000 000 Forte 995 000 KI 534 969 STINT 375 000 EU 386 155 Gillbergska 40 000 HKH Kronprinsessan Lovisas förening för barnsjukvård/Stift A Tielmans minnesfond 40 000

# Improving neonatal health and survival

# Mats Målqvist, Ashish KC, Nisha Rana, Ola Andersson, Anna Bergström, Leif Eriksson, Johan Wrammert, Uwe Ewald, Lars Åke Persson

#### **NeoKIP**

#### Lars Åke Persson (PI), Mats Målqvist, Anna Bergström, Leif Eriksson, Uwe Ewald

A persistent problem in many countries is a high neonatal mortality, and inequity in neonatal survival chances. This has been addressed in a collaborative project in the Quang Ninh province in

Vietnam, where a community-based cluster randomized trial has tested a facilitation approach for improved neonatal health and survival; the NeoKIP trial, Neonatal health Knowledge Into Practice, trial registration number ISRCTN44599712. Local stakeholder groups employed a Plan-Do-Study-Act method to identify local perinatal health problems and act accordingly. The main outcome of the trial was a reduction in neonatal mortality by half in the intervention clusters In 2014 we conducted a follow-up of the NeoKIP trial, three years after its completion, and found that the low level of neonatal mortality in the intervention clusters was sustained. During the year a pilot study for scale up in Cao Bang province of the intervention at commune level in combination with a facilitated participatory approach at district hospitals has been performed

#### NepCord

#### Ola Andersson (PI), Mats Målqvist, Ashish KC, Nisha Rana

In Nepal there is an on-going research collaboration focusing on interventions during the neonatal period. During the year a trial investigating the effects of timing of cord clamping on heart rate in the newborn has been performed (NepCord 2 and 3). More than 1500 newborns have been included in the study. In parallel, a randomized controlled study including neonates in need of resuscitation has been completed, where one group received the standard resuscitation performed at a resuscitation table, separated from the mother, and one group received resuscitation with the umbilical cord still intact. Analysis of data is under way. Results from NepCord 1, a randomized controlled trial on the evaluation of delayed versus early cord clamping and its effects on the prevalence of anemia when the newborn has reached the age of eight to twelve months was published in JAMA Pediatrics early 2017. A total of 540 live births were included in the trial and a significant reduction of anemia at 8 and 12 months of age could be seen in the group with delayed cord clamping. Further analyses of bilirubin levels and neurodevelopment at 12 and 24 months are under way.

#### Helping Babies Breathe – Quality Improvement Cycle (HBB-QIC) in Nepal

# Mats Målqvist (PI), Ashish KC (PI/Nepal), Anna Bergström, Leif Eriksson, Johan Wrammert, Uwe Ewald

Previous trials within the research collaboration with Nepal have included an evaluation of Helping Babies Breathe (HBB) coupled to a quality improvement approach (QIC). The trial demonstrated a substantial reduction of intra-partum stillbirths and first day mortality after introduction on HBB-QIC at a tertiary hospital in Kathmandu. Results were published in Pediatrics in June 2016. Ashish KC defended his PhD thesis based in study findings in February 2016. Currently plans for a scale-up of the intervention is under way and together with the Ministry of Health and UNICEF an intervention package for improved quality of maternal and newborn care will be delivered to 12 public hospitals in Nepal.

# Community Kangaroo Mother Care (C-KMC) in Uganda

#### Mats Målqvist (PI), Anna Bergström, Leif Eriksson

In Uganda initial data collection on Kangaroo Mother Care (KMC) practices at district hospital level has been initiated in collaboration with Makerere University Centre of Excellence for Maternal and Newborn Health. This baseline survey will form the foundation for a project to develop a community KMC intervention

# **Global Nutrition**

Eva-Charlotte Ekström, Katarina Selling, Shirin Ziaiei, Pernilla Svefors, Lars Åke Persson, Hanna Yemane Berhane, Elazar Tadesse, Amare Worku, Jill Trenholm, Amy Frith, Kajsa Åsling, Moshfiqur Rahman

# Developmental origin of health and disease: MINIMat prenatal nutrition intervention trial rural Bangladesh

## Eva-Charlotte Ekström (PI), Katarina Selling, Shirin Ziaiei, Lars Åke Persson, Amy Frith, Moshfiqur Rahman

In an extensive prenatal nutrition intervention trial in Matlab, Bangladesh, effects of food and micronutrient supplements are investigated in a short- and long-term perspective. In this project, that has got the acronym MINIMat (Maternal and Infant Nutrition Interventions in Matlab, trial registration number ISRCTN16581394). So far, the trial and its cohort of women and children have generated more than 100 publications (http://www.kbh.uu.se/digitalAssets/96/c\_96956-1\_1k\_170215-bibliography-minimat-feb-15-2017.pdf). We have shown that food supplementation early in pregnancy combined with multiple micronutrient supplementation substantially improves survival of the offspring. We have also evaluated research questions related to the DOHaD hypotheses (Developmental Origin of Health and Disease) by studying the impact of the interventions on child growth, body composition, metabolic markers at 4.5 and 10 years and oxidative stress in pregnancy and birth weight. An ongoing add-on study evaluates the trans-generational effects of poor nutrition in fetal life. The publications from MINIMat also include micronutrient status in pregnancy and infancy, risk factors for infant anemia, breastfeeding and micronutrient status, maternal-infant interaction, household food security and child growth and development, morbidity and psychomotor development, and violence against women and child growth and morbidity. Results from the 10years follow-up of these children have been published. The data collection for the 15-years followup is scheduled to start in September 2017 where the intention is to capture the influence of three dimensions of the Sustainable Development Goals; environment, economic and social influence on the children's health and development at 15 years. A key component in this follow-up is assessment of physical activity and strength. The key collaborative institution in this project is icddr,b in Bangladesh, but we also collaborate with Karolinska Institutet, Tsukuba University, Japan, Ithaca College, USA, the National Institute of Health and Welfare, Finland. The Swedish Research Council and Sida have, among others, provided funding over the years.

# EAT Addis, Women, children and the food environment in Addis Ababa, Ethiopia

#### Eva-Charlotte Ekström (PI), Katarina Selling, Jill Trenholm

Food and nutrition security is a cornerstone for achieving global sustainable development. In Africa's rapidly growing cities, unemployment and widespread poverty currently leads to high levels of food and nutrition insecurity for a large share of the population. Undernutrition as well as overnutrition cause health related problems affecting individuals and society at large. In spite of these pressing challenges, the factors influencing the access to and consumption of food among urban people in low-income countries, remain insufficiently studied and understood. In the research project EAT Addis we aim to evaluate the social, economic and gender stratification of household food security and their accessibility to safe and nutritious foods with a particular focus on young children. The influence of the urban food environment and its seasonal dynamic will be evaluated as well as the role of women empowerment in their role as gatekeeper between the food environment and the family. The first round of data collection is scheduled for July 2017. The study is funded by Swedish Research Council and FORMAS.

#### Community based management of severe undernutrition

#### Eva-Charlotte Ekström (PI), Elazar Tadesse

Effective nutrition interventions exist to prevent and manage mother and child malnutrition. Scaling up of such interventions is less successful and influenced by the context where it is implemented. This study was done within Ethiopia's community-based program for management of severe acute malnourished children. The study was done within a nationally scaled up nutrition program. It analyses the influence of women's empowerment on the outcome of rehabilitation of their severely malnourished children as well as the importance of the quality of the program. One of the PhD students defended her thesis in 2016 and the results from the study have been reported in a number of scientific publications as well as conferences. Swedish Agency for Research Cooperation (SAREC), and Uppsala University have supported these studies.

## Gender-based violence and child nutrition

#### Eva-Charlotte Ekström (PI), Shirin Ziaiei, Lars Åke Persson, Amy Frith, Kajsa Åsling

The health consequences – also for children – of violence against women (VAW) have been studied in a series of studies. We have earlier shown an association between VAW and child mortality, size at birth, child growth and morbidity. More recently papers have been published on association with breastfeeding practices and maternal mental health and stress. The Swedish Research Council and Sida have, among others, provided funding.

#### Betel chewing in pregnancy, Bangladesh

#### Eva-Charlotte Ekström (PI), Moshfiqur Rahman

Betel chewing is prevalent in Asia including among women in pregnancy. Betel is known as carcinogenic but little is known about health risks for mother and fetus. Studies suggest that health risks are similar to that of undernourishment in early life; adverse pregnancy outcome, poor fetal and infant growth and increased risk for metabolic syndrome in adulthood. Thus if poor nutrition and betel chewing are combined synergetic affects are plausible. Set in a rural Bangladesh our aim of this project is to evaluate the health consequences for mother and offspring of betel chewing. Two years of data collection is to be completed during 2017. The project is funded by Swedish Research Council.

# Improved childhood fever and malaria case management

# Stefan Peterson, Katarina Selling, Emily White Johansson, Freddy Kitutu, Nina Linder, Juliana Inoue, Chris Cotter, Andreas Mårtensson

#### Malaria rapid diagnostic testing

#### Stefan Peterson (PI), Katarina Selling, Emily White Johansson, Freddy Kitutu

In 2010, the World Health Organization revised malaria treatment guidelines to recommend diagnostic testing of all suspected malaria cases prior to treatment. Recent studies, however, suggest that the full potential of malaria rapid diagnostic tests (mRDT) are not being achieved given poor adherence to test results by health workers in areas of intense malaria transmission. Emily White Johansson (PhD 2016), using a national health facility census in Malawi, demonstrated that singular use of mRDTs, in the absence of other diagnostic tests and alternative appropriate treatment guidance, leads to irrational use of Antibiotics, when mRDTs are negative. Integrated testing and treatment strategies are required, such as Integrated Management of Childhood Illness strategy addressing the febrile child for a range of disorders, rather than singular malaria management.

#### Integrated fever case management in private drug shops in Uganda

# Stefan Peterson (PI), Katarina Selling, Emily White Johansson, Freddy Kitutu, Andreas Mårtensson

Together with Makerere University and other collaborators, we are conducting studies to increase coverage and penetration of the integrated community case management (iCCM) intervention for febrile children in rural areas in Uganda. Our studies have shown improvement in the quality of diagnosis and management of febrile children and findings have contributed to changing the policy on community case management of malaria, pneumonia, and diarrhoea at national level, in UNICEF, WHO and Global Fund. Currently, together with collaborators in Uganda, we are evaluating how to embed the iCCM intervention in the existing health systems and scale it up while applying real-world supervision models and medicine supply chains. In addition, we have proposed to develop and implement a franchise model for the drug shops implementing iCCM intervention and management of moderate malnutrition.

# Is it possible to eliminate malaria in Zanzibar?

#### Andreas Mårtensson (PI), Chris Cotter

We are involved in a multidisciplinary research project studying whether malaria elimination is possible in Zanzibar, a previously high endemic area, as a case study for sub-Saharan Africa. The background to the project is that Zanzibar has been able to reduce the burden of malaria significantly following combined modern malaria control interventions, i.e. artemsinin based combination therapies, mRDTs, long lasting insecticidal treated nets and indoor residual spraying. This project, which is a joint venture between the Zanzibar Malaria Elimination Programme, Karolinska Institutet, the Presidents Malaria Initiative (PMI)/Centers for Disease Control and Prevention (CDC), London School of Hygiene and Tropical Medicine and Uppsala University, is assessing temporal and spatial trends of various malariometric indicies by triangulating data from community-based cross-sectional surveys, health facility data and vital statistics. The role of molecular based malaria diagnostic tools,

such as PCR and loop-mediated isothermal amplification (LAMP), to assist malaria elimination efforts and to improve the understanding of molecular epidemiology is also studied. Following the decline of malaria burden in Zanzibar, we have been involved in fever etiology studies to get a better understanding of the nature of uncomplicated childhood fevers in the new context of very low malaria transmission, and based on this how fever case management potentially can be improved in primary health care facilities.

# Sida bilateral research collaboration Tanzania - Malaria

#### Andreas Mårtensson (PI), Nina Linder, Juliana Inoue

In a Sida sponsored bilateral malaria research project between Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, and Swedish partners we are involved in studies aiming to improve malaria case management, assessment of antimalarial drug resistance and the diagnostic accuracy of new point-of care diagnostic tools in Tanzania. A special focus in the project is on potential evolution and spread of artemisinin and long acting partner drug tolerance/resistance in artemisinin-based combination therapies, which we assess using both standard in vivo studies and molecular surveillance of antimalarial drug resistance of *Plasmodium falciparum*.

# Health systems research

Mats Målqvist, Anna Bergström, Ann-Charlotte Almblad, Ali Saidi, Dorcus Kiwanuka Henriksson, Stefan Peterson, Meena Davidsson, Carina Källestål, Wilton Perez, Eva-Charlotte Ekström, Mariela Contreras, Lars Åke Persson, Katarina Selling

# Pediatric Early Warning Score (PEWS)

#### Mats Målqvist (PI), Ann-Charlotte Almblad

Recognition of danger signs and deteriorated state of admitted patients is vital to prevent adverse event and improve survival chances. At the University Pediatric Hospital in Uppsala, Sweden, an evaluation of a Pediatric Early Warning System (PEWS) has been completed. This simple tool has shown promising results in reducing admittance to intensive care unit and reducing time to initiation of adequate treatment. Trial results are expected to be published in 2017.

# Sida bilateral research collaboration Tanzania – Health systems and reproductive health

#### Mats Målqvist (PI), Ali Saidi, Stefan Peterson

In Tanzania, there is a bilateral Sida financed research collaboration with Muhimbili University of Health and Allied Sciences (MUHAS). The reproductive health group of the collaboration has a health systems focus and has enrolled 5 PhD students and 3 Master's students. Research projects include evaluating Audit and Feedback mechanisms within the health system, performing policy analysis and trying new methods of group antenatal care.

# Community and District Empowerment for Scale up (CODES)

#### Stefan Peterson (PI), Dorcus Kiwanuka Henriksson

In Uganda, evidence-based district planning is the focus for the UNICEF-Gates funded study CODES – Community and District Empowerment for Scale up. Focusing on child health and child health care this study set in Uganda is a randomized controlled trial of a governance intervention on coverage of essential child health services.

# **Essential Quality Improvement Using Information Power (EQUIP)**

#### Stefan Peterson (PI), Dorcus Kiwanuka Henriksson

An EU-funded project EQUIP – essential quality improvement using information power – has been completed in Uganda and Tanzania. It demonstrated the capacity of quality improvement to improve facility level care, but also that community level dialogue with expecting parents can increase care seeking for delivery care beyond what the health facilities can meet. In a pilot study funded by the Einhorn Family Foundation we are now pursuing quality improvement at hospital level, and IDRC has funded an EQUIP scale-up in Tanzania with 1 million dollars.

# Self Management of Diabetes mellitus type 2 (SMART2D)

#### Stefan Peterson (PI)

A study of health system aspects of the rapidly increasing diabetes prevalence in low- and middleincome countries was funded by EU Horizon 2020. Entitled SMART2D – self management and reciprocal learning for type 2 diabetes management – the study will run over the next four years with partners in South Africa, Uganda, Belgium, Finland and Sweden.

#### Community development work and health effects

## Carina Källestål (PI), Wilton Perez, Eva-Charlotte Ekström, Mariela Contreras, Lars Åke Persson, Katarina Selling

In a post-war frontier area in north-western Nicaragua that was severely hit by the hurricane Mitch in 1998 local stakeholders embarked on multidimensional initiatives to break the cycles of poverty. A series of studies have analyzed poverty reduction and different health outcomes in the area, based on a Health and Demographic Surveillance System that was initiated in 2004. The achievements and lessons learned from the Cuatro Santos initiative underlines the importance of a bottom-up approach and local ownership of the development process, the importance of collection of local data for monitoring and evaluation, and the importance of multi-dimensional local interventions to break the cycles of poverty and gain better health and welfare. We are now embarking on an equity analysis using data mining methods.

# Implementation research

#### Anna Bergström, Leif Eriksson, Mats Målqvist, Lars-Åke Persson

Researchers at IMCH have an interest to advance the field of implementation research. Since 2014 a 5 credit Master/PhD-level course in Implementation Science in Global Health is offered.

# Context Assessment for Community Health (COACH) project

#### Anna Bergström (PI), Mats Målqvist, Lars-Åke Persson

The COACH project initially aimed to develop a tool that focused on modifiable aspects of local health care context in low- and middle-income settings, i.e. aspects of context that could be intervened upon to enhance health system strengthening. The development of the COACH tool was undertaken with partners in Bangladesh, Vietnam, Uganda, South Africa and Nicaragua. The application and continued psychometric evaluation of the COACH tool (© Bergström and Estabrooks 2015) is still ongoing.

<u>Collaborators (during the development to the tool)</u>: ICDDR,B (Bangladesh), Hanoi University of Public Health (Vietnam), Makerere University College of Health Sciences (Uganda), Stellenbosch University (South Africa), Fundacion Coordinación de Hermanamientos e Iniciativas de Cooperación (Nicaragua), University of Alberta (Canada) and Dalarna University (Sweden). The tool is currently being used in Vietnam and Mozambique. Weblink: http://www.kbh.uu.se/imch/coach

# Perinatal Knowledge Into Practice (PeriKIP) project

#### Anna Bergström (PI), Leif Eriksson, Lars-Åke Persson

Similar to other community-based initiatives, the research groups behind the NeoKIP (below) identified the need to implement processes aimed to improve quality of care also at higher levels of the health system. This PeriKIP project thus responds to the need of a community and health facility intervention with the potential of health system integration for sustained effects. This project aims to investigate the feasibility of implementing facilitated local stakeholder groups applying the same methodology as that previously tested in NeoKIP but implementing it on commune, district and provincial level.

<u>Collaborators:</u> Research Institute for Child Health at the Vietnam National Children's Hospital (Vietnam), Cao Bang Provincial Health Bureau (Vietnam).

# Reorientation of the Health System towards Primary Diabetes Care in Sudan

#### Mats Målqvist (PI), Anna Bergström, Abubakr Mohamed

In 2015, 415 million individuals were living with diabetes, 75% of them in low- and middle-income countries. Estimates suggest that the burden of diabetes will increase to 642 million by 2040. The majority of health systems in low resources settings are organized for the treatment of acute rather than chronic conditions and face an immense challenge to tackle an increasing number of patients

with life-long conditions. Diabetes educators has been a successful strategy adopted in several highincome countries and has been put forward as the most cost-effective intervention for low- and middle-income countries. The project aim to investigate diabetes care in Sudan and to evaluate the effect of diabetes educators in governmental primary health care centers in Khartoum towards quality and efficiency of diabetes care.

<u>Collaborators:</u> Ahfad University for Women (Sudan) and Diabetes Prevention Promotion Organization (Sudan).

## International Maternal and Reproductive Health and Migration

## Birgitta Essén

More than a third of the ill-health in women is related to their reproduction. Research must address both individual and structural factors contributing to these health problems, as well as the health interventions and programs that can be effective to alleviate the suffering, both in low- and high-income countries.

The research is approached in an interdisciplinary way involving gynaecological and obstetrical issues, nursing, and epidemiology with public health aspects. These also include political, legal, social, and cultural aspects of medicine as well as theoretical frameworks in social anthropology.

#### Members of the group during 2016

Arousell, Jonna, Doctoral student Arvidsson, Anna, Doctoral student August, Furaha, PhD, MD Axemo, Pia, associate professor, MD Binder Finnema, Pauline, PhD, Researcher Bjerneld, Magdalena, PhD, Guest researcher Byrskog, Ulrika, PhD, post doc Darj, Elisabeth, Guest professor Essén, Birgitta, Professor, Research group leader Kaime Atterhög, Wanjiku, PhD, Researcher Klingberg-Allvin, Marie, Senior lecturer Larsson, Camilla, Doctoral student Larsson, Elin, PhD, Post doc Lesio Kidanto, Hussein, PhD, MD, Researcher Lindmark, Gunilla, Professor emeritus Litorp, Helena, PhD, MD Maina Ahlberg, Beth, adjunct Professor Mgava, Andrew, Doctoral student Mohammadi, Soheila, PhD, MD Muganyizi Abeid, Muzdalifat, PhD, MD Muganyizi, Projestine, MD PhD Nor, Barni, PhD Paul, Mandira, PhD, Researcher Pembe, Andrea, PhD, MD, Researcher Puthoopparambil, Soorej Jose, PhD Post doc Påfs, Jessica, PhD Rööst, Mattias PhD, MD Trenholm, Jill, PhD, Researcher Ugarte Guevara, William José, PhD, MD, Researcher Wahlberg, Anna, Doctoral student

#### Publications 2014-2016

#### 2016

 Abeid M, Muganyizi P, Mpembeni R, Darj E, Axemo P. Evaluation of a training program for health care workers to improve the quality of care for rape survivors: a quasi-experimental design study in Morogoro, Tanzania. Global health action. 2016;9. http://www.globalhealthaction.net/index.php/gha/article/view/31735

- Adolphson K, Axemo P, Högberg U. Midwives' experiences of working conditions, perceptions of professional role and attitudes towards mothers in Mozambique. Midwifery. 2016 Sep 30;40:95-101. <u>http://www.sciencedirect.com/science/article/pii/S0266613816301012</u>
- Ahlberg BM, Maina F, Kubai A, Khamasi W, Ekman M, Lundqvist-Persson C. "A child, a tree": Challenges in building collaborative relations in a community research project in a Kenyan context. Action Research. 2016 Sep;14(3):257-75. http://journals.sagepub.com/doi/abs/10.1177/1476750315607607
- Arousell J, Carlbom A. Culture and religious beliefs in relation to reproductive health. Best Practice & Research Clinical Obstetrics & Gynaecology. 2016 Apr 30;32:77-87. <u>http://www.sciencedirect.com/science/article/pii/S1521693415001558</u>
- Arvidsson A, Johnsdotter S, Emmelin M, Essén B. Gauging the interests of birth mother and child: a qualitative study of Swedish social workers' experiences of transnational gestational surrogacy. European Journal of Social Work. 2016 Nov 23:1-4. http://www.tandfonline.com/doi/full/10.1080/13691457.2016.1256869
- 6. August F, Pembe AB, Mpembeni R, Axemo P, Darj E. Effectiveness of the Home Based Life Saving Skills training by community health workers on knowledge of danger signs, birth preparedness, complication readiness and facility delivery, among women in Rural Tanzania. BMC pregnancy and childbirth. 2016 Jun 2;16(1):129. http://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-016-0916-x
- August F, Pembe AB, Mpembeni R, Axemo P, Darj E. Community health workers can improve male involvement in maternal health: evidence from rural Tanzania. Global health action. 2016 Jan 1;9(1):30064. <u>http://www.tandfonline.com/doi/full/10.3402/gha.v9.30064</u>
- 8. Berglund A, Lindmark G. Preconception health and care (PHC)—a strategy for improved maternal and child health. Upsala Journal of Medical Sciences. 2016 Oct 1;121(4):216-21. http://www.tandfonline.com/doi/full/10.1080/03009734.2016.1191564
- Byrskog U, Essén B, Olsson P, Klingberg-Allvin M. 'Moving on'Violence, wellbeing and questions about violence in antenatal care encounters. A qualitative study with Somali-born refugees in Sweden. Midwifery. 2016 Sep 30;40:10-7. http://www.sciencedirect.com/science/article/pii/S0266613816300614
- Cleeve A, Oguttu M, Ganatra B, Atuhairwe S, Larsson EC, Makenzius M, Klingberg-Allvin M, Paul M, Kakaire O, Faxelid E, Byamugisha J. Time to act—comprehensive abortion care in east Africa. The Lancet Global Health. 2016 Sep 30;4(9):e601-2. <u>http://www.sciencedirect.com/science/article/pii/S2214109X1630136X</u>
- Esscher A, Essén B, Innala E, Papadopoulos FC, Skalkidou A, Sundström-Poromaa I, Högberg U. Suicides during pregnancy and 1 year postpartum in Sweden, 1980–2007. The British Journal of Psychiatry. 2016 May 1;208(5):462-9. <u>http://bjp.rcpsych.org/content/208/5/462</u>
- Fernbrant C, Essén B, Esscher A, Östergren PO, Cantor-Graae E. Increased risk of mortality due to interpersonal violence in foreign-born women of reproductive age: a Swedish registerbased study. Violence against women. 2016 Oct;22(11):1287-304. <u>http://journals.sagepub.com/doi/abs/10.1177/1077801215623380</u>
- 13. Högberg U, Claeson C, Krebs L, Svanberg AS, Kidanto H. Breech delivery at a University Hospital in Tanzania. BMC pregnancy and childbirth. 2016 Nov 8;16(1):342. http://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-016-1136-0
- 14. Iyengar K, Klingberg Allvin M, Iyengar SD, Danielsson KG, Essén B. "Who Wants to Go Repeatedly to the Hospital?" Perceptions and Experiences of Simplified Medical Abortion in

Rajasthan, India. Global Qualitative Nursing Research. 2016 Dec 19;3:2333393616683073. http://journals.sagepub.com/doi/abs/10.1177/2333393616683073

- Iyengar K, Klingberg-Allvin M, Iyengar SD, Paul M, Essén B, Gemzell-Danielsson K. Home use of misoprostol for early medical abortion in a low resource setting: secondary analysis of a randomized controlled trial. Acta obstetricia et gynecologica Scandinavica. 2016 Feb 1;95(2):173-81 <u>http://onlinelibrary.wiley.com/doi/10.1111/aogs.12815/abstract</u>
- 16. Johansson MM, Lundin E, Qian X, Mirzazadeh M, Halvardson J, Darj E, Feuk L, Nilsson M, Jazin E. Spatial sexual dimorphism of X and Y homolog gene expression in the human central nervous system during early male development. Biology of sex differences. 2016 Jan 12;7(1):5. <u>http://bsd.biomedcentral.com/articles/10.1186/s13293-015-0056-4</u>
- Johnsdotter S, Essén B. Cultural change after migration: Circumcision of girls in Western migrant communities. Best Practice & Research Clinical Obstetrics & Gynaecology. 2016 Apr 30;32:15-25. <u>http://www.sciencedirect.com/science/article/pii/S1521693415001959</u>
- Kaime-Atterhög W, Persson LÅ, Ahlberg BM. "With an open heart we receive the children": Caregivers' strategies for reaching and caring for street children in Kenya. Journal of Social Work. 2012:1468017316651989. http://journals.sagepub.com/doi/abs/10.1177/1468017316651989
- Kalengayi FK, Hurtig AK, Nordstrand A, Ahlm C, Ahlberg BM. Perspectives and experiences of new migrants on health screening in Sweden. BMC health services research. 2016 Jan 15;16(1):14. <u>http://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-015-1218-0</u>
- Larsson EC, Fried S, Essén B, Klingberg-Allvin M. Equitable abortion care–A challenge for health care providers. Experiences from abortion care encounters with immigrant women in Stockholm, Sweden. Sexual & Reproductive Healthcare. 2016 Dec 31;10:14-8. http://www.sciencedirect.com/science/article/pii/S1877575616301719
- 21. Litorp H, Rööst M, Kidanto HL, Nyström L, Essén B. The effects of previous cesarean deliveries on severe maternal and adverse perinatal outcomes at a university hospital in Tanzania. International Journal of Gynecology & Obstetrics. 2016 May 1;133(2):183-7. http://onlinelibrary.wiley.com/doi/10.1016/j.ijgo.2015.10.009/abstract
- 22. Mgaya AH, Litorp H, Kidanto HL, Nyström L, Essén B. Criteria-based audit to improve quality of care of foetal distress: standardising obstetric care at a national referral hospital in a low resource setting, Tanzania. BMC pregnancy and childbirth. 2016 Nov 8;16(1):343. http://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-016-1137-z
- Mgaya AH, Kidanto HL, Nystrom L, Essén B. Improving Standards of Care in Obstructed Labour: A Criteria-Based Audit at a Referral Hospital in a Low-Resource Setting in Tanzania. PloS one. 2016 Nov 28;11(11):e0166619. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0166619
- 24. Mohammadi S, Essén B, Fallahian M, Taheripanah R, Saleh Gargari S, Källestål C. Maternal near-miss at university hospitals with cesarean overuse: an incident case-control study. Acta obstetricia et gynecologica Scandinavica. 2016 Jul 1;95(7):777-86. http://onlinelibrary.wiley.com/doi/10.1111/aogs.12881/abstract
- 25. Paul M, Iyengar SD, Essén B, Gemzell-Danielsson K, Iyengar K, Bring J, Klingberg-Allvin M. Does mode of follow-up influence contraceptive use after medical abortion in a low-resource setting? Secondary outcome analysis of a non-inferiority randomized controlled trial. BMC public health. 2016 Oct 17;16(1):1087. http://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-016-3726-1

- 26. Paul M, Näsström SB, Klingberg-Allvin M, Kiggundu C, Larsson EC. Healthcare providers balancing norms and practice: challenges and opportunities in providing contraceptive counselling to young people in Uganda–a qualitative study. Global health action. 2016;9. http://www.tandfonline.com/doi/full/10.3402/gha.v9.30283
- 27. Pun KD, Infanti JJ, Koju R, Schei B, Darj E, ADVANCE Study Group. Community perceptions on domestic violence against pregnant women in Nepal: a qualitative study. Global health action. 2016;9. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5122230/</u>
- Puthoopparambil SJ, Bjerneld M. Detainees, staff, and health care services in immigration detention centres: a descriptive comparison of detention systems in Sweden and in the Benelux countries. Global health action. 2016;9. <u>http://www.tandfonline.com/doi/full/10.3402/gha.v9.30358</u>
- 29. Påfs J, Musafili A, Binder-Finnema P, Klingberg-Allvin M, Rulisa S, Essén B. Beyond the numbers of maternal near-miss in Rwanda–a qualitative study on women's perspectives on access and experiences of care in early and late stage of pregnancy. BMC Pregnancy and Childbirth. 2016 Sep 2;16(1):257. http://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-016-1051-4
- 30. Påfs J, Rulisa S, Musafili A, Essén B, Binder-Finnema P. 'You try to play a role in her pregnancy'-a qualitative study on recent fathers' perspectives about childbearing and encounter with the maternal health system in Kigali, Rwanda. Global Health Action. 2016;9. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5002034/</u>
- Sjöström S, Essén B, Gemzell-Danielsson K, Klingberg-Allvin M. Medical students are afraid to include abortion in their future practices: in-depth interviews in Maharastra, India. Bmc medical education. 2016 Jan 12;16(1):8. http://bmcmededuc.biomedcentral.com/articles/10.1186/s12909-016-0532-5
- Kitching GT, Haavik HJ, Tandstad BJ, Zaman M, Darj E. Exploring the Role of Ad Hoc Grassroots Organizations Providing Humanitarian Aid on Lesvos, Greece. PLoS Currents. 2016 Nov 17;8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5145811/
- Trenholm J, Olsson P, Blomqvist M, Ahlberg BM. The global, the ethnic and the gendered war: women and rape in eastern Democratic Republic of Congo. Gender, Place & Culture. 2016 Apr 2;23(4):484-502. <u>http://www.tandfonline.com/doi/full/10.1080/0966369X.2015.1013440</u>
- Wiberg-Itzel E, Pembe AB, Järnbert-Pettersson H, Norman M, Wihlbäck AC, Hoesli I, Bernasconi MT, Azria E, Åkerud H, Darj E. Lactate in Amniotic Fluid: Predictor of Labor Outcome in Oxytocin-Augmented Primiparas' Deliveries. PloS one. 2016 Oct 26;11(10):e0161546. <u>http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0161546</u>
- 35. Åkerman E, Essén B, Westerling R, Larsson E. Healthcare-seeking behaviour in relation to sexual and reproductive health among Thai-born women in Sweden: a qualitative study. Culture, Health & Sexuality. 2017 Feb 1;19(2):194-207. http://www.tandfonline.com/doi/full/10.1080/13691058.2016.1214746
- 36. Åkerman E, Östergren PO, Essén B, Fernbrant C, Westerling R. Knowledge and utilization of sexual and reproductive healthcare services among Thai immigrant women in Sweden. BMC international health and human rights. 2016 Oct 10;16(1):25. <u>https://bmcinthealthhumrights.biomedcentral.com/articles/10.1186/s12914-016-0100-4</u>

#### 2015

- 1. Arousell, J., Carlbom, A. (2015). Culture and religious beliefs in relation to reproductive health. Baillière's Best Practice & Research
- Arvidsson, A., Johnsdotter, S., Essén, B. Views of Swedish commissioning parents relating to the exploitation discourse in using transnational surrogacy. PLoS ONE, vol. 10, 2015. <u>http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0126518</u>
- 3. Binder-Finnema, P., Lien, P., Hoa, D., Målqvist, M. Determinants of marginalization and inequitable maternal health care in North-Central Vietnam: a framework analysis. Global health action, vol. 8, 2015. http://www.globalhealthaction.net/index.php/gha/article/view/27554
- 4. Bjerneld, M. Western Health Workers in Humanitarian Aid: Chapter 14. I Pat Gibbons and Hans-Joachim Heintze (red.) The humanitarian Chanllenge 20 years European Network on Humanitarian Action (NOHA). 2015. http://link.springer.com/book/10.1007%2F978-3-319-13470-3
- Byrskog, U., Olsson, P., Essén, B., Allvin, M. Being a bridge: Swedish antenatal care midwives' encounters with Somali-born women and questions of violence; a qualitative study. BMC Pregnancy and Childbirth, vol. 15, ss. 1-. 2015 http://www.biomedcentral.com/1471-2393/15/1
- Esscher, A., Essén, B., Innala, E., Papadopoulos, F., Skalkidou, A. et al. (2015). Suicides during pregnancy and one year postpartum in Sweden, 1980–2007. British Journal of Psychiatry
- Essén, B., Johnsdotter, S. Transnational surrogacy: reproductive rights for whom? Acta Obstetricia et Gynecologica Scandinavica, vol. 94, ss. 449-450, 2015. http://onlinelibrary.wiley.com/doi/10.1111/aogs.12636/abstract;jsessionid=21B6FDD995E364 A88C5F83A822BD2F68.f01t04
- Ivarsson, A., Kinsman, J., Johansson, K., Mohamud, K., Weinehall, L. et al. Healing the health system after civil unrest. Global health action, vol. 8, 2015. http://www.globalhealthaction.net/index.php/gha/article/view/27381
- Iyengar, K., Paul, M., Iyengar, S., Klingberg-Allvin, M., Essén, B. et al. Self-assessment of the outcome of early medical abortion versus clinic follow-up in India: a randomised, controlled, non-inferiority trial. LANCET GLOBAL HEALTH, vol. 3, ss. E537-E545, 2015. http://www.sciencedirect.com/science/article/pii/S2214109X15001503
- 10. Johnsdotter, S., Essén, B. (2015). Cultural change after migration: Circumcision of girls in Western migrant communities. Baillière's Best Practice & Research
- Jordal, M., Wijewardena, K., Öhman, A., Essén, B., Olsson, P. 'Disrespectful men, disrespectable women': Men's perceptions on heterosexual relationships and premarital sex in a Sri Lankan Free Trade Zone - A qualitative interview study. BMC International Health and Human Rights, vol. 15, 2015. <u>http://www.biomedcentral.com/1472-698X/15/3</u>
- 12. Khanolkar, A., Wedrén, S., Essén, B., Sparén, P., Koupil, I. Preterm and postterm birth in immigrant- and Swedish-born parents: a population register-based study. European Journal of Epidemiology, vol. 30, ss. 435-447, 2015. <u>http://link.springer.com/article/10.1007%2Fs10654-014-9986-0</u>
- Litorp, H., Mgaya, A., Kidanto, H., Johnsdotter, S., Essén, B. "What about the mother?": Women's and caregivers' perspectives on caesarean birth in a low-resource setting with rising caesarean section rates. Midwifery, vol. 31, ss. 713-720, 2015. http://www.sciencedirect.com/science/article/pii/S0266613815000947
- 14. Litorp, H., Mgaya, A., Mbekenga, C., Kidanto, H., Johnsdotter, S. et al. Fear, blame and transparency: Obstetric caregivers' rationales for highcaesarean section rates in a low-resource

setting. Social Science and Medicine, ss. 232-240, 2015. http://www.sciencedirect.com/science/article/pii/S0277953615301088

- Musafili, A., Essén, B., Baribwira, C., Binagwaho, A., Persson, L. et al. Trends and social differentials in child mortality inRwanda 1990–2010: results from three demographicand health surveys. Journal of Epidemiology and Community Health, vol. 69, ss. 834-840, 2015. <u>http://jech.bmj.com/content/69/9/834</u>
- Musafili, A., Essén, B., Baribwira, C., Ekholm Selling, K., Persson, L. Social equity in perinatal survival: a case-control study at hospitals in Kigali, Rwanda. Acta Paediatrica, 2015. http://onlinelibrary.wiley.com/doi/10.1111/apa.12951/abstract
- Paul, M., Danielsson, K., Essén, B., Allvin, M. The importance of considering the evidence in the MTP 2014 Amendment debate in India: unsubstantiated arguments should not impede improved access to safe abortion. Global health action, vol. 8, ss. 27512-, 2015. http://www.globalhealthaction.net/index.php/gha/article/view/27512
- Paul, M., Essén, B., Sariola, S., Iyengar, S., Soni, S. et al. (2015). Negotiating Collective and Individual Agency: A Qualitative Study of Young Women's Reproductive Health in Rural India. Qualitative health research
- Paul, M., Iyengar, K., Essén, B., Gemzell-Danielsson, K., Iyengar, S. et al. Acceptability of Home-Assessment PostMedical Abortion and Medical Abortion in aLow-Resource Setting in Rajasthan, India.: Secondary Outcome Analysis of a Non-Inferiority Randomized Controlled Trial. PLoS ONE, 2015. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0133354
- Puthoopparambil, S., Bjerneld, M., Källestål, C. Quality of life among immigrants in Swedish immigration detention centres: a cross-sectional questionnaire study. Global health action, vol. 8, 2015. http://www.globalhealthaction.net/index.php/gha/article/view/28321
- Puthoopparambil, S., Ahlberg, B., Bjerneld, M. (2015). A prison with extra flavours : Experiences of immigrants in Swedish immigration detention centres. International Journal of Migration, Health and Social Care, vol. 11, ss. 73-85
- Puthoopparambil, S., Ahlberg, B., Bjerneld, M. "It is a thin line to walk on": challenges of staff working at Swedish immigration detention centres. International Journal of Qualitative Studies on Health and Well-being, vol. 10, ss. 25196-, 2015. http://www.ijqhw.net/index.php/qhw/article/view/25196
- Påfs, J., Musafili, A., Finnema, P., Allvin, M., Rulisa, S. et al. (2015). 'They would never receive you without a husband': Paradoxical barriers to antenatal care scale-up in Rwanda. Midwifery, vol. 31, ss. 1149-1156
- Urquia, M., Glazier, R., Mortensen, L., Nybo-Andersen, A., Small, R. et al. Severe maternal morbidity associated with maternal birthplace in three high-immigration settings. European Journal of Public Health, vol. 25, ss. 620-625, 2015. http://eurpub.oxfordjournals.org/content/25/4/620

#### 2014

- 1. Borne, Y., Hedblad, B., Essén, B., Engstrom, G. (2014). Anthropometric measures in relation to risk of heart failure hospitalization: a Swedish population-based cohort study. European Journal of Public Health, vol. 24, ss. 215-220
- Byrskog U, Olsson P, Essén B, Klingberg Allvin M. Violence and reproductive health preceding flight from war: accounts from Somali born women in Sweden. BMC Public Health 2014, 14:892. http://biomedcentral.com/1471-2458/14/892
- Degni, F., Suominen, S., El Ansari, W., Vehviläinen-Julkunen, K., Essén, B. (2014). Reproductive and maternity health care services in Finland: perceptions and experiences of Somali-born immigrant women. Ethnicity and Health, vol. 19, ss. 348-366
- 4. Esscher A, Binder-Finnema P, Bödker B, Högberg U, Mulic-Lutvica A, Essén B. Suboptimal care and maternal mortality among foreign-born women in Sweden: maternal death audit with application of the "migration three delays" model. BMC Pregnancy and Childbirth 2014, 14:141. <u>http://www.biomedcentral.com/1471-2393/14/141</u>
- 5. Fernbrant C, Emmelin M, Essén B, Östergren PO, Cantor-Graae E. Intimate partner violence and poor mental health among Thai women residing in Sweden. Global Health Action 2014, 7:24991. <u>http://dx.doi.org/10.3402/gha.v7.24991</u>
- Gagnon AJ, DeBruyn R, Essén B, Gissler M, Heaman M. Jeambey Z, Korfker D, McCourt C, Roth C, Zeitlin J, Small R. Development of the Migrant Friendly Maternity Care Questionnaire (MFMCQ) for migrants to Western societies: an international Delphi consensus process. BMC Pregnancy and Childbirth 2014,14:200. <u>http://www.biomedcentral.com/1471-2393/14/200</u>
- Jordal, M., Wijewardena, K., Öhman, A., Essén, B., Olsson, P. (2014). Negotiating Respectability: Migrant Women Workers' Perceptions on Relationships and Sexuality in Free Trade Zones in Sri Lanka. Health Care for Women International, vol. 35, ss. 658-676
- Litorp H, Kidanto HL, Rööst M, Abeid M, Nyström L, Essén B. Maternal near-miss and death and their association with caesarean section complications: a cross-sectional study at a university hospital and a regional hospital in Tanzania. BMC Pregnancy and Childbirth 2014, 14:244. <u>http://www.biomedcentral.com/1471-2393/14/244</u>
- 9. Litorp, H., Mgaya, A., Mbekenga, C., Kidanto, H., Johnsdotter, S. et al. (2014). Fear, Blame and Transparency: Caregivers' rationales for high caesarean section rates in a low-resource setting.
- Paul M, Gemzell-Danielsson K, Kiggundu C, Klingberg-Allvin M, Barriers and facilitators in the provision of post-abortion care at district level in central Uganda: A qualitative study focusing on task sharing between physicians and midwives. BMC Health Serv Res 2014 Jan 21;14(1):28. (E-pub ahead of print) <u>http://www.biomedcentral.com/content/pdf/1472-6963-14-28.pdf</u>
- Paul M, Iyengar K, Iyengar S, Gemzell-Danielsson K, Essén B, Klingberg-Allvin M. Simplified follow-up after medical abortion using a low-sensitivity urinary pregnancy test and a pictorial instruction sheet in Rajasthan, India – study protocol and intervention adaptation of a randomised control trial. BMC Women's Health 2014, 14:98. http://www.biomedcentral.com/1472-6874/14/98.
- Sjöström S, Essén B, Sydén F, Gemzell-Danielsson K, Klingberg-Allvin M. Medical students' attitudes and perceptions on abortion: a cross-sectional survey among medical interns in Maharastra, India. Contraception 2014. E-pub ahead of print. http://www.sciencedirect.com/science/article/pii/S0010782414000523#
- Wahlberg A, Källestål C, Lundgren AC, Essén B. Causes of death among undocumented migrants in Sweden, 1997-2010. Global Health Action 2014, 7:24464. <u>http://www.globalhealthaction.net/index.php/gha/article/view/24464</u>

#### **Dissertations 2016**

- 1. Furaha August: Effect of Home Based Life Saving Skills education on knowledge of obstetric danger signs, birth preparedness, utilization of skilled care and male involvement: A Community-based intervention study in rural Tanzania
- 2. Soorej Jose Puthoopparambil: Life in Immigration Detention Centers: An exploration of health of immigrant detainees in Sweden and three other EU member states.

3. Jessica Påfs: The Quest for Maternal Survival in Rwanda: Paradoxes in Policy and Practice from the Perspective of Near-Miss Women, Recent Fathers and Healthcare Providers.

#### Agencies that support the work/Funding

ALF 1 485 679 VR 1 969 000 Forte 2 680 000 Familjeplaneringsfonden 120 000 Gillbergska 42 000 Länsstyrelsen 50 000

#### Collaborating centres

Karolinska institutet Malmö Högskola Uppsala universitet, Department of Public Health and Caring Sciences All India Institute of Medical Science and the WHO - collaborating centre in New Delhi Ipas – Indien Muhimbili National Hospital, Dar es Salaam, Tanzania Läkare utan gränser – MSF National University of Rwanda (NUR) Umeå University, Public Health and Clinical Medicine Universidad Nacional Autótoma de Nicaragua UNAN - Leon, Nicaragua Shahid Beheshti University of Medical Sciences/ Infertility Reproductive Health Research Center

#### Maternal mortality and severe obstetric morbidity in a globalized world

#### Birgitta Essén, Mattias Rööst, Pauline Binder, Annika Esscher, Helena Litorp, Soheila Mohammadi, Jessica Påfs, Anna Wahlberg, Sara Johnsdotter, Lennart Nyström, Eliette Valladares. Joseph Vyankakander, Aimable Musafili, Hussein Kidanto

Maternal mortality is a well-known quality indicator of obstetric care, and maternal near miss is fast gaining interest as a complementary indicator, particularly among vulnerable groups with a lack of social networks in situations of general instability or poverty in low-income settings (Rwanda and Tanzania), or after migration to high resource settings (Sweden, UK). Our current research activities include analyses of maternal and perinatal ill-health in low-, middle- and high-income settings from a migration perspective. Partner's role in the provision of support during antenatal and obstetric decision-making is also explored as an influence on birth outcome barriers. The overall aim is to develop tools for comprehensive maternal health services to women living in underprivileged situations. The research program is interdisciplinary and uses multiple mixed methods, including epidemiological, audit, as well as anthropological methods to define the social and cultural aspects of these medical phenomena.

The significance of these findings yields improved medical and culturally relevant ways to understand and prevent the tragic incidence of maternal or perinatal loss of life. The multidisciplinary group has previously shown effects of ethnic background, suboptimal care and socio-cultural factors, such as female circumcision, on the risk of perinatal mortality and maternal morbidity and results have been implemented in health care practices among ethnic groups in Latin America and in Sweden. The findings have contributed to theoretical knowledge, but have also been implemented through guidelines in order to reduce health inequalities in an ethnic perspective.

#### Too many caesarean deliveries challenge Safe Motherhood

#### Birgitta Essén, Ulf Högberg, Mattias Rööst, Pauline Binder, Helena Litorp, Soheila Mohammadi, Lennart Nyström, Eliette Valladares, Hussein Kidanto

There is a global trend of increasing rates of caesarean delivery due to such reasons as medicalization, economic incitements and parental autonomy, whilst from an equity and priority perspective, safe motherhood is not implied. Hospital caesarean section rates of 24 - 75% are reported from Latin America, Asia and Africa. This project is focused on Iran, Nicaragua and Tanzania.

The study designs are hospital based: audits, demographic health surveillance site, interviews of mothers at hospital delivery and follow-up; maternal and child outcomes, including Robson 10-group classification; and sampling of parents and doctors for anthropological interviews to explore decision making, attitudes, birth experiences and health economic analysis.

#### Genitals, gender and ethnicity: The Politics of Genital Modifications

#### Birgitta Essén, Sara Johnsdotter, Anna Arvidsson

This study, conducted by an anthropologist and a gynecologist, aims at reaching an understanding of societal views of the relation between 'sex', 'gender' and genitals, through analyzing the political positions that have given rise to decisions to advocate, accept or criminalize certain surgical genital modifications. The phenomena analyzed are male and female circumcision, cosmetic genital surgery, hymenoplasty and operations on transsexual adults/intersexual infants. Society's views of these procedures have their own social, medical and political history, and as yet there is no systematic analysis juxtaposing them. The theoretical approach is social constructivist, inspired by gender theory and critical medical anthropology. Empirical data include legislative texts and qualitative interviews with professionals in medicine and with key activists. Through discourse analysis we will explore the social values about 'sex' and 'gender' that are conveyed in legal decisions and medical practice in this field, and in alternative discourses. The study adds to our research about female genital cutting and cosmetic genital surgery. Procedures involving the genitals provide an arena where medicine and culture converge. Understandings of 'sex' are interwoven with politicized socio-cultural constructions of 'gender'. What is 'given by nature' can be modified through surgery, but medical practice itself develops within a norm structure that is time- and culture-bound.

## Daily life and wellbeing for irregular immigrants in detention centres in three EU countries

#### Magdalena Bjerneld, Soorej Jose Puthoopparambil

Sweden receives a major share group of asylum seekers in the world. In year 2007 the EU member states had together about 3,8 million irregular migrants form countries outside EU. Most of the European countries use detention centers in order to facilitate deportation of irregular migrants who have been captured.

The time spent in the detention unit is important for a detainee as it affects his/her life at present and in the future. The health situation of the detainees, which is already deteriorated, is worsened when they are detained at the detention centers. They need support to handle the stressful situation in the detention. In order to provide this support, an understanding of the detainee's daily life is required. Most of the EU states use a comparatively similar system for handling irregular immigrants. In this project the system in Sweden, France and the Netherlands will be analyzed and compared.

The overall aim of the project is to create a knowledge base for the development of the care of detainees in three EU countries with a focus on the Swedish detention system. The objectives are to: describe how the detainees experience the daily life, well-being and received care: describe the staff's and the volunteer's perspectives on the care of provided for the detainees; compare the experiences of detainees from the three countries; identify factors which support or prevent the well-being of the detainees; develop a model for promoting the well-being for detainees. Qualitative methods are used for the data collection in the project, which is run as a PhD project in the area of International health with the PhD student Soorej Jose Puthoopparambil.

#### Unaccompanied Somali refugee girls in Sweden – a follow-up study

#### Magdalena Bjerneld

Sweden has received unaccompanied children since the end of 1980ths. During the period 1980 - 2010 around 11000 unaccompanied children arrived in Sweden. The tendency is that this group of children will increase in the future. In the beginning of 1990th the Somali children was the largest group and they still are, together with children from Afghanistan. The majority is boys but one third is girls. The majority of the children have received asylum and have therefore lived their fist years as young adults in Sweden. During 1998-1999 we performed a study in Sweden where unaccompanied girls from Somalia were interviewed. They experienced great cultural differences concerning the expectations on girls. They had difficulties to learn Swedish and lack of trust in new people.

The overall aim with this study is to document and to analyze how a group of unaccompanied girls from Somalia look back on their first years in Sweden as young adults. The objectives are to document how they have experienced the reception of the authorities, how they have been received by the Swedish health care system, how they self-rate their own health and how they have developed their social network in Sweden. Their experiences will identify factors important for a good reception and integration. This knowledge can be useful for authorities and caretakers when they plan for other groups of unaccompanied children today and in the future.

#### Sri Lankan Males Perspective of Gender

#### Elisabeth Darj, Pia Axemo, Gunilla Lindmark, Kumudu Wijwardena

'Gender' is defined by WHO as 'the socially constructed roles, behaviour, activities and attributes that a particular society considers appropriate for men and women'. The distinct roles and behavior may give rise to gender inequality, which are differences between men and women that systematically favor one group. Such inequalities build up the foundation for gender related issues such as gender based violence (GBV), social, economic and health inequalities between men and women. Partner violence is the most frequent form of GBV in societies, and efforts are made to get evidence based interventions. The Government in Sri Lanka has adopted several policies around GBV and calls for service points to provide care to abused women. GBV among ever married women and intimate partner violence (IPV) in Sri Lanka is estimated to be between 20 - 60 percent.

The Aim of the present study is to investigate in collaboration with University of Sri Jayawardenapura in Colombo, male university student's perception on GBV, as it is the young generation that will have to make a change.

Objectives are to explore young men's perceptions on GBV, on male dominance and female subordination and to investigate their willingness to actively engage in prevention of GBV in their future occupations.

The study design is qualitative, using focus group discussion (FGD). An experienced Sri Lankan moderator on qualitative research will lead the discussions and an additional research assistant will observe and take notes. The study will contribute to build capacity at the University of Sri Jayawardenapura on sexual and intimate partner violence.

Expected outcomes are to get a deeper understanding of the new generation of men and their understandings on GBV and primary prevention to reduce partner violence. The results will strengthen the evidence base for prevention of sexual and intimate partner violence in South East Asia. This is a pilot study, which will serve as the base of a later application for funding of an intervention study

## Intervention to increase university students' knowledge on Gender Based Violence (GBV)

#### Elisabeth Darj, Pia Axemo

Pilot study to plan and test an educational program on GBV at the University Sri Jayewardenepura, Colombo, Sri Lanka. Studies in Sri Lanka has shown that university students have poor understanding of gender, GBV, its' prevalence, contributing factors and possible preventive measures.

An educational program will be pilot-tested and evaluated in order to later introduce a computerized program accessible to all students and teachers at the University Sri Jayewardenepura.

Questionnaires before and after finalizing the program will be analysed, as well as Focus Group discussions with teachers and students.

## Infertility and assisted reproductive technology (ART), with focus on surrogacy in Assam, India

#### Birgitta Essén, Sara Johnsdotter, Anna Arvidsson

Infertility often creates social and financial problems because of the importance of having children to secure the support in old age and ensure the continuation of the lineage. Especially women suffer from not being able to bear children and childlessness carries social stigma. Even though infertility treatment can be found within the public health care system in India it is in a very small scale and difficult to access. ART is mainly provided to a high cost in private clinics, and there has been a rapid increase of clinics. Many clinics also provide surrogacy but the service is in large part used by childless couples outside of India. The enormous increase in ART clinics providing surrogacy also means that they are no longer located only in big cities, but have spread all over India even to places where they lack basic health care facilities.

Assam is one of seven North-East states in India and borders Bhutan and Bangladesh. Assam is considered to be one of the poorest states in India. Reproductive health care is in many ways insufficient and no government hospital has a department for In-vitro-fertilization (IVF). The study

has a qualitative approach and is focusing on different perspectives of the issues on options to parenthood in Assam. Special emphasize is on surrogacy as a solution to childlessness. The study is carried out in collaboration with Gauhati University, Assam, The Department of Women's studies.

## Accessibility and Acceptability of Medical Abortion and Contraception in Low-resource India

#### Marie Klingberg Allvin, Birgitta Essén, Kristina Gemzell, Mandira Paul

Maternal mortality is high in India (178/100000 LB), especially in Rajasthan (255/100000 LB), one of the government's priority states due to its poor health outcomes. Although abortion was legalized in 1971, access to safe abortion services is still inadequate. Unsafe abortions are estimated to account for 8-18% of maternal deaths in India, in addition to substantial morbidity. Contraceptive use is low and so is women's general awareness of their reproductive health and available reproductive health services. This project aims to simplify medical abortion and make it more acceptable to women as well as to health care providers. Simplifying and demedicalising medical abortion can decrease service costs and make services more affordable to women in low-resource settings. Moreover, combining medical abortion with contraceptive counseling and health promotion may enhance women's motivation to adapt a contraceptive method post-abortion. In addition, making abortion services from the public health system, something that is not widely seen today.

A randomized control trial is carried out to investigate the efficacy, safety and acceptability of a simplified medical abortion regime in a rural and urban low-resource setting in Rajasthan, India. Studies in Europe and USA have shown an increased acceptability among both women and providers when fewer clinical visits are required for a medical abortion, however, these studies do neither take the low-resource setting, the lack of mobile phones and infrastructure, and the low literacy level into account. This study aims to fill the knowledge gap and investigate the feasibility of simplified follow-up in low-resource settings. Additionally, the contraceptive use among women post-abortion will be investigated, and barriers to access to safe abortion services and contraceptive use will be explored. Furthermore young women's reproductive choices and partner involvement in the reproductive decision-making process among rural youth will also be explored outside of the randomized control trial.

#### International Sexual and Reproductive Health

#### **Christine Rubertsson**

Our research group studies women's health and rights, youth health as well as care and support related to pregnancy, birth, post-natal care, breast-feeding and parenthood. The group collaborates with scientists from several disciplines such as medicine, public health, social science, gender studies, nursing and midwifery. Three PhD students defended their thesis during 2016 and new doctoral students have been registered. Our projects span over the following main areas:

#### **Reproductive Health and Healthcare**

This area focuses on quality of care throughout the continuum of care from home, through the community and on to health services and referral hospitals. The different projects are described in more detail below.

**Sexual Health and Rights** includes projects among young people in different contexts, in Sweden as well as in other countries. Several projects are related to gender-based violence and interventions for prevention of violence. The projects are described in more detail below.

Nutrition and Women's Health is another focus of the group. Studies are on-going in several countries and described in more detail below.

#### Members of the group during 2016

Abeid Muzdalifat PhD Ahlberg Beth Maina PhD, Adjunct Professor Furaha August Doctoral student Axemo Pia PhD, Associate Professor Berglund Anna PhD Blixt Ingrid Doctoral student Bodin Maja Doctoral student Cato Karin Doctoral student Darj Elisabeth PhD, Guest Professor **Ekstrand Maria PhD** Haines Helen PhD Hildingsson Ingegerd PhD, Professor Högberg Hjördis Med lic Höglund Berit PhD Jordal Malin PhD Kaime-Atterhög Wanjiku PhD Larsson Birgitta Doctoral student Larsson Margareta PhD, Associate Professor, Senior Lecturer Lindmark Gunilla PhD, Professor emerita Makenzius Marlene PhD Malm Mari-Cristin PhD Mattebo Magdalena PhD Mbekenga Kokusiima Colomba PhD Olsson Pia RNM, PhD, Associate Professor, Senior Lecturer Omer-Salim Amal PhD Pallangyo Eunice Doctoral student Pembe Andrea PhD Rubertsson Christine PhD, Associate Professor, Senior Lecturer Svensson Liisa Doctoral student Tydén Tanja Professor Ternström Elin Doctoral student

Trenholm Jill PhD Helena Volgsten Wickström Maria Doctoral student Annika Åhman PhD

#### Publications 2014-2016

- 1. Abeid M, Muganyizi P, Mpembeni R, Darj E, Axemo P. Evaluation of a training program for health care workers to improve the quality of care for rape survivors: a quasi-experimental design study in Morogoro, Tanzania. Glob Health Action. 2016 Jan;9(1):31735. doi: 10.3402/gha.v9.31735.
- Adolphson K, Axemo P, Högberg U. Midwives' experiences of working conditions, perceptions of professional role and attitudes towards mothers in Mozambique. Midwifery. 2016 Sep;40:95-101.
- Andersson, E., Hildingsson, I. (2016). Mother's postnatal stress: an investigation of links to various factors during pregnancy and post-partum. Scandinavian Journal of Caring Sciences, vol. 30, ss. 782-789
- 4. August F, Pembe AB, Mpembeni R, Axemo P, Darj E. Effectiveness of the Home Based Life Saving Skills training by community health workers on knowledge of danger signs, birth preparedness, complication readiness and facility delivery, among women in Rural Tanzania. BMC Pregnancy Childbirth. 2016 Jun 2;16(1):129.
- 5. August F, Pembe AB, Mpembeni R, Axemo P, Darj E. Community health workers can improve male involvement in maternal health: evidence from rural Tanzania. Glob Health Action. 2016 Jan;9(1):30064.
- 6. Blomqvist, Y., Nyqvist, K., Rubertsson, C., Funkquist, E. (2016). Parents need support to find ways to optimise their own sleep without seeing their preterm infant's sleeping patterns as a problem. Acta Paediatrica
- 7. Byrskog U, Essén B, Olsson P, Klingberg-Allvin M. 'Moving on' Violence, wellbeing and questions about violence in antenatal care encounters. A qualitative study with Somali-born refugees in Sweden. Midwifery. 2016;40:10-17.
- 8. Edqvist M, Blix E, Hegaard H K, Olafsdottir O A, Hildingsson I, Ingversen K, et al. Perineal injuries and birth positions among 2992 women with a low risk pregnancy who opted for a homebirth. BMC Pregnancy and Childbirth. 2016;16:196.
- 9. Ehrsson Y T, Stenhammar C, Rosenblad A, Åkerud H, Larsson M, Tydén T. Self-reported sexually transmitted infections among female university students.. Upsala Journal of Medical Sciences. 2016;121(1):45-49.
- 10. Ekstrand Ragnar M, Tydén T, Kihlbom U, Larsson M. Swedish parents' interest in preconception genetic carrier screening. Taylor & Francis; Upsala Journal of Medical Sciences. 2016;121(4):289-294.
- 11. Grandahl M, Rosenblad A, Stenhammar C, Tydén T, Westerling R, Larsson M, et al. Schoolbased intervention for the prevention of HPV among adolescents : a cluster randomised controlled study. BMJ Open. 2016;6(1):e009875.
- 12. Halfdansdottir B, Olafsdottir O A, Hildingsson I, Smarason A K, Sveinsdottir H. Maternal attitudes towards home birth and their effect on birth outcomes in Iceland : A prospective cohort study. Midwifery. 2016;34:95-104.
- 13. Hauck Y L, Blixt I, Hildingsson I, Gallagher L, Rubertsson C, Thomson B, et al. Australian, Irish and Swedish women's perceptions of what assisted them to breastfeed for six months : exploratory design using critical incident technique. BMC Public Health. 2016;16:1067.
- 14. Hedqvist M, Brolin L, Tyden T, Larsson M. Women's experiences of having an early medical abortion at home. Sexual & Reproductive HealthCare. 2016;9:48-54.

- Hildingsson I, Gamble J, Sidebotham M, Creedy D K, Guilliland K, Dixon L, et al. Midwifery empowerment : National surveys of midwives from Australia, New Zealand and Sweden. Midwifery. 2016;40:62-69.
- 16. Hildingsson I, Karlstrom A, Haines H, Johansson M. Swedish women's interest in models of midwifery care Time to consider the system? : A prospective longitudinal survey. Sexual & Reproductive HealthCare. 2016;7:27-32.
- 17. Högberg H, Skagerström J, Spak F, Nilsen P, Larsson M. Alcohol Consumption among partners of pregnant women in Sweden : a cross sectional study. BMC Public Health. 2016;16:694.
- 18. Jha P, Christensson K, Svanberg A S, Larsson M, Sharma B, Johansson E. Cashless childbirth, but at a cost : A grounded theory study on quality of intrapartum care in public health facilities in India. Midwifery. 2016;39:78-86.
- 19. Johansson M, Thomas J, Hildingsson I, Haines H. Swedish fathers contemplate the difficulties they face in parenthood. Sexual & Reproductive HealthCare. 2016;8:55-62.
- 20. Kerstis B, Aarts C, Tillman C, Persson H, Engström G, Edlund B, et al. Association between parental depressive symptoms and impaired bonding with the infant. Springer; Archives of Women's Mental Health. 2016;19(1):87-94.
- 21. Larsson B, Karlström A, Rubertsson C, Hildingsson I. Counseling for childbirth fear : a national survey. Sexual & Reproductive HealthCare. 2016;8:82-87.
- 22. Malm M, Hildingsson I, Rubertsson C, Rådestad I, Lindgren H. Prenatal attachment and its association with foetal movement during pregnancy : A population based survey. Women and Birth. 2016;
- 23. Mattebo M, Tydén T, Häggström-Nordin E, Nilsson K W, Larsson M. Pornography consumption among adolescent girls in Sweden. European journal of contraception & reproductive health care. 2016;21(4):295-302.
- 24. Mogilevkina I, Stern J, Melnik D, Getsko E, Tydén T. Ukrainian medical students' attitudes to parenthood and knowledge of fertility. European journal of contraception & reproductive health care. 2016;21(2):189-194.
- 25. Oras P, Thernström Blomqvist Y, Hedberg Nyqvist K, Gradin M, Rubertsson C, Hellström-Westas L, et al. Skin-to-skin contact is associated with earlier breastfeeding attainment in preterm infants. Acta Paediatrica. 2016;105(7):783-789.
- 26. Salih Joelsson L, Berglund A, Wånggren K, Lood M, Rosenblad A, Tydén T. Do subfertile women adjust their habits when trying to conceive?. Upsala Journal of Medical Sciences. 2016;121(3):184-191.
- 27. Stern J, Salih Joelsson L, Tydén T, Berglund A, Ekstrand M, Hegaard H, et al. Is pregnancy planning associated with background characteristics and pregnancy planning behavior?. Acta Obstetricia et Gynecologica Scandinavica. 2016;95(2):182-189.
- Sørensen Olsén, N., Marcussen, S., Grønbæk Backhausen, M., Juhl, M., Schmidt, L. et al. (2016). Fertility awareness and attitudes towards parenthood among Danish university college students. Reproductive Health, vol. 13(1):146.
- 29. Ternström E, Hildingsson I, Haines H, Rubertsson C. Pregnant women's thoughts when assessing fear of birth on the Fear of Birth Scale. Women and Birth. 2016;29(3):E44-E49.
- 30. Trenholm J, Olsson P, Blomqvist M, Ahlberg B M. The global, the ethnic and the gendered war: women and rape in eastern Democratic Republic of Congo. Gender, Place and Culture: A Journal of Feminist Geography. 2016;23(4):484-502.
- Tydén, T., Verbiest, S., van Achterberg, T., Larsson, M., Stern, J. (2016). Using the Reproductive Life Plan in contraceptive counselling. Upsala Journal of Medical Sciences, vol. 121, ss. 299-303
- Wiberg-Itzel E, Pembe AB, Järnbert-Pettersson H, Norman M, Wihlbäck AC, Hoesli I, Todesco Bernasconi M, Azria E, Åkerud H, Darj E. Lactate in Amniotic Fluid: Predictor of Labor Outcome in Oxytocin-Augmented Primiparas' Deliveries. PLoS One. 2016 Oct 26;11(10):e0161546.

33. Åhman A, Sarkadi A, Lindgren P, Rubertsson C. 'It made you think twice' : an interview study of women's perception of a web-based decision aid concerning screening and diagnostic testing for fetal anomalies. BMC Pregnancy and Childbirth. 2016;16:267.

- 1. Abeid, M., Muganyizi, P., Massawe, S., Mpembeni, R., Darj, E. et al. (2015). Knowledge and attitude towards rape and child sexual abuse a community-based cross-sectional study in Rural Tanzania. BMC Public Health. Apr 28;15:428. doi: 10.1186/s12889-015-1757-7.
- Abeid, M., Muganyizi, P., Mpembeni, R., Darj, E., Axemo, P. (2015). A community-based intervention for improving health-seeking behavior among sexual violence survivors: A controlled before and after design study in rural Tanzania. Glob Health Action, 8: 28608 http://dx.doi.org/10.3402/gha.v8.28608.
- 3. Ahlberg, B., Maina, F., Kubai, A., Khamasi, W., Ekman, M. et al. (2015). "A child, a tree': Challenges in building collaborative relations in a community research project in a Kenyan context. Action Research. E-pub September 29, , doi: 10.1177/1476750315607607
- 4. Ahlberg, B. M. (2015). Rights, sexual and reproductive. The International Encyclopedia of Human Sexuality. 1059–1114.
- Angeby, K., Wilde-Larsson, B., Hildingsson, I., Sandin-Bojo, A. (2015). Primiparous women's preferences for care during a prolonged latent phase of labour. Sexual & Reproductive HealthCare, vol. 6, ss. 145-150
- 6. August, F., Pembe, A., Kayombo, E., Mbekenga, C., Axemo, P. Darj., E. (2015). Birth preparedness and complication readiness a qualitative study among community members in rural Tanzania. Global health action, vol. 8, ss. 1-U12
- August, F., Pembe, A., Mpembeni, R., Axemo, P., Darj, E. (2015). Men's Knowledge of Obstetric Danger Signs, Birth Preparedness and Complication Readiness in Rural Tanzania. PLoS One. May 7;10(5):e0125978. doi: 10.1371/journal.pone.0125978. eCollection 2015.
- Bodin, M., Stern, J., Käll, L., Tydén, T., Larsson, M.(2015). Coherence of pregnancy planning within couples expecting a child. Midwifery, vol. 31, ss. 973-978
- Byrskog, U., Olsson, P., Essén, B., Allvin, M. (2015). Being a bridge: Swedish antenatal care midwives' encounters with Somali-born women and questions of violence; a qualitative study. BMC Pregnancy and Childbirth, vol. 15, ss. 1-
- Contreras, M., Blandón, E., Persson, L., Hjern, A., Ekström, E. (2015). Socio-economic resources, young child feeding practices, consumption of highly processed snacks and sugarsweetened beverages: a population-based survey in rural northwestern Nicaragua. BMC Public Health. 2015 Jan 21;15:25. doi: 10.1186/s12889-015-1374-5.
- 11. Darj, E., Infanti, J., Ahlberg, B., Okumu, J. (2015). "The fairer the better?": Use of potentially toxic skin bleaching products. African Health Sciences, vol. 15, ss. 1074-1080
- 12. Drevin, J., Stern, J., Annerbäck, E., Peterson, M., Butler, S. et al. (2015). Adverse childhood experiences influence development of pain during pregnancy. Acta Obstetricia et Gynecologica Scandinavica, vol. 94, ss. 840-846
- 13. Forsén, E., Tadesse, E., Berhane, Y., Ekström, E. (2015). Predicted implications of using percentage weight gain as single discharge criterion in management of acute malnutrition in rural southern Ethiopia. Maternal and Child Nutrition, vol. 11, ss. 962-972
- 14. Gottvall, M., Tydén, T., Larsson, M., Stenhammar, C., Höglund, A. (2015). Informed Consent for HPV Vaccination: A Relational Approach. Health Care Analysis, vol. 23, ss. 50-62
- 15. Grandahl, M., Tyden, T., Gottvall, M., Westerling, R., Oscarsson, M. (2015). Immigrant women's experiences and views on the prevention of cervical cancer: a qualitative study. Health Expectations, vol. 18, ss. 344-354
- Haines, H., Pallant, J., Toohill, J., Creedy, D, Gamble, J., Hildingsson, I., Fenwick, J. Identifying women who are afraid of giving birth: A comparison of the fear of birth scale with the WDEQ-A in a large Australian cohort. Sexual and Reproductive Health Care 2015; 6(4): 204-210.

- 17. Halfdansdottir B, Olafsdottir O, Hildingsson I, Smarason A, Sveinsdottir H. Maternal attitudes towards home birth and their effect on birth outcomes in Iceland: A prospective cohort study. Midwifery (in press)
- Halfdansdottir, B., Smarason, A., Olafsdottir, O., Hildingsson, I., Sveinsdottir, H. (2015). Outcome of Planned Home and Hospital Births among Low-Risk Women in Iceland in 2005-2009: A Retrospective Cohort Study. Birth, vol. 42, ss. 16-26
- Halfdansdottir, B., Wilson, M., Hildingsson, I., Olafsdottir, O., Smarason, A. et al. (2015). Autonomy in place of birth: a concept analysis. Medicine, Health care and Philosophy, vol. 18, ss. 591-600
- 20. Hildingsson, I. (2015). Women's birth expectations, are they fulfilled?: Findings from a longitudinal Swedish cohort study. Women and Birth, vol. 28, ss. e7-e13
- 21. Hildingsson I, Haines H, Karlström A, Johansson M. Parents prefer continuity of midwifery care –Time to change the Swedish system? A prospective longitudinal cohort study. Sexual and Reproductive HealthCare 2016; 7: 27-32
- Hildingsson, I., Blix, E., Hegaard, H., Huitfeldt, A., Ingversen, K. et al. (2015). How Long Is a Normal Labor?: Contemporary Patterns of Labor and Birth in a Low-Risk Sample of 1,612 Women from Four Nordic Countries. Birth, vol. 42, ss. 346-353
- 23. Hildingsson, I., Fenwick, J. (2015). Swedish midwives' perception of their practice environment - A cross sectional study. Sexual & Reproductive HealthCare, vol. 6, ss. 174-181
- Högberg, H., Spak, F., Larsson, M. (2015). Dialogue between Midwives and Parents-to-Be about Alcohol, from a Life Cycle Perspective—An Intervention Study. Creative Education, vol. 6, ss. 489-500.
- 25. Höglund, B., Larsson, M. (2015). Midwives' comprehension of care for women with intellectual disability during pregnancy and childbirth: An open-ended questionnaire study in Sweden. Women Birth. Sep;28(3):e57-62. doi: 10.1016/j.wombi.2015.03.002.
- 26. Johansson M, Edvardsson C, Hildingsson I. The pregnant man. Journal of Men's health 2015 (11(6):8-18.
- Jordal, M., Wijewardena, K., Öhman, A., Essén, B., Olsson, P. (2015). 'Disrespectful men, disrespectable women': Men's perceptions on heterosexual relationships and premarital sex in a Sri Lankan Free Trade Zone - A qualitative interview study. BMC Int Health Hum Rights. Feb 7;15:3. doi: 10.1186/s12914-015-0040-4.
- Karlstrom, A., Nystedt, A., Hildingsson, I. (2015). The meaning of a very positive birth experience: focus groups discussions with women. BMC Pregnancy Childbirth. Oct 9;15:251. doi: 10.1186/s12884-015-0683-0.
- Khan, A., Kabir, I., Hawkesworth, S., Ekström, E., Arifeen, S. et al. (2015). Early invitation to food and/or multiple micronutrient supplementation in pregnancy does not affect body composition in offspring at 54 months: follow-up of the MINIMat randomized trial, Bangladesh. Maternal and Child Nutrition, vol. 11, ss. 385-397
- 30. Larsson, B., Karlström, A., Rubertsson, C., Hildingsson, I. (2015). The effects of counseling on fear of childbirth. Acta Obstetricia et Gynecologica Scandinavica, vol. 94, ss. 629-636
- Lindholm, A., Hildingsson, I. (2015). Women's preferences and received pain relief in childbirth: A prospective longitudinal study in a northern region of Sweden. Sexual & Reproductive HealthCare, vol. 6, ss. 74-81
- 32. Lindström, A., Näslund, S., Rubertsson, C. (2015). The interactional organization of sex assignment after childbirth. Gender and Language, vol. 9, ss. 189-222
- Litorp, H., Mgaya, A., Mbekenga, C., Kidanto, H., Johnsdotter, S. et al. (2015). Fear, blame and transparency: Obstetric caregivers' rationales for highcaesarean section rates in a lowresource setting. Social Science and Medicine, vol. 143, ss. 232-240
- Mattsson, E., Funkquist, E., Wickström, M., Nyqvist, K., Volgsten, H. (2015). Healthy late preterm infants and supplementary artificial milk feeds: Effects on breast feeding and associated clinical parameters. Midwifery, vol. 31, ss. 426-431
- 35. Omer-Salim, A., Suri, S., Dadhich, J., Faridi, M., Olsson, P. (2015). 'Negotiating the tensions of having to attach and detach concurrently': A qualitative study on combining breastfeeding

and employment in public education and health sectors in New Delhi, India. Midwifery, vol. 31, ss. 473-481

- Oras, P., Thernström Blomqvist, Y., Hedberg Nyqvist, K., Gradin, M., Rubertsson, C. et al. (2015). Breastfeeding Patterns in Preterm Infants Born at 28-33 Gestational Weeks. Journal of Human Lactation, vol. 31, ss. 377-385
- Palmqvist, H., Zather, J., Larsson, M. (2015). Fathers' and co-mothers' voices about breastfeeding and equality - A Swedish perspective. Women Birth. Sep;28(3):e63-9. doi: 10.1016/j.wombi.2015.03.005
- Puthoopparambil, S., Ahlberg, B., Bjerneld, M. (2015). A prison with extra flavours : Experiences of immigrants in Swedish immigration detention centres. International Journal of Migration, Health and Social Care, vol. 11, ss. 73-85
- 39. Puthoopparambil, S., Ahlberg, B., Bjerneld, M. (2015). "It is a thin line to walk on": challenges of staff working at Swedish immigration detention centres. International Journal of Qualitative Studies on Health and Well-being, vol. 10, ss. 25196
- 40. Rubertsson, C., Pallant, J., Sydsjö, G., Haines, H., Hildingsson, I. (2015). Maternal depressive symptoms have a negative impact on prenatal attachment: findings from a Swedish community sample. Journal of Reproductive and Infant Psychology, vol. 33, ss. 153-164
- 41. Sharma, B., Hildingsson, I., Johansson, E., Prakasamma, M., Ramani, K. et al. (2015). Do the pre-service education programmes for midwives in India prepare confident 'registered midwives'?: A survey from India. Global Health Action, vol. 8
- 42. Shawe, J., Delbaere, I., Ekstrand, M., Hegaard, H., Larsson, M. et al. (2015). Preconception care policy, guidelines, recommendations and services across six European countries: Belgium (Flanders), Denmark, Italy, the Netherlands, Sweden and the United Kingdom. European journal of contraception & reproductive health care, vol. 20, ss. 77-87
- 43. Soderberg, M., Christensson, K., Lundgren, I., Hildingsson, I. (2015). Women's attitudes towards fertility and childbearing A study based on a national sample of Swedish women validating the Attitudes to Fertility and Childbearing Scale (AFCS). Sexual & Reproductive HealthCare, vol. 6, ss. 54-58
- 44. Stenhammar, C., Ehrsson, Y., Åkerud, H., Larsson, M., Tydén, T. (2015). Sexual and contraceptive behavior among female university students in Sweden: repeated surveys over a 25-year period. Acta Obstetricia et Gynecologica Scandinavica, vol. 94, ss. 253-259
- 45. Stern, J., Bodin, M., Grandahl, M., Segeblad, B., Axen, L. et al. (2015). Midwives' adoption of the reproductive life plan in contraceptive counselling: a mixed methods study. Human Reproduction, vol. 30, ss. 1146-1155
- 46. Tadesse, E., Berhane, Y., Hjern, A., Olsson, P., Ekström, E. (2015). Perceptions of usage and unintended consequences of provision of ready-to-use therapeutic food for management of severe acute child malnutrition: A qualitative study in Southern Ethiopia. Health Policy Plan. Dec;30(10):1334-41. doi: 10.1093/heapol/czv003.
- 47. Ternström, E., Hildingsson, I., Haines, H., Rubertsson, C. (2015). Higher prevalence of childbirth related fear in foreign born pregnant women: Findings from a community sample in Sweden. Midwifery, vol. 31, ss. 445-450
- Ternström, E., Hildingsson, I., Haines, H., Rubertsson, C. (2015). Pregnant women's thoughts when assessing fear of birth on the Fear of Birth Scale. Women Birth. Dec 19. pii: S1871-5192(15)00357-1. doi: 10.1016/j.wombi.2015.11.009
- 49. Thomas, J., Hildingsson, I. (2015). Chapter 12. Sweden. I Patricia Kennedy and Naonari Kodate (red.) Maternity Services and Policy in an International Context .

- 1. Ahman A, Axelsson O, Maras G, Rubertsson C, Sarkadi A, Lindgren P. Ultrasonographic fetal soft markers in a low-risk population: prevalence, association with trisomies and invasive tests. Acta Obstet Gynecol Scand. 2014 Apr;93(4):367-73.
- 2. Andersson E, Christensson K, Hildingsson I. Swedish midwives' perspectives on group based antenatal care. International Journal of Childbirth 2014; 4: 240-249.

- 3. Backhausen, M., Ekstrand, M., Tydén, T., Magnussen, B., Shawe, J. et al. (2014). Pregnancy planning and lifestyle prior to conception and during early pregnancy among Danish women. European journal of contraception & reproductive health care, vol. 19, ss. 57-65
- 4. Baylis, R., Ewald, U., Gradin, M., Hedberg Nyqvist, K., Rubertsson, C. et al. (2014). First-time events between parents and preterm infants are affected by the designs and routines of neonatal intensive care units. Acta Paediatrica, vol. 103, ss. 1045-1052
- 5. Byrskog, U., Olsson, P., Essén, B., Allvin, M. (2014). Violence and reproductive health preceding flight from war: accounts from Somali born women in Sweden. BMC Public Health. Aug 30;14:892. doi: 10.1186/1471-2458-14-892
- Cato, K., Sylvén, S., Skalkidou, A., Rubertsson, C. (2014). Experience of the First Breastfeeding Session in Association with the Use of the Hands-On Approach by Healthcare Professionals: A Population-Based Swedish Study. Breastfeeding Medicine, vol. 9, ss. 294-300
- Contreras M, Zelaya Blandón E, Persson LA, Ekström EC. Consumption of highly processed snacks, sugar-sweetened beverages and child feeding practices in a rural area of Nicaragua. Matern Child Nutr. 2014 Aug 19. doi: 10.1111/mcn.12144. [Epub ahead of print
- 8. Darj E. Global helse og onkologi. Onkonytt 2014;1.
- Doherty T, Jackson D, Swanevelder S, Lombard C, Engebretsen IM, Tylleskär T, Goga A, Ekström EC, Sanders D; PROMISE EBF study group. Severe events in the first 6 months of life in a cohort of HIV-unexposed infants from South Africa: effects of low birthweight and breastfeeding status. Trop Med Int Health. 2014 Oct;19(10):1162-9.
- 10. Engebretsen IM, Jackson D, Fadnes LT, Nankabirwa V, Diallo AH, Doherty T, Lombard C, Swanvelder S, Nankunda J, Ramokolo V, Sanders D, Wamani H, Meda N, Tumwine JK, Ekström EC, Van de Perre P, Kankasa C, Sommerfelt H, Tylleskär T; PROMISE EBF-study group. Growth effects of exclusive breastfeeding promotion by peer counsellors in sub-Saharan Africa: the cluster-randomised PROMISE EBF trial. BMC Public Health. 2014 Jun 21;14:633.
- 11. Engebretsen IM, Nankabirwa V, Doherty T, Diallo AH, Nankunda J, Fadnes LT, Ekström EC, Ramokolo V, Meda N, Sommerfelt H, Jackson D, Tylleskär T, Tumwine JK; PROMISE-EBF study group. Early infant feeding practices in three African countries: the PROMISE-EBF trial promoting exclusive breastfeeding by peer counsellors. Int Breastfeed J. 2014 Nov 18;9:19.
- 12. Eriksson, E., Lindmark, G., Haddad, B., Axemo, P. (2014). Young people, sexuality, and HIV prevention within Christian faith communities in South Africa: a cross-sectional survey. Journal of religion and health, vol. 53, ss. 1662-1675
- 13. Gerhardsson, E., Nyqvist, K., Mattsson, E., Volgsten, H., Hildingsson, I. et al. (2014). The Swedish Version of the Breastfeeding Self-Efficacy Scale-Short Form: Reliability and Validity Assessment. Journal of Human Lactation, vol. 30, ss. 340-345
- 14. Grandahl, M., Oscarsson, M., Stenhammar, C., Nevéus, T., Westerling, R. et al. (2014). Not the right time: why parents refuse to let their daughters have the human papillomavirus vaccination. Acta Paediatrica, vol. 103, ss. 436-441
- 15. Grandahl, M., Tydén, T., Rosenblad, A., Oscarsson, M., Nevéus, T. et al. (2014). School nurses' attitudes and experiences regarding the human papillomavirus vaccination programme in Sweden: a population-based survey. BMC Public Health, . vol. 14, ss. 1-9
- 16. Henriksson, C., Larsson, M., Herlitz, J., Karlsson, J., Wernroth, L. et al. (2014). Influence of health-related quality of life on time from symptom onset to hospital arrival and the risk of readmission in patients with myocardial infarction. Open Heart, vol. 1, ss. e000051-
- 17. Hildingsson, I. (2014). Swedish couples' attitudes towards birth, childbirth fear and birth preferences and relation to mode of birth: A longitudinal cohort study. Sexual & Reproductive HealthCare, vol. 5, ss. 75-80
- Hildingsson, I., Andersson, E., Christensson, K. (2014). Swedish women's expectations about antenatal care and change overtime: A comparative study of two cohorts of women. Sexual & Reproductive HealthCare, vol. 5, ss. 51-57
- 19. Hildingsson, I., Haines, H., Johansson, M., Rubertsson, C., Fenwick, J. (2014). Childbirth fear in Swedish fathers is associated with parental stress as well as poor physical and mental health. Midwifery, vol. 30, ss. 248-254

- Hildingsson, I., Johansson, M., Fenwick, J., Haines, H., Rubertsson, C. (2014). Childbirth fear in expectant fathers: Findings from a regional Swedish cohort study. Midwifery, vol. 30, ss. 242-247
- 21. Hildingsson, I., Thomas, J. (2014). Parental stress in mothers and fathers one year after birth. Journal of Reproductive and Infant Psychology, vol. 32, ss. 41-56
- Höglund, B., Larsson, M. (2014). Professional and social support enhances maternal well-being in women with intellectual disability: a Swedish interview study. Midwifery, vol. 30, ss. 1118-1123
- Jansen J. P, Jong M, Hildingsson I, Jong, M. C. (2014). A Minimum Protocol for a Randomised Homeopathic Drug Proving as basis for further research. Research in Complementary Medicine, 21(4), 232-238.
- 24. Johansson, M., Hildingsson, I., Fenwick, J. (2014). 'As long as they are safe Birth mode does not matter' Swedish fathers' experiences of decision-making around caesarean section. Women and Birth, vol. 27, ss. 208-213
- 25. Jordal M, Essén B, Wijewardena K, Öhman A. Olsson P. Negotiating respectability: Migrant women workers' perceptions on relationships and sexuality in Free Trade Zones in Sri Lanka. Health Care Women Int. 2014;35(6):658-76.
- Jordal, M., Wijewardena, K., Öhman, A., Essén, B., Olsson, P. (2014). Negotiating Respectability: Migrant Women Workers' Perceptions on Relationships and Sexuality in Free Trade Zones in Sri Lanka. Health Care for Women International, vol. 35, ss. 658-676
- 27. Larsson, M. (2014). Interventions during pregnancy and birth Call for papers. Sexual & Reproductive HealthCare, vol. 5, ss. 1-1.
- 28. Larsson, M. (2014). Interventions during pregnancy and childbirth Challenges and opportunities. Sexual & Reproductive HealthCare, vol. 5, ss. 159-159
- Litorp, H., Kidanto, H., Rööst, M., Abeid, M., Nyström, L. et al. (2014). Maternal near-miss and death and their association with caesarean section complications: a cross-sectional study at a university hospital and a regional hospital in Tanzania. BMC Pregnancy Childbirth. Jul 23;14:244. doi: 10.1186/1471-2393-14-244.
- Malm, M., Lindgren, H., Rubertsson, C., Hildingsson, I., Rådestad, I. (2014). Development of a tool to evaluate fetal movements in full-term pregnancy. Sexual & Reproductive HealthCare, vol. 5, ss. 31-35.
- Malm, M., Rådestad, I., Rubertsson, C., Hildingsson, I., Lindgren, H. (2014). Women's experiences of two different self-assessment methods for monitoring fetal movements in fullterm pregnancy: a crossover trial. BMC Pregnancy Childbirth. 2014 Oct 7;14:349. doi: 10.1186/1471-2393-14-349.
- 32. Mattebo, M., Grün, N., Rosenblad, A., Larsson, M., Häggström-Nordin, E. et al. (2014). Sexual experiences in relation to HPV vaccination status in female high school students in Sweden. European journal of contraception & reproductive health care, vol. 19, ss. 86-92
- Mattebo, M., Larsson, M., Tydén, T., Häggström-Nordin, E. (2014). Professionals' perceptions of the effect of pornography on Swedish adolescents. Public Health Nursing, vol. 31, ss. 196-205
- Mattebo, M., Tydén, T., Häggström-Nordin, E., Nilsson, K., Larsson, M. (2014). Pornography and sexual experiences among high school students in Sweden. Journal of Developmental and Behavioral Pediatrics, vol. 35, ss. 179-188
- 35. Nkonki LL, Daviaud E, Jackson D, Chola L, Doherty T, Chopra M, Robberstad B; Promise-EBF Study Group.Costs of promot ng exclusive breastfeeding at community level in three sites in South Africa.PLoS One. 2014 Jan 10;9(1):e79784.
- Nystedt, A., Hildingsson, I. (2014). Diverse definitions of prolonged labour and its consequences with sometimes subsequent inappropriate treatment. BMC Pregnancy Childbirth. 2014 Jul 16;14:233. doi: 10.1186/1471-2393-14-233.
- Nystedt A, Kristiansen L, Ehrenstråle K, Hildingsson I. Exploring some Swedish women's experiences of support during childbirth. International Journal of Childbirth 2014; 4(3):183-190.

- Omer-Salim, A., Suri, S., Dadhich, J., Faridi, M., Olsson, P. (2014). Theory and social practice of agency in combining breastfeeding and employment: A qualitative study among health workers in New Delhi, India. Women and Birth, vol. 27, ss. 298-306
- Pallant, J., Haines, H., Hildingsson, I., Cross, M., Rubertsson, C. (2014). Psychometric evaluation and refinement of the Prenatal Attachment Inventory. Journal of Reproductive and Infant Psychology, vol. 32, ss. 112-125
- Radestad, I., Malm, M., Lindgren, H., Pettersson, K., Larsson, L. (2014). Being alone in silence - Mothers' experiences upon confirmation of their baby's death in utero. Midwifery. Mar;30(3):e91-5. doi: 10.1016/j.midw.2013.10.021
- 41. Rubertsson, C., Hellström, J., Cross, M., Sydsjö, G. (2014). Anxiety in early pregnancy: prevalence and contributing factors. Archives of Women's Mental Health, vol. 17, ss. 221-228
- 42. Rydbeck F, Rahman A, Grandér M, Ekström EC, Vahter M, Kippler M. Maternal urinary iodine concentration up to 1.0 mg/L is positively associated with birth weight, length, and head circumference of male offspring. J Nutr. 2014 Sep;144(9):1438-44.
- 43. Shawe J, Delbaere I, Ekstrand M, Hegaard HK, Larsson M, Mastroiacovo P, Stern J, Steegers E, Stephenson J, Tydén T. Preconception care policy, guidelines, recommendations and services across six European countries: Belgium (Flanders), Denmark, Italy, the Netherlands, Sweden and the United Kingdom. Eur J Contracept Reprod Health Care. 2014 Dec 30:1-11. 37.
- 44. Sjöblom I, Idvall E, Lindgren H and The Nordic Homebirth research group#. Creating a safe haven - Women's experiences of the midwife's professional skills during planned home birth in four Nordic countries. Birth 2014; 41(1):100-107. #Nordic Homebirth Reserach group members in alphabetic order: Ellen Blix, Norway, Olof Asta Olafsdottir, Inceland, Karen Ingversen, Denmark, Ingegerd Hildingsson, Sweden, Ingela Rådestad, Sweden, Ingela Lundgren, Sweden, Anette Huitfeldt, Noway, Hanne Kjaergaard, Denmark, Ingela Sjöblom, Sweden and Helena Lindgren, Sweden
- 45. Talungchit, P., Liabsuetrakul, T., Lindmark, G. (2014). Multifaceted intervention to implement indicators of quality of care for severe pre-eclampsia/eclampsia. International Journal of Gynecology & Obstetrics, vol. 124, ss. 106-111
- 46. Wiberg-Itzel, E., Pembe, A., Wray, S., Wihlbäck, A., Darj, E. et al. (2014). Level of lactate in amniotic fluid and its relation to the use of oxytocin and adverse neonatal outcome. Acta Obstetricia et Gynecologica Scandinavica, vol. 93, ss. 80-85
- 47. Ziaei S, Naved RT, Ekström EC. Women's exposure to intimate partner violence and child malnutrition: findings from demographic and health survey in Bangladesh, Matern Child Nutr. 2014 Jul;10(3):347-59.
- 48. Ziaei S, Contreras M, Zelaya Blandón E, Persson LA, Hjern A, Ekström EC Women's autonomy and social support and their associations with infant and young child feeding and nutritional status: community-based survey in rural Nicaragua. Public Health Nutr. 2014 Nov 20:1-12.

#### Dissertations 2016

- 1. Hjördis Högberg (lic.)
- 2. Mari-Cristin Malm
- 3. Furaha August

#### Agencies that support the work/Funding

ALF 2 384 617 VR 1 000 000 Promobilia 300 000 Sveriges Lantbruksuniv 370 262 Familjeplaneringsfonden 235 000 Aga Khan University, Tz 127 200 Gillbergska 100 000

## Reproductive Health and Healthcare

#### Child Birth related fear

#### PI: Ingegerd Hildingsson and Christine Rubertsson

Childbirth related fear (CBRF) is a growing area of concern. All women in Sweden are offered counseling for such fear, although the effect of the treatment is unknown. Following a prevalence study, a randomized controlled trial comparing two different treatments of CBRF; standard care and internet-based cognitive behavioral treatment are ongoing. Recently a clinical study has been introduced where fearful women will have additional support in terms of having a known midwife at birth.

#### Dysfunctional labour in a National Hospital in Dar es Salaam

#### PI: Elisabeth Darj

In this project at Muhimbili National Hospital in Tanzania we analysed lactate in amniotic fluid in 1000 women. The aim was to test the hypothesis, that if lactate levels are low, it is possible to attain a normal vaginal delivery by augmentation of labour with oxytocin. It was also investigated whether high levels of lactate indicate an increased risk of caesarean section.

## Home based lifesaving skill education within maternal and newborn care in Tanzania

#### PI: Elisabeth Darj and Pia Axemo

The study was a cluster randomised structured education intervention to investigate the impact of community based education on knowledge and behaviour in seeking professional care for mother and child during pregnancy and birth. Furthermore, the involvement of men during pregnancy and birth and the views of health care workers have been studied.

#### Preconception health and care

#### PI: Margareta Larsson and Tanja Tydén

Preconception care aims to improve pregnancy outcomes and women's health in general through prevention of disease and management of risk factors. A longitudinal survey on life style and health, the Swedish Pregnancy Planning Study is on-going in collaboration with partners in Sweden and Europe (the PrePreg Network). Parents' interest in Preconception Genetic Carrier Screening is investigated as well as satisfaction with the couple relationship after childbirth. Fertility awareness is measured among young adults. The Reproductive Life Plan (RLP) is a plan for having children or not and how to achieve these goals. Studies among women and men using the RLP are ongoing. An RLP-web page is developed and will be evaluated.

#### Intervention to improve post partum care in Tanzania PI: Pia Olsson

Maternal and infant mortality in Tanzania is highest during the postnatal period, when care is weakest. This intervention project is a pre and post comparison assessment of a low-cost, participatory, facility based model for improving quality in postpartum care in Ilala District, Dar se

# Sexual/reproductive health among young people with intellectual disability – the health of their children

Salaam, Tanzania. The project is a collaboration with Aga Khan University, Tanzania.

### PI: Margareta Larsson and Berit Höglund

Women with intellectual disability (ID) and their children are risk groups. We have reported increased health risks among children born to mothers with ID. Interview studies regarding sexual health and reproduction among young adults with ID are ongoing. Professionals have been be interviewed and parents and young individuals will also be interviewed. A randomized intervention study will evaluate the effect of using a specially designed toolkit and a Real Care Baby simulator among students with ID.

## The quality of referrals of pregnant women in rural Tanzania

### PI: Elisabeth Darj

Women have little or no influence following the advice from the antenatal clinic to go to the hospital for delivery. In-depth-interviews of referred women or relatives to deceased women, who did not follow advice to go to the hospital for care have been performed.

## The midwife's dialogue about alcohol with parents-to-be

### PI: Margareta Larsson

The aim of the project is to evaluate a method about social and psychosocial support for an alcoholfree pregnancy and for responsible alcohol consumption during parenthood, involving both parentsto-be. It has also evaluated the feasibility of the implementation of such a method.

## School-based HPV vaccination

### PI: Maria Grandahl

HPV vaccination is in Sweden provided to 12-year old girls within the school-based vaccination program. Several studies are ongoing; follow up of an education intervention about HPV in high schools, school nurses attitudes and experiences of working with the program and young men's interest in HPV vaccination- a qualitative study.

## Prospective follow-up study five years after undergoing ART

### PI: Helena Volgsten

Undergoing assisted reproductive technology (ART) treatment is a psychological burden for infertile couples according to our baseline study. A longitudinal cohort study was undertaken to describe live birth outcome, spontaneous pregnancies and adoption and to assess mood disorders up to five years after ART, to evaluate if there was any difference in mood disorders in women and men if living with or without children.

## Sexual Health and Rights

#### **Clitoris reconstruction after Female Genital Mutilation**

#### **PI: Malin Jordal**

Female genital mutilation/cutting (FGM/C) is a violation of girls' and women's human rights and may involve several health consequences. An estimate of 38 000 girls and women living in Sweden may have undergone FGM/C. Reconstructive surgery of the clitoris is recently introduced in Sweden, but has long been available in Burkina Faso. The effects of such surgery are still unclear. In-depth interviews with women who request a clitoris reconstruction surgery are ongoing.

#### Pornography, youth and health

#### **PI: Margareta Larsson**

A prospective longitudinal questionnaire study among 800 high school students showed that pornography has become a part of everyday life for many adolescents and the use is associated with some risky behaviours and sexual preoccupanccy. In the longitudinal analyses frequent use of pornography was more associated to psychosomatic symptoms compared with depressive symptoms.

#### Sri Lankan males perspectives of Gender Based Violence

#### PI: Pia Axemo, Elisabeth Darj and Gunilla Lindmark

The **aim** of study is to investigate male university student's perception on GBV, male dominance and female subordination and the willingness to actively engage in prevention of GBV in future occupations. Focus group interviews have been performed, and will serve as the base for a later intervention study.

#### Inclusive and culturally aligned sexual reproductive health and rights

#### PI: Beth Maina Ahlberg

Since most communities in developing countries juxtapose between their indigenous – and western health care systems, it is important to research where these two systems meet or diverge from each other. This project endeavours to facilitate Sexual Reproductive Health and Rights education through community-based participative action research and is a partnership between Northern Cape and Uppsala Universities.

#### Gender Mainstreaming

#### PI: Beth Maina Ahlberg

This project is collaboration between Universidade Eduardo Mondlane Mozambique, University of Zambeze, Mozambique and Uppsala University in developing competencies in higher education for gender equality, peacebuilding and gender sensitive research.

## Nutrition and Women's Health

### Initiation of breastfeeding

#### **PI Christine Rubertsson**

Although breastfeeding initiation rates in Sweden are high, the majority of women do not exclusively breastfeed for the six months recommended by WHO. The first breastfeeding session can be essential for continuation and duration of breastfeeding as well as professional and social support. The overall aim of this project is to increase knowledge about breastfeeding support. One study focuses on the very first breastfeeding session and the second on women's perceptions of what enabled them to continue breastfeeding for at least six months.

### A world on the move

#### PI: Beth-Maina Ahlberg

This project studies challenges and opportunities for HIV/AIDS/Tuberculosis care and prevention among immigrants from countries in Sub-Saharan Africa and another ethnographic study of war rape in Eastern Democratic Republic of Congo has been performed.

#### **Jigger infestation**

#### PI: Beth-Maina Ahlberg

This is a project with a transdisciplinary approach for understanding a visibly deforming but simultaneously invisible and neglected public health problem in the East African Region.

#### Pediatric Endocrinology

#### **Ingemar Swenne**

Our research in the field of pediatric endocrinology contributes to the understanding of how hormones and nutrition influences metabolism, growth and development before birth and during infancy, childhood and puberty and how pertubations of development influences adult health.

We study conditions causing intrauterine growth retardation and increased fetal growth. The substrate metabolism of such newborn infants is studied. In Swedish registers we study how conditions at birth are associated with growth, intellectual performance and development of disease in adulthood. Eating disorders are known to influence growth and pubertal development and the endocrine and metabolic consequences of anorexia nervosa are studied. Obesity during childhood, which represents a globally increasing problem is studied in large cohorts of obese children in the projects ULSCO and Beta JUDO. Aspects of type 1 diabetes during childhood are also studied with focus on neurodevelopmental problems and metabolic control and on weight gain during treatment and remaining endogenous insulin production. Endocrine aspects of Down's syndrome and its association with neuropsychiatric disease are studied.

#### Members of the group during 2016

Swenne, Ingemar, Senior lecturer, Associate professor Ahlsson, Fredrik, MD, Associate professor Ciba, Iris MD, Doctoral student Diderholm, Barbro, MD, PhD Forslund, Anders MD, PhD Gebre-Medhin, Mehari, Professor em Grönberg, Annika MD, Doctoral student Gustafsson, Jan, Senior Professor Halldin-Stenlid, Maria, MD, PhD Hedberg Nykvist, Kerstin, RN, Associate professor Heyman, Maria, MD Lundgren, Maria, MD, PhD Lundqvist, Thomas, MD Myrelid, Åsa MD, PhD Nylander, Charlotte MD, PhD Proos, Lemm MD, PhD Staaf, Johan, MD, Doctoral student Strand-Brodd, Katarina, MD, PhD Tindberg, Ylva. MD, PhD, Associate professor Tuvemo, Torsten. Professor em Wahlström Jonsson, Inger MD, Doctoral student Wester Oxelgren, Ulrika MD, Doctoral student

#### Publications 2014-2016

#### 2016

 Andersson AK, Martin L, Strand Brodd K, Almqvist L. Predictors for everyday functioning in preschool children born preterm and at term. Early Hum Dev. 2016;103:147-53. doi: 10.1016/j.earlhumdev.2016.09.011.

- Albertsson-Wikland K, Mårtensson A, Sävendahl L, Niklasson A, Bang P, Dahlgren J, Gustafsson J, Kriström B, Norgren S, Pehrsson NG, Odén A .Mortality Is Not Increased in Recombinant Human Growth Hormone-treated Patients When Adjusting for Birth Characteristics. J Clin Endocrinol Metab. 2016;101:2149-59. doi: 10.1210/jc.2015-3951.
- Dalin F, G. Nordling Eriksson, P. Dahlqvist, Å. Hallgren, J. Wahlberg, O. Ekwall, S. Söderberg, J. Rönnelid, P. Olcén, O. Winqvist, S-B. Catrina, T. Olsson, B. Kriström, M. Laudius, M. Isaksson, M. Halldin Stenlid, J. Gustafsson, G. Gebre-Medhin, S. Björnsdottir, A. Janson, R. Zetterström, A-K. Åkerman, J. Åman, K. Duchen, R. Bergthorsdottir, G. Johannsson, E. Lindskog, M. Landin-Olsson, M. Elfving, E. Waldenström, J. Svensson, K. Link, A-L. Hulting, O. Kämpe, S. Bensing. Clinical and immunological characteristics of Autoimmune Addison's disease in Sweden: a nationwide multicenter analysis of 660 patients. J Clin Endocrinol Metab 2016; doi: jc20162522. [Epub ahead of print]
- Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Body Mass Index, Overweight, and Obesity in Swedish Women Born Post-term.Paediatr Perinat Epidemiol. 2016;30:320-4. doi: 10.1111/ppe.12292.
- Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women. PLoS One. 2016;11:e0154304. doi: 10.1371/journal.pone.0154304.
- 6. Derraik JG, Ahlsson F, Lundgren M, Jonsson B, Cutfield WS. First-borns have greater BMI and are more likely to be overweight or obese: a study of sibling pairs among 26,812 Swedish women. J Epidemiol Community Health. 2016;70:78-81. doi: 10.1136/jech-2014-205368.
- Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Association Between Preterm Birth and Lower Adult Height in Women. Am J Epidemiol. 2017;185:48-53. doi: 10.1093/aje/kww116. [Epub 2016 Dec 9]
- Fahnehjelm KT, Liu Y, Olsson D, Amrén U, Haglind CB, Holmström G, Halldin M, Andreasson S, Nordenström A. Most patients with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency develop pathological or subnormal retinal function..Acta Paediatr. 2016;105:1451-1460. doi: 10.1111/apa.13536.
- 9. Grönberg A, Swenne I. Recovery of premorbid BMI trajectory without overshoot during the first year of treatment of children with type 1 diabetes. BMJ Open Diabetes Res Care. 2016:26;4:e000209. doi: 10.1136/bmjdrc-2016-000209.
- Landegren N, Sharon D, Freyhult E, Hallgren Å, Eriksson D, Edqvist PH, Bensing S, Wahlberg J, Nelson LM, Gustafsson J, Husebye ES, Anderson MS, Snyder M, Kämpe O. Proteome-wide survey of the autoimmune target repertoire in autoimmune polyendocrine syndrome type 1. Sci Rep. 2016;6:20104. doi: 10.1038/srep20104.
- 11. Landegren N, Pourmousa Lindberg M, Skov J, Hallgren Å, Eriksson D, Lisberg Toft-Bertelsen T, MacAulay N, Hagforsen E, Räisänen-Sokolowski A, Saha H, Nilsson T, Nordmark G, Ohlsson S, Gustafsson J, Husebye ES, Larsson E, Anderson MS, Perheentupa J, Rorsman F, Fenton RA, Kämpe O. Autoantibodies Targeting a Collecting Duct-Specific Water Channel in Tubulointerstitial Nephritis. J Am Soc Nephrol. 2016;27:3220-3228. Epub 2016 Mar 16.
- Lucas S, Jernbro C, Tindberg Y, Janson S. Bully, bullied and abused. Associations between violence at home and bullying in childhood. Scand J Public Health. 2016;44:27-35. doi: 10.1177/1403494815610238.
- Manell H, Staaf J, Manukyan L, Kristinsson H, Cen J, Stenlid R, Ciba I, Forslund A, Bergsten P. Altered Plasma Levels of Glucagon, GLP-1 and Glicentin During OGTT in Adolescents With Obesity and Type 2 Diabetes. J Clin Endocrinol Metab. 2016;101:1181-9. doi: 10.1210/jc.2015-3885.
- Massad S, Deckelbaum RJ, Gebre-Medhin M, Holleran S, Dary O, Obeidi M, Bordelois P, Khammash U. Double Burden of Undernutrition and Obesity in Palestinian Schoolchildren: A Cross-Sectional Study. Food Nutr Bull. 2016;37:144-52. doi: 10.1177/0379572116637720.
- 15. Oras P, Thernström Blomqvist Y, Hedberg Nyqvist K, Gradin M, Rubertsson C, Hellström-Westas L, Funkquist EL. Skin-to-skin contact is associated with earlier breastfeeding attainment in preterm infants. Acta Paediatr. 2016;105:783-9. doi: 10.1111/apa.13431.

- Norlin M, J. Lundqvist, M. Ellfolk, M. Hellström Pigg, J. Gustafsson, and K. Wikvall. Drug-Mediated Gene Regulation of Vitamin D3 Metabolism in Primary Human Dermal Fibroblasts. Basic Clin Pharmacol Toxicol. 2016; doi: 10.1111/bcpt.12641. [Epub ahead of print]
- 17. Nylander C. Protective factors, health-risk behaviours and the impact of coexisiting ADHD among adolescents with diabete and other chronic conditions. Thesis. Digital Comprensive Summaries of Uppsdala Dissertatiosn from the Faculty of Medicine. 2016;1213:1-75.
- 18. Paulmichl K, Hatunic M, Højlund K, Jotic A, Krebs M, Mitrakou A, Porcellati F, Tura A, Bergsten P, Forslund A, Manell H, Widhalm K, Weghuber D, Anderwald CH; Beta-JUDO Investigators; RISC Investigators. Modification and Validation of the Triglyceride-to-HDL Cholesterol Ratio as a Surrogate of Insulin Sensitivity in White Juveniles and Adults without Diabetes Mellitus: The Single Point Insulin Sensitivity Estimator (SPISE). Clin Chem. 2016;62:1211-9. doi: 10.1373/clinchem.2016.257436.
- 19. Rosling A, Salonen Ros H, Swenne I. One-year outcome and incidence of anorexia nervosa and restrictive eating disorders among adolescent girls treated as out-patients in a family-based setting. Ups J Med Sci. 2016;121:50-9. doi: 10.3109/03009734.2016.1141810.
- Sjöström E S, Öhlund I, Ahlsson F, Domellöf M. Intakes of Micronutrients are Associated with Early Growth in Extremely Preterm Infants - A Population-Based Study.. J Pediat Gastroenterol Nutr. 2016;62:885-92.
- Solstrand Dahlberg L, Wiemerslage L, Swenne I, Larsen A, Stark J, Rask-Andersen M, Salonen-Ros H, Larsson EM, Schiöth HB, Brooks SJ. Adolescents newly diagnosed with eating disorders have structural differences in brain regions linked with eating disorder symptoms. Nord J Psychiatr. 2017 Apr;71(3):188-196. doi: 10.1080/08039488.2016.1250948. [Epub 2016 Nov 15]
- 22. Späth C, Sjöström ES, Ahlsson F, Ågren J, Domellöf M. Sodium supply influences plasma sodium concentration and the risks of hyper- and hyponatremia in extremely preterm infants. Pediatr Res. 2017;81:455-460. doi: 10.1038/pr.2016.264. [Epub 2016 Dec 9]
- Staaf J, Ubhayasekera SJ, Sargsyan E, Chowdhury A, Kristinsson H, Manell H, Bergquist J, Forslund A, Bergsten P. Initial hyperinsulinemia and subsequent β-cell dysfunction is associated with elevated palmitate levels. Pediatr Res. 2016;80:267-74. doi: 10.1038/pr.2016.80.
- 24. Swenne I. Plasma cholesterol is related to menstrual status in adolescent girls with eating disorders and weight loss. Acta Paediatr. 2016;105:317-23. doi: 10.1111/apa.13258.
- 25. Swenne I. Evaluation of the Compulsive Exercise Test (CET) in Adolescents with Eating Disorders: Factor Structure and Relation to Eating Disordered Psychopathology. Eur Eat Disord Rev. 2016;24:334-40. doi: 10.1002/erv.2439.
- 26. Swenne I. Influence of premorbid BMI on clinical characteristics at presentation of adolescent girls with eating disorders. BMC Psychiatry. 2016;16:81. doi: 10.1186/s12888-016-0788-7.
- Wackernagel D, Dube M, Blennow M, Tindberg Y. Continuous subcutaneous glucose monitoring is accurate in term and near-term infants at risk of hypoglycaemia. Acta Paediatr. 2016;105:917-23. doi: 10.1111/apa.13479.
- 28. Wallin U, Swenne I. Tidig viktuppgång vid anorexia nervosa ger god prognos Intensiv familjebaserad behandling ger bäst resultat. Lakartidningen. 2016;113. pii: DWWX.
- Wester Oxelgren U, Myrelid Å, Annerén G, Ekstam B, Göransson C, Holmbom A, Isaksson A, Åberg M, Gustafsson J, Fernell E. Prevalence of autism and attention-deficit-hyperactivity disorder in Down syndrome: a population-based study. Dev Med Child Neurol. 2017;59:276-283. doi: 10.1111/dmcn.13217. [Epub 2016 Aug 19]

#### 2015

1. Ahlsson F, Åkerud H, Schijven D, Olivier J, Sundström Poromaa I. Gene Expression in Placentas From Nondiabetic Women Giving Birth to Large for Gestational Age Infants. Reproduct Sci. 2015;22:1281-88.

- 2. Ahlsson F, Kaijser M, Adami J, Lundgren M, Palme M. School performance after preterm birth. Epidemiology. 2015;26:106-11.
- 3. Chaplin J E, Kristrom B, Jonsson B, Tuvemo T, Albertsson-Wikland K. Growth Hormone Treatment Improves Cognitive Function in Short Children with Growth Hormone Deficiency. Hormne Res Paediatr. 2015;83:390-99.
- 4. Chiavaroli V, Cutfield W S, Derraik J G, Pan Z, Ngo S, Sheppard A, et al. Infants born largefor-gestational-age display slower growth in early infancy, but no epigenetic changes at birth. Sci Rep. 2015;5:14540.
- 5. Derraik J G, Ahlsson F, Diderholm B, Lundgren M. Obesity rates in two generations of Swedish women entering pregnancy, and associated obesity risk among adult daughters. Scientific Reports. 2015;5:16692.
- 6. Ellonen N, Jernbro C, Janson S, Tindberg Y, Lucas S. Current parantal attitudes towards upbringing practices in Finland and Sweden thirty years afer the ban on corporal punishment. Child Abuse Rev. 2015:24:409-17.
- Freda P U, Gordon M B, Kelepouris N, Jonsson P, Koltowska-Häggström M, van der Lely A J. Long-Term Treatment with Pegvisomant as Monotherapy in Patients with Acromegaly: Experience from Acrostudy. Endocrine Pract. 2015;21:264-74.
- Gardner C J, Mattsson A F, Daousi C, Korbonits M, Koltowska-Häggström M, Cuthbertson D J. GH deficiency after traumatic brain injury: improvement in quality of life with GH therapy: analysis of the KIMS database. Eur J Endocrinol. 2015;172:371-81.
- Haglind C B, Nordenström A, Ask S, von Döbeln U, Gustafsson J, Stenlid M H. Increased and early lipolysis in children with long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency during fast. J Inher Metab Dise. 2015;38:315-22.
- 10. Haglind C B, Ask S, von Dobeln U, Engvall M, Ekblom O, Stenlid M H, et al. Energy expenditure and lipid metabolism in very long-chain Acyl-CoA dehydrogenase (VLCAD) deficiency. Mol Gen Metab 2015;114:333.
- 11. Hansson T, Dahlbom I, Tuvemo T, Frisk G. Silent coeliac disease is over-represented in children with type 1 diabetes and their siblings. Acta Paediatr. 2015;104:185-91.
- 12. Jernbro C, Tindberg Y, Lucas S, Janson S. Quality of life among Swedish school children who experienced multi-type child maltreatment. Acta Paediatrica. 2015;104:320-25.
- 13. Johnsson IW, Haglund B, Ahlsson F, Gustafsson J. A high birth weight is associated with increased risk of type 2 diabetes and obesity. Pediatric Obesity. 2015;10(2):77-83.
- 14. Landegren N, Sharon D, Shum A K, Khan I S, Fasano K J, Hallgren Å, et al. Transglutaminase 4 as a prostate autoantigen in male subfertility. Sci Transl Med. 2015;7:292ra101.
- van der Lely AJ, Gomez R, Heissler J F, Åkerblad A, Jönsson P, Camacho-Hübner C, et al. Pregnancy in acromegaly patients treated with pegvisomant. Endocrine (Basingstoke). 2015;49:769-73.
- 16. Lindblad F, Eickhoff M, Forslund A H, Isaksson J, Gustafsson J. Fasting blood glucose and HbA1c in children with ADHD. Psychiat Res. 2015;226:515-16.
- Mattsson E, Funkquist E, Wickström M, Nyqvist K H, Volgsten H. Healthy late preterm infants and supplementary artificial milk feeds: Effects on breast feeding and associated clinical parameters. Midwifery. 2015;31:426-31.
- 18. Nylander C, Fernell E, Tindberg Y. Chronic conditions and coexisting ADHD-a complicated combination in adolescents. Eur J Pediatr. 2015;174:1209-15.
- 19. Nylander C, Tindberg Y, Fernell E. Risky sexual behaviour among adolescents may be related to ADHD. Acta Paediatr. 2015;104:E235-E235.

- Oras P, Thernström Blomqvist Y, Hedberg Nyqvist K, Gradin M, Rubertsson C, Hellström-Westas L, et al. Breastfeeding Patterns in Preterm Infants Born at 28-33 Gestational Weeks. J Hum Lactation. 2015;31:377-85.
- 21. Swenne I, Stridsberg M. Bone metabolism in adolescent girls with eating disorders and weight loss : independent effects of weight change, insulin-like growth factor-1 and oestradiol. Eating and Weight Disorders. 2015;20:33-41.
- 22. Tollerz L U, Forslund A H, Olsson R M, Lidström H, Holmbäck U. Children with cerebral palsy do not achieve healthy physical activity levels. Acta Paediatr. 2015;104:1125-29.
- 23. Welch E, Ghaderi A, Swenne I. A comparison of clinical characteristics between adolescent males and females with eating disorders. BMC Psychiatry. 2015;15:45.
- 24. Wikiera B, Mulak M, Koltowska-Häggström M, Noczynska A. The presence of eye defects in patients with Turner syndrome is irrespective of their karyotype. Clin Endocrinol. 2015;83:842-48.

- 1. Albertsson-Wikland K, Kriström B, Lundberg E, Aronson A S, Gustafsson J, Hagenäs L et al. Growth hormone dose-dependent pubertal growth: a randomized trial in short children with low growth hormone secretion. Horm Res Paediatr. 2014;82:158-170.
- 2. Baylis R, Ewald U, Gradin M, Hedberg Nyqvist K, Rubertsson C, Thernström Blomqvist Y. First-time events between parents and preterm infants are affected by the designs and routines of neonatal intensive care units. Acta Paediatr. 2014;103:1045-52.
- Benyi E, Kieler H, Linder M, Ritzén M, Carlstedt-Duke J, Tuvemo T, Westphal O, Sävendahl L. Risks of malignant and non-malignant tumours in tall women treated with high-dose oestrogen during adolescence. Horm Res Paediatr. 2014;82:89-96
- 4. Brooks SJ, Solstrand Dahlberg L, Swenne I, Aronsson M, Zarei S, Lundberg L, Jacobsson JA, Rask-Andersen M, Salonen-Ros H, Rosling A, Larsson EM, Schiöth HB. Obsessive-compulsivity and working memory are associated with differential prefrontal cortex and insula activation in adolescents with a recent diagnosis of an eating disorder. Psychiatr Res. 2014;224:246-53.
- Freda P U, Gordon M B, Kelepouris N, Jonsson P, Koltowska-Häggström M, van der Lely A J. Long-Term Treatment with Pegvisomant as Monotherapy in Patients with Acromegaly: Experience from Acrostudy. Endocrine Pract. 2014;1-32.
- 6. Gerhardsson E, Nyqvist K H, Mattsson E, Volgsten H, Hildingsson I, Funkquist E. The Swedish Version of the Breastfeeding Self-Efficacy Scale-Short Form: Reliability and Validity Assessment. J Hum Lactation. 2014;30:340-45.
- Jonsson P, Jonsson B, Eeg-Olofsson O. Psychological and social outcome of epilepsy in wellfunctioning children and adolescents. A 10-year follow-up study. European J Paediatr Neur. 2014;18:381-90.
- Koltowski L, Koltowska-Häggström M, Filipiak K J, Kochman J, Golicki D, Pietrasik A, et al. Quality of Life in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention-Radial Versus Femoral Access (from the OCEAN RACE Trial). Am J Cardiol. 2014;114:516-21
- 9. Lundgren M, Morgården E, Gustafsson J. Is obesity a risk factor for impaired cognition in young adults with low birth weight? Pediatr Obesity. 2014;9:319-26.

- 10. Merks P, Kazmierczak J, Olszewska A E, Koltowska-Häggström M. Comparison of factors influencing patient choice of community pharmacy in Poland and in the UK, and identification of components of pharmaceutical care. Patient Preference and Adherence. 2014;8:715-26.
- 11. Nylander C, Seidel C, Tindberg Y. The triply troubled teenager chronic conditions associated with fewer protective factors and clustered risk behaviours. Acta Paediatr. 2014;103:194-200.
- 12. Proos L A, Gustafsson J, Tuvemo T. Catch-up growth following undernutrition a risk factor for early puberty in internationally adopted children. Pediatrics. 2014;
- 13. Ragnarsson O, Mattsson A F, Monson J P, Filipsson Nyström H, Akerblad A, Koltowska-Häggström M, et al. The relationship between glucocorticoid replacement and quality of life in 2737 hypopituitary patients. European Journal of Endocrinology. 2014;171:571-79.
- 14. Reinehr T, Lindberg A, Koltowska-Häggström M, Ranke M. Is growth hormone treatment in children associated with weight gain? Longitudinal analysis of KIGS data. Clin Endocrinol. 2014;81:721-26.
- 15. Ridefelt P, Gustafsson J, Aldrimer M, Hellberg D. Alkaline phosphatase in healthy children: reference intervals and prevalence of elevated levels. Horm Res Paediatr. 2014;82:399-404.
- 16. Ridefelt P, Hellberg D, Aldrimer M, Gustafsson J. Estimating reliable paediatric reference intervals in clinical chemistry and haematology. Acta Paediatr. 2014;103:10-15.
- Skogberg G, Lundberg V, Lindgren S, Gudmundsdottir J, Sandström K, Kämpe O, Annerén G, Gustafsson J, Sunnegårdh J, van der Post S, Telemo E, Berglund M, Ekwall O. Altered Expression of Autoimmune Regulator in Infant Down Syndrome Thymus, a Possible Contributor to an Autoimmune Phenotype. J Immunol. 2014;193:2187-95.
- 18. Stenlid M H, Ahlsson F, Forslund A H, von Döbeln U, Gustafsson J. Energy substrate metabolism in pyruvate dehydrogenase complex deficiency. J Pediatr Endocrinol Metab 2014;27:1059-64.
- 19. Strand H, Blomqvist Y T, Gradin M, Nyqvist K H. Kangaroo mother care in the neonatal intensive care unit: staff attitudes and beliefs and opportunities for parents. Acta Paediatr. 2014;103:373-78.
- 20. Tindberg Y. Handfasta råd för möte med ungdomar. In: Ungdomars hälsa, pp 44-45 Studentlitteratur; 2014.
- 21. Tindberg Y, Otterman G. Skador av våld på små barn tecken, handläggning och diagnostik. Läkartidningen. 2014;111:2098-101.
- 22. Westin V, Stoltz Sjöström E, Ahlsson F, Domellöf M, Norman M. Perioperative nutrition in extremely preterm infants undergoing surgical treatment for patent ductus arteriosus is suboptimal. Acta Paediatr. 2014;103:282-88.

#### **Dissertations 2016**

Nylander C. Protective factors, health-risk behaviours and the impact of coexisiting ADHD among adolescents with diabete and other chronic conditions. Thesis. Digital Comprensive Summaries of Uppsdala Dissertatiosn from the Faculty of Medicine. 2016;1213:1-75.

#### Agencies that support the work/Funding

Barndiabetesfonden Childhood Cancer Foundation Drottning Silvias jubileumsfond EU Exodiab First of May Flower Annual Campaign **Gillberg** Foundation HRH Crown Princess Lovisa's Fund Merck AB **Regional Research Council** Selanders Stiftelse Sven Jerring Foundation Stiftelsen samariten Sävstaholmsföreningen Wera Ekström stiftelse ALF

#### Energy substrate metabolism during infancy and childhood

#### Fredrik Ahlsson, Barbro Diderholm, Inger Wahlström Johnsson and Jan Gustafsson

After birth the newborn infant has to produce its own glucose to supply the brain with energy. Infants, born small as well as large for gestational age, are at risk for neonatal hypoglycemia but also metabolic disease later in life. Research is now directed towards the metabolism of infants, children and adults. Over recent years there has been an increase of birth weight associated with maternal overweight. Presently a line of research is now the long term metabolic and cardiovascular consequences of being born large for gestational age.

## Young adult outcome of infants born with extremely low birth weight (<1000 g).

#### Barbro Diderholm, Maria Heyman, Jan Gustafsson and Fredrik Ahlsson

Improvement in modern neonatal care has increased survival of preterm and extremely preterm infants over the last 2-3 decades. Few studies have assessed outcomes in adulthood of infants born extremely preterm or with extremely low birth weight. Studies based mainly on preterm infants with higher birth weights have shown that survivors of preterm birth have an increased risk of short- and long-term mental and physical health impairments as well as of educational underachievement. Preterm infants are more prone to develop impaired glucose tolerance, high blood pressure and cardiovascular and pulmonary disease during early years. A former Swedish cohort of extremely-low-birth-weight (ELBW <1000g) infants born 1990-1992 will be re-examined concerning their mental, cardio-vascular, pulmonary and metabolic health. The project is run together with dr Helena Grönkvist, U-Care and with professor Tord Naessen, Gynecological Endocrinology, professor Kjell Alving, Paediatric Inflammation Research and professor Fredrik Serenius, Neonatal Research group.

## Uppsala Longitudinal Study of Childhood Health and Disease (ULSCHED) – A pediatric cohort studying metabolic disease

#### Barbro Diderholm, Fredrik Ahlsson, Jan Gustafsson and Anders Forslund

A large number of children with obesity develop type 2 diabetes mellitus (T2DM) and other metabolic diseases. An important aspect of childhood obesity is the fact that mothers giving birth to children who develop overweight/obesity are often overweight/obese themselves. In order to develop strategies for early detection, prevention and intervention, it is necessary to study various biological mechanisms associated with obesity, metabolism and beta-cell function. The purpose of this study is to identify mechanisms, by which glucose, free fatty acids and amino acids stimulate insulin secretion, in some cases hypersecretion, in infancy and childhood, which may contribute to the development of obesity and, in some individuals, beta-cell failure leading to T2DM.

#### Childhood obesity

#### Anders Forslund and Johan Staaf

Overweight and obesity during childhood are major health problems both in Sweden and in a global perspective. The research groupof of the regional childhood obesity centre at Uppsala University Hospital has during 2017 completed the EU-sponsered project Beta-JUDO. The parallel study Combat-JUDO, started in 2016, is a double-blinded, randomized, 6-month study comparing lifestyle interventions + exenatide (a GLP 1-analoge) with lifestyle interventions + placebo in adolescents with obesity. The aim is to explore differences between the groups with regard to change in BMI. Studies of hypersecretion of insulin as a possible mechanism leading to childhood overweight and obesity are also ongoing in collaboration with professor Peter Bergsten, Department of Medical Cell Biology.

#### Register based studies on fetal origin of adult disease

#### Maria Lundgren, Jan Gustafsson, Inger Wahlström Johnson and Fredrik Ahlsson

We use Swedish registers for epidemiological studies - the Medical Birth Register, the Conscript Register, the Inpatient Care Register, the Drug Register and the Causes of Death Register. Circumstances during fetal life may influence morbidity during childhood and adult life. We have therefore studied effects of conditions during fetal life and childhood on growth, development of obesity and cognitive function in adulthood. We have demonstrated an association between overweight/obesity and impaired intellectual performance in young adults, particularly in those with a low birth weight. In collaboration with a group at University of Auckland studies on the effect of the intrauterine milieu for later life are ongoing. We have shown that first-borns are more likely to be overweight or obese in adulthood compared to their siblings. A study on school performance following preterm birth was performed in collaboration with Stockholm University. Studies on the effect of being born large for gestational age have pointed out long term risks for adult metabolic disease. An epidemiological project on development and health of children born to mothers with intellectual disability is ongoing in collaboration with the research group of International Sexual and Reproductive Health at our department.

#### Mechanisms behind precocious puberty

#### Lemm Proos, Margareta Dahl and Jan Gustafsson

Precocious puberty has for several years been a field of research in the group. Particularly girls with hydrocephalus and myelomeningocele are prone to develop early or precocious puberty. This may lead to practical and psychological problems in addition to those caused by the myelomeningocele.

In an ongoing project which is performed in collaboration with pediatric neurologist Margareta Dahl predictors for development of precocious puberty in cases of myelomeningocele and hydrocephalus are studied.

#### Down syndrome

#### Ulrika Wester Oxelgren, Åsa Myrelid and Jan Gustafsson

The pediatric endocrinology research group has for many years studied endocrine disease in Down syndrome (DS) in collaboration with professor Göran Annéren. Growth hormone secretion and effects of growth hormone treatment on growth and psychomotor performance has been studied. Causes of death in DS have been investigated i register studies. Presently the association between DS and neuropsychiatric disorders such as ADHD and ASD is studied in collaboration with professor Elisabeth Fernell, Univesity of Gothenburg. Within this project the prevalence of ADHD and ASD is investigated and the effect of pharmacological treatment of ADHD in people with DS is analysed.

#### Endocrine consequences of stem cell transplantation

#### Per Frisk, Anders Öberg and Jan Gustafsson

Individuals who have been treated with stem cell transplantation (SCT) during childhood due to hematological malignancies may develop metabolic disease later in life. In collaboration with associate professor Per Frisk, dr Anders Öberg and researchers in Stockholm we study long term effects of SCT on insulin sensitivity and parameters related to the metabolic syndrome.

#### Growth and endocrine function in eating disorders

#### Ingemar Swenne

At the Child and Adolescent Eating Disorders Unit adolescentss with eating disorders are treated according to a protocol, which enables continuous evaluation of the course of the disease and the outcome of treatment. Models for the prediction of growth, menarche and subsequent menstruations during the treatment of eating disorders have been created. Markers for bone accretion and breakdown are studied in relation to changes of weight changes and circulating hormones. In investigations of the relationship between somatic factors and psychiatric morbidity it has been possible to demonstrate how diet and weight changes influence thyroid hormones and essential fatty acids. The changes predispose for depression and thus influence the expression of the eating disorder. The effect of decisive interventions at the start of treatment have been evaluated. It has then been possible to show that forceful interventions by the parents at the very start of treatment influence outcome in a longer perspective. In an extensive collaborative study with professor Helgi Shiöth's group it has been possible to study brain function with functional magnetic resonance (fMRI) imaging and relate findings to eating disturbed psychopathology.

#### Inborn errors of metabolism

#### Maria Halldin, Thomas Lundqvist and Jan Gustafsson

Disorders of fatty acid oxidation are diseases, which impair energy production from  $\beta$ -oxidation of fatty acids. The patients risk organ accumulation of non-metabolized acylcarnitines, hypoglycemia and brain damage. In collaboration with Dept of Women's and Children's Health, Karolinska Institute we study growth, energy balance, neurocognitive outcome and long term complications of children with defects in the oxidation of long chain and very long chain fatty acids. A similar protocol is used for the investigation of patients with defects in the urea cycle (UCD). Such patients

risk brain damage and organ insufficiencies from hyperammonemia and focus is on their protein and energy metabolism.

#### Diabetes

#### Charlotte Nylander, Ylva Tindberg, Annika Grönberg and Ingemar Swenne

Factors influencing treatment adherence of adolescents with type 1 diabetes has been studied, particularly factors behind the development of risk behaviours. The importance of diagnosing poor executive functions, as in ADHD, is high-lighted since adherence to treatment may be influenced. The project is collaboration with with professor Elisabeth Fernell, University of Gothenburg.

In a further project on pediatric type 1 diabetes metabolic control, weight gain and remaining endogenous insulin production are studied. Weight gain during treatment is analysed and related to different aspects of insulin therapy and metabolic control. Remaining endogenous insulin production, which may protect against long-term complications of diabetes, is analysed by use of an ultrasensitive C-peptide assay and related to insulin treatment, metabolic control and genetic predisposition.

#### Perinatal, Neonatal and Paediatric Cardiology Research

#### Lena Hellström-Westas

The perinatal, neonatal and paediatric cardiology research group spans over a broad research field but has a main focus on perinatal outcomes and neonatal intensive care of term and preterm infants, which includes neurocritical care and studies of brain physiology (EEG, NIRS, vision), cardiology and lung physiology, pain and stress responses, skin-to-skin care and breast feeding.

#### Members of the group

Lena Hellström-Westas, Professor Fredrik Serenius, Guest professor Eva-Lotta Funkquist, RN, PhD, Senior lecturer Anders Jonzon, Associate professor Kristina Persson, Associate professor Ann Edner, MD, PhD Laszlo Markasz, MD, PhD Erik Normann, MD, PhD Richard Sindelar, MD, PhD Gunnar Sjörs, MD, PhD Ylva Thernström Blomqvist, RN, PhD Johan Ågren, MD, PhD Josanne Munsters. MD. Guest researcher Victoria Karlsson, RN, PhD student Ylva Fredriksson Kaul, MSc, PhD student Cecilia Montgomery, MSc, PhD student Karl Wilhelm Olsson, MD, PhD student Paola Oras, RN, PhD student Maria Stålhammar, MSc, PhD student Linda Wallström, MD, PhD student Nima Naseh, MD, PhD student

#### Publications 2014-2016

- Stålhammar ME, Sindelar R, Douhan Håkansson L. Neutrophil receptor response to bacterial N-formyl peptides is similar in term newborn infants and adults in contrast to IL-8. *Scand J Immunol* 2016; 84(6):332-337.
- 2. Stålhammar ME, Douhan Håkansson L, Jonzon A, Sindelar R. Differential neutrophil chemotactic response towards IL-8 and bacterial N-formyl peptides in term newborn infants. *Ups J Med Sci* 2017; 122(1):35-42.
- 3. Larsson C, Wågström U, Normann E, Thernström Blomqvist Y. Parents experiences of discharge readiness from a Swedish neonatal intensive care unit. *Nurs Open* 2016; 4(2):90-95.
- 4. Separation and Closeness Experiences in Neonatal Environment (SCENE) research group (incl Normann E). Parent and nurse perceptions on the quality of family-centred care in 11 European NICUs. *Aust Crit Care* 2016; 29(4):201-209.
- Shah PS, Lui K, Sjörs G, Mirea L, Reichman B, Adams M, Modi N, Darlow BA, Kusuda S, San Feliciano L, Yang J, Håkansson S, Mori R, Bassler D, Figueras-Aloy J, Lee SK; International Network for Evaluating Outcomes (iNeo) of Neonates. Neonatal outcomes of very low birth weight and very preterm neonates: an international comparison. *J Pediatr* 2016; 177:144-152.e6.

- 6. Späth C, Sjöström ES, Ahlsson F, Ågren J, Domellöf M. Sodium supply influences plasma sodium concentration and the risks of hyper- and hyponatremia in extremely preterm infants. *Pediatr Res* 2017; 81(3):455-460.
- 7. Karlsson V, Sporre B, Ågren J. Transcutaneous PCO2 Monitoring in Newborn Infants During General Anesthesia Is Technically Feasible. *Anesth Analg* 2016; 123(4):1004-7.
- Oras P, Thernström Blomqvist Y, Hedberg Nyqvist K, Gradin M, Rubertsson C, Hellström-Westas L, Funkquist EL. Skin-to-skin contact is associated with earlier breastfeeding attainment in preterm infants. *Acta Paediatr* 2016; 105(7):783-9.
- Ericson J, Flacking R, Hellström-Westas L, Eriksson M. Changes in the prevalence of breast feeding in preterm infants discharged from neonatal units: a register study over 10 years. *BMJ Open* 2016; 6(12):e012900.
- 10. Stevenson NJ, Boylan GB, Hellström-Westas L, Vanhatalo S. Treatment trials for neonatal seizures: the effect of design on sample size. *PLoS One* 2016;11(11):e0165693.
- 11. Andersson O, Hellström-Westas L, Domellöf M. Elective caesarean: does delay in cord clamping for 30 s ensure sufficient iron stores at 4 months of age? A historical cohort control study. *BMJ Open* 2016; 6(11):e012995.
- 12. Kaul YF, Rosander K, von Hofsten C, Brodd KS, Holmström G, Kaul A, Böhm B, Hellström-Westas L. Visual tracking in very preterm infants at 4 mo predicts neurodevelopment at 3 y of age. *Pediatr Res* 2016;80(1):35-42.
- 13. Weeke LC, Toet MC, van Rooij LG, Groenendaal F, Boylan GB, Pressler RM, Hellström-Westas L, van den Broek MP, de Vries LS. Lidocaine response rate in aEEG-confirmed neonatal seizures: Retrospective study of 413 full-term and preterm infants. *Epilepsia* 2016;57(2):233-42.
- 14. Nörby U, Forsberg L, Wide K, Sjörs G, Winbladh B, Källén K. Neonatal morbidity after maternal use of antidepressant drugs during pregnancy. *Pediatrics* 2016;138(5). pii: e20160181.
- Gemmell L, Martin L, Murphy KE, Modi N, Håkansson S, Reichman B, Lui K, Kusuda S, Sjörs G, Mirea L, Darlow BA, Mori R, Lee SK, Shah PS. Hypertensive disorders of pregnancy and outcomes of preterm infants of 24 to 28 weeks' gestation. *J Perinatol* 2016;36(12):1067-1072.
- 16. Martin LJ, Sjörs G, Reichman B, Darlow BA, Morisaki N, Modi N, Bassler D, Mirea L, Adams M, Kusuda S, Lui K, Feliciano LS, Håkansson S, Isayama T, Mori R, Vento M, Lee SK, Shah PS; International Network for Evaluating Outcomes (iNeo) of Neonates Investigators. Country-specific vs. common birthweight-for-gestational age references to identify small for gestational age infants born at 24-28 weeks: an international study. *Paediatr Perinat Epidemiol* 2016;30(5):450-61.
- Rysavy MA, Marlow N, Doyle LW, Tyson JE, Serenius F, Iams JD, Stoll BJ, Barrington KJ, Bell EF. Reporting outcomes of extremely preterm births. *Pediatrics* 2016;138(3): pii: e20160689.
- Serenius F, Ewald U, Farooqi A, Fellman V, Hafström M, Hellgren K, Maršál K, Ohlin A, Olhager E, Stjernqvist K, Strömberg B, Ådén U, Källén K; Extremely Preterm Infants in Sweden Study Group. Neurodevelopmental outcomes among extremely preterm infants 6.5 years after active perinatal care in Sweden. *JAMA Pediatr 2016*;170(10):954-963.
- 19. Holsti A, Adamsson M, Serenius F, Hägglöf B, Farooqi A. Two-thirds of adolescents who received active perinatal care after extremely preterm birth had mild or no disabilities. *Acta Paediatr* 2016;105(11):1288-1297.
- Hellgren KM, Tornqvist K, Jakobsson PG, Lundgren P, Carlsson B, Källén K, Serenius F, Hellström A, Holmström G. Ophthalmologic outcome of extremely preterm infants at 6.5 years of qge: Extremely Preterm Infants in Sweden Study (EXPRESS). *JAMA Ophthalmol* 2016 Mar 24. doi: 10.1001/jamaophthalmol.2016.0391. [Epub ahead of print]
- 21. Farooqi A, Adamsson M, Serenius F, Hägglöf B. Executive functioning and learning skills of adolescent children born at fewer than 26 weeks of gestation. *PLoS One* 2016;11(3):e0151819.

#### 2015

- 1. Andersson O, Lindquist B, Lindgren M, Stjernqvist K, Domellöf M, Hellström-Westas L. Delayed cord clamping improves fine motor skills at four years: follow-up of a randomized trial. *JAMA Pediatrics* 2015; 169: 631-8.
- 2. Olsson KW, Sindelar R. Future benefits of sequential echocardiography: Unmasking the indications for treatment of patent ductus arteriosus in extremely preterm infants. *Neonatology* 2015;108(2):99.
- 3. Steen E, Bonamy A-K, Norman M, Hellström-Westas L. Preterm birth may be a larger risk factor for increased blood pressure than intrauterine growth restriction. *Acta Paediatr* 2015:104:1098-103. (*Emma Elsmén Steen received Acta Paediatrica Young Investigator 2016 prize for this work*)
- 4. Iyer KK, Roberts JA, Hellström-Westas L, Wikström S, Hansen Pupp I, Ley D, Vanhatalo S, Breakspear M. Cortical burst dynamics predict clinical outcome early in extremely preterm infants. *Brain* 2015; 138:2206-18.
- Pressler RM, Boylan GB, Marlow N, Blennow M, Chiron C, Cross JH, de Vries LS, Hallberg B, Hellström-Westas L, et al ; NEonatal seizure treatment with Medication Off-patent (NEMO) consortium. Bumetanide for the treatment of seizures in newborn babies with hypoxic ischaemic encephalopathy (NEMO): an open-label, dose finding, and feasibility phase 1/2 trial. *Lancet Neurol* 2015; 14: 469-77.
- 6. Oras P, Blomqvist YT, Nyqvist KH, Gradin M, Rubertsson C, Hellström-Westas L, Funkquist EL. Breastfeeding patterns in preterm infants born at 28-33 gestational weeks. *J Hum Lact* 2015; 31:377-85.
- 7. Mattsson E, Funkquist EL, Wickström M, Nyqvist KH, Volgsten H. Healthy late preterm infants and supplementary artificial milk feeds: Effects on breast feeding and associated clinical parameters. *Midwifery* 2015; 31(4):426-31.
- 8. Hövel H, Partanen E, Tideman E, Stjernqvist K, Hellström-Westas L, Huotilainen M, Fellman V. Auditory event-related potentials are related to cognition at preschool age after very preterm birth. *Pediatr Res* 2015;77:570-8.
- 9. Iyer KK, Roberts JA, Hellström-Westas L, Wikström S, Hansen Pupp I, Ley D, Breakspear M, Vanhatalo S. Early detection of preterm intraventricular hemorrhage from clinical electroencephalography. *Crit Care Med* 2015;43:2219-27.
- 10. Carlsson T, Bergman G, Melander Marttala U, Wadensten B, Mattsson E. Information following a diagnosis of congenital heart defect: experiences among parents to prenatally diagnosed children. *PLoS One* 2015;10(2):e0117995.
- 11. Källén K, Serenius F, Westgren M, Maršál K; EXPRESS Group. Impact of obstetric factors on outcome of extremely preterm births in Sweden: prospective population-based observational study (EXPRESS). *Acta Obstet Gynecol Scand* 2015 Nov;94(11):1203-14.
- 12. Ohlin A, Björkman L, Serenius F, Schollin J, Källén K. Sepsis as a risk factor for neonatal morbidity in extremely preterm infants. *Acta Paediatr* 2015 Nov;104(11):1070-6.
- Serenius F, Blennow M, Maršál K, Sjörs G, Källen K; EXPRESS Study Group. Intensity of perinatal care for extremely preterm infants: outcomes at 2.5 years. *Pediatrics* 2015 May;135(5):e1163-72.
- 14. Dedinszki D, Kiss A, Márkász L, Márton A, Tóth E, Székely L, Erdődi F. Inhibition of protein phosphatase-1 and -2A decreases the chemosensitivity of leukemic cells to chemotherapeutic drugs. *Cell Signal* 2015 Feb;27(2):363-72.
- 15. Ander M, Grönqvist H, Cernvall M, Engvall G, Hedström M, Ljungman G, Lyhagen J, Mattsson E, von Essen L. Development of health-related quality of life and symptoms of anxiety and depression among persons diagnosed with cancer during adolescence: a 10-year follow-up study. *Psychooncology* 2015 Sep 10. doi: 10.1002/pon.3965. [Epub ahead of print]

#### 2014

1. Chetaille P, Preuss C, Burkhard S, .....Jonzon A, et al. Mutations in SGOL1 cause a novel cohesinopathy affecting heart and gut rhythm. *Nat Genet* 2014;46(11):1245-9.

- 2. Andersson O, Domellöf M, Andersson D, Hellström-Westas L. Effect of delayed vs early umbilical cord clamping on iron status and neurodevelopment at age 12 months: a randomized clinical trial. *JAMA Pediatr* 2014;168(6):547-54.
- 3. Jonsson M, Ågren J, Nordén Lindeberg S, Ohlin A, Hanson U. Suboptimal care and metabolic acidemia is associated with neonatal encephalopathy but not with neonatal seizures alone: A population based clinical audit. *Acta Obstet Gynecol Scand* 2014; 93(5):477-82
- 4. Jonsson M, Ågren J, Nordén Lindeberg S, Ohlin A, Hanson U. Neonatal encephalopathy and the association to asphyxia in labor. *Am J Obstet Gynecol* 2014; 211(6):667.e1-667.
- 5. Holmström GE, Källen K, Hellström A, Jakobsson PG, Serenius F, Stjernqvist K, Tornqvist K. Ophthalmologic outcome at 30 months' corrected age of a prospective Swedish cohort of children born before 27 weeks of gestation: the extremely preterm infants in sweden study. *JAMA Ophthalmol* 2014 Feb;132(2):182-9.
- 6. Steen EE, Källén K, Maršál K, Norman M, Hellström-Westas L. Impact of sex on perinatal mortality and morbidity in twins. *J Perinat Med* 2014; 42(2):225-31.
- Stevenson NJ, Palmu K, Wikström S, Hellström-Westas L, Vanhatalo S. Measuring brain activity cycling (BAC) in long term EEG monitoring of preterm babies. *Physiol Meas* 2014; 35(7):1493-508.
- 8. Lundqvist P, Kleberg A, Edberg AK, Larsson BA, Hellström-Westas L, Norman E. Development and psychometric properties of the Swedish ALPS-Neo pain and stress assessment scale for newborn infants. *Acta Paediatr* 2014; 103(8):833-9.
- 9. Ignell Modé R, Mard E, Nyqvist KH, Blomqvist YT. Fathers' perception of information received during their infants' stay at a neonatal intensive care unit. *Sex Reprod Healthc* 2014;5(3):131-6.
- 10. Strand H, Blomqvist YT, Gradin M, Nyqvist KH. Kangaroo mother care in the neonatal intensive care unit: staff attitudes and beliefs and opportunities for parents. Acta Paediatr 2014;103(4):373-8.
- 11. Gerhardsson E, Nyqvist KH, Mattsson E, Volgsten H, Hildingsson I, Funkquist EL. The Swedish version of the Breastfeeding Self-Efficacy Scale-Short Form: reliability and validity assessment. *J Hum Lact* 2014; 30(3):340-345.
- 12. Holmström GE, Källen K, Hellström A, Jakobsson PG, Serenius F, Stjernqvist K, Tornqvist K. Ophthalmologic outcome at 30 months' corrected age of a prospective Swedish cohort of children born before 27 weeks of gestation: the extremely preterm infants in Sweden study. *JAMA Ophthalmol* 2014; 132(2):182-9.
- Serenius F, Sjörs G, Blennow M, Fellman V, Holmström G, Maršál K, Lindberg E, Olhager E, Stigson L, Westgren M, Källen K; EXPRESS study group. EXPRESS study shows significant regional differences in 1-year outcome of extremely preterm infants in Sweden. *Acta Paediatr* 2014;103(1):27-37.
- 14. Baylis R, Ewald U, Gradin M, Hedberg Nyqvist K, Rubertsson C, Thernström Blomqvist Y. First-time events between parents and preterm infants are affected by the designs and routines of neonatal intensive care units. *Acta Paediatr* 2014; 103(10):1045-52.
- 15. Shah PS, Lee SK, Lui K, Sjörs G, Mori R, Reichman B, Håkansson S, Feliciano LS, Modi N, Adams M, Darlow B, Fujimura M, Kusuda S, Haslam R, Mirea L; International Network for Evaluating Outcomes of Neonates (iNeo). The International Network for Evaluating Outcomes of very low birth weight, very preterm neonates (iNeo): a protocol for collaborative comparisons of international health services for quality improvement in neonatal care. *BMC Pediatr* 2014;14:110.
- 16. Lundqvist P, Hellström-Westas L, Hallström I. Reorganizing life: A qualitative study of fathers' lived experience in the 3 years subsequent to the very preterm birth of their child. *J Pediatr Nurs* 2014; 29(2):124-31.

#### Reviews 2014-2016

1. Hellström-Westas L, Boylan G, Ågren J. Systematic review of neonatal seizure management strategies provides guidance on anti-epileptic treatment. *Acta Paediatr* 2015; 104:123-9.

#### **Dissertations 2016**

Maria Stålhammar: Neutrophil Chemotaxis and Respiratory Burst in Term and Preterm Newborn Infants (main supervisor Richard Sindelar)

#### Collaboration

Professor Geraldine Boylan, Cork, Ireland Professor Raffaele Dellaca, Milano, Italy Professor Magnus Domellöf, Umeå Associate professor Lena Douhan Håkansson, Uppsala Associate professor Renée Flacking, Falun/Uppsala Professor em Claes von Hofsten, Uppsala Professor Karin Källén, Lund Professor Anders Larsson, Uppsala Professor Liisa Lehtonen, Turkku/Åbo, Finland Professor David Ley, Lund Professor Mikael Norman, Stockholm Professor Karin Stjernqvist, Lund Professor Sampsa Vanhatalo, Helsinki, Finland Professor Linda de Vries, Utrecht, The Netherlands

#### Agencies that support the work/Funding

HRH Crown Princess Lovisa Foundation (several grants of 100-120.000 SEK each) Linnéa and Josef Carlsson Foundation (several grants of 50-100.000 SEK each) Jerring Foundation (300.000 SEK) Hjärnfonden (500.000 SEK) Heart and Lung Foundation Josephine Neyman Stipend (300.000 SEK) Gillbergska Foundation (several stipends up to 50.000 SEK each)

#### Inflammation and neonatal lung injury

#### Richard Sindelar, Lena Douhan Håkansson, Maria Stålhammar

Acute and chronic lung injury is common in very preterm infants. The underlying mechanisms are only partly understood and include inflammation, oxygen toxicity, and barotrauma from mechanical ventilation. This study investigates migration of inflammatory cells in newborn infants under agarose (simulating tissue migration), migratory influence on respiratory burst, and the receptor expression for adherence, inflammatory state, phagocytosis and migration in response to different inflammatory stimulators encountered in preterm newborn infants with evolving bronchopulmonary dysplasia (BPD).

#### Mechanical ventilation and pulmonary function

## Richard Sindelar, Anders Jonzon, Raffaele Dellaca, Chiara Veneroni, Liisa Lehtonen, Hanna Soukka, Linda Wallström

Barotrauma is considered to be a major cause of preterm lung injury. This clinical project investigates effects of different modes of assisted ventilation (intermittent mandatory ventilation, patient-triggered ventilation, proportional assisted ventilation, and neurally adjusted ventilatory assistance [NAVA]) to minimize airway pressure while maintaining adequate ventilation. The effect of end-expiratory pressure on lung mechanics and regulation of breathing during invasive and non-invasive assisted ventilation is studied with forced oscillatory technique and with electrical activity of the diaphragm. A randomized multicenter clinical study (Uppsala and Åbo) will investigate early effects on breathing activity and the early ventilatory outcome during nCPAP and non-invasive NAVA in newborn infants born at less than 32 gestational weeks.

## Early clinical predictors of response to pharmacological treatment of persistent ductus arteriosus in extremely preterm infants

#### Richard Sindelar, Anders Jonzon, Anders Larsson, Karl Wilhelm Olsson

Newborn infants born before 28 gestational weeks have a high incidence of patent ductus arteriosus (PDA). The postnatal presence of a haemodynamically significant left to right shunt through the duct is associated with a lower survival rate and an increased incidence of intraventricular haemorrhage (IVH), necrotizing enterocolitis, and BPD. We have previously shown that a high maximal flow in ductus arteriosus is associated with successful pharmacological closure of PDA in 22-27 gestational weeks. The present study investigates early haemodynamical effects of PDA in extremely preterm infants by assessing early sequential echochardiographic examinations and biochemical markers for pulmonary circulation and cardiac load. The aim is to elucidate prognostic factors for successful pharmacological treatment with cyclooxygenase inhibitors, and to evaluate new therapeutical approaches for the closure of PDA.

## Oxygenation, heat exchange and fluid balance in extremely preterm infants in the NICU and during surgery

#### Johan Ågren, Victoria Karlsson, Laszlo Markasz

These investigations measure oxygenation, heat exchange and fluid balance in extremely preterm infants cared for during different clinical conditions (skin-to skin with parent, incubator, surgery). The aim is to better understand the dynamics of heat and fluid balance in very low birth-weight infants and to better support postnatal circulatory, respiratory and metabolic adaptation. The studies also include assessments of both parental and infant comfort and stress.

## Maternal, neonatal and long-term effects of delayed, as compared to early, cord clamping in healthy term infants

### Lena Hellström-Westas, Ola Andersson

In this project, 400 healthy women with normal pregnancies were randomized to delayed or early cord clamping after delivery. Infants subjected to delayed cord clamping had higher neonatal haemoglobin, and at four months they had higher ferritin and lower risk for iron deficiency. At 12 months, delayed cord clamping was associated with a modest, but statistically significant positive effect on neurodevelopment in boys. The four-year follow up is in press 2015. There were no effects on maternal haemorrhage from time to cord clamping.

#### Neonatal neurocritical care

#### Lena Hellström-Westas, Johan Ågren

We have introduced neonatal neurocritical care in the NICU at Uppsala University Hospital, and will investigate mechanisms for perinatal brain injury in high-risk infants, including asphyxiated infants, infants with seizures and very preterm infants. These infants are at increased risk for developing neurodevelopmental handicaps with life-long consequences. Mechanisms for such brain injury are

multifactorial, but a significant proportion of brain injury probably occurs around and soon after birth. We have previously shown that subclinical seizures are prevalent also in extremely preterm infants, and effective treatment may limit brain injury in infants with seizures. Methods include monitoring of amplitude-integrated EEG (aEEG), EEG, NIRS, cerebral ultrasound, MRI, and measurement of various biomarkers.

#### Early oculomotor function and long-term outcome in very preterm infants Lena Hellström-Westas, Katarina Strand-Brodd, Ylva Fredriksson Kaul, Cecilia

**Montgomery, Nima Naseh, Claes von Hofsten, Kerstin Rosander, Kristina Persson** This project follows a population-based cohort of very preterm infants, born in Uppsala in 2004-2007. The infants have been followed with repeated evaluation of motor function (the Structured Observation of Motor Performance, SOMP-I), neurological assessment and psychological assessment at 2<sup>1</sup>/<sub>2</sub> and 6<sup>1</sup>/<sub>2</sub> years. Visual eye tracking ability was tested at two and four months, and ability to reach for a moving object at eight months, and in half of the infants MRI was performed at 2<sup>1</sup>/<sub>2</sub>-5 years. We are currently investigating cognition, motor function, visual function and cerebral MRI in a new follow-up of these children at the age of 12 years.

#### Breastfeeding and family-centred care in term and preterm infants

**Eva-Lotta Funkquist, Ylva Thernström Blomqvist, Paola Oras, Jenny Ericson, Erik Normann** Rates of breastfeeding are decreasing in Sweden, both among term and preterm infants, but the reasons for this are not known. The current projects aim at investigating factors that promote successful breast-feeding and parental bonding, and includes evaluation of skin-to-skin care, observations of development of breast-feeding patterns in moderately preterm and term infants, and specific interventions for promoting breast-feeding in NICU graduates and healthy infants in the postnatal ward. We also participate in a multi-centre collaborative project, the Separation and Closeness Experiences in the Neonatal Environment (SCENE) group, on family-centred care.

#### **Epidemiological research**

**Fredrik Serenius, Gunnar Sjörs, Lena Hellström-Westas, Johan Ågren, Kristina Persson** This project includes long-term follow up of three cohorts of extremely preterm infants: the national EXPRESS study group (infants born 2004-2007), the "1000 gram study" (infants born 1992-93), a regional cohort of infants born in the south of Sweden in 1985-86, and a regional Uppsala cohort of infants born 1986-89, who required neonatal intensive care. We are currently performing a 12-year follow-up of the EXPRESS study group. The project also includes register-based research on perinatal risk factors, quality of care, neonatal seizures and postnatal epilepsy, and benchmarking in the International Network for Evaluating Outcomes (iNeo) of Neonates.

#### Hyaluronan and RHAMM

#### Richard Sindelar, Rashmin Savani, Laszlo Markasz

Hyaluronan, a major component of the extracellular matrix with a high capacity to immobilize water, but is also involved in proliferation of cells, interaction with cell receptors and migrations of cells. HA appears in abundance in the lung and also other tissues during fetal development The receptor for hyaluronan-mediated motility (RHAMM) is expressed in endothelial cells, fibroblasts, smooth muscle cells, and immune cells. It regulates signaling pathways that influence cell motility, and proliferation in inflammatory and tumorigenic responses. The role of RHAMM in fetal lung development is not well established. The aim of this project to understand the role of HA content and RHAMM expression in postnatal lung development by analyzing human lung specimens from ventilated newborn infants at different gestational and postnatal ages with a variety of different lung diseases.
### Pain assessment during neonatal intensive care interventions and possible pain reducing treatments

**Richard Sindelar, Johan Ågren, Lena Hellström-Westas, Gerd Holmström, Josanne Munsters** Extremely preterm infants are subjected to an intensive care that is characterized by many painful procedures and environmental disturbances. It is important to reliably assess pain and fore mostly find ways to reduce painful exposure, in order to reduce harmful short and long term effects on brain development. This project studies both new pain assessment methods such as skin conductance (SC), NIRS and aEEG compared to observational pain assessment scores during potential painful procedures such as heel stick, investigation for retinopathy of the preterm (ROP), hypothermia treatment, gavage placement, endotracheal intubation etc and possible pain alleviating treatments such as skin-to-skin care, facilitated tucking, swaddling, dextrose, nitrous gas etc.

#### Pediatric Oncology and Neurology

#### **Gustaf Ljungman**

#### Pediatric Oncology

Intensive international research focus on pediatric oncology has resulted in a dramatic increase in overall survival of pediatric cancer diseases- yet these rare diseases still today account for the main medical cause of death in children aged 1-15 years. Increased understanding of the biology, molecular basis and treatment of leukemia, the main cancer disease in children, now results in 80% cure of the disease. Research interest is now focusing on pediatric neural tumors, the second largest group of pediatric malignancies, accounting for the highest mortality and morbidity in children with cancer, and at present the main challenge in pediatric oncology.

The research of the Pediatric Oncology research group deals with clinical cancer diseases of children, their biology, treatment, and consequences. The research of the group comprises a wide range of scientific questions.

#### **Research group**

Ljungman, Gustaf MD, Associate professor, adjunct lecturer, research group leader Arvidson, Johan MD, Associate professor Englund, Annika MD, PhD student Engvall, Gunn RN, PhD, lecturer Frisk, Per MD, Associate professor Frost, Britt-Marie MD, Associate professor Georgantzi, Clary MD, PhD student Giraud, Geraldine MD, PhD Gustafsson, Britt MD, Adjunct professor Hedén, Lena RN, PhD, lecturer Jackmann Natalja MD, PhD student Jakobson Åke MD, Associate professor, Kamsvåg-Magnusson, Tove MD, PhD student Lönnerholm, Gudmar MD, Professor emeritus Palle, Josefine MD, PhD Paulsson, Mattias, PhD Pfeifer, Susan Adjunct professor Thorsell Cederberg, Jenny MS, PhD student Öberg, Anders MD PhD student.

#### Publications 2014-2016

- 1. Cernvall M, Skogseid E, Carlbring P, Ljungman L, Ljungman G, von Essen L. Experiential Avoidance and Rumination in Parents of Children on Cancer Treatment : Relationships with Posttraumatic Stress Symptoms and Symptoms of Depression. Journal of clinical psychology in medical settings 2016;23(1):67–76.
- 2. Holm S, Ljungman G, Åsenlöf P, Linton SJ, Söderlund A. Treating youth in pain : Comparing tailored behavioural medicine treatment provided by physical therapists in primary care with physical exercises. European Journal of Pain 2016;20(4):626–38.
- 3. Hedén L, von Essen L, Ljungman G. The relationship between fear and pain levels during needle procedures in children from the parents' perspective. European Journal of Pain 2016;20(2):223–30.

- 4. Ander M, Grönqvist H, Cernvall M, Engvall G, Hedström M, Ljungman G, et al. Development of health-related quality of life and symptoms of anxiety and depression among persons diagnosed with cancer during adolescence : a 10-year follow-up study. Psycho-Oncology 2016;25(5):582–9.
- Lychou SE, Gustafsson GG, Ljungman GE. Higher rates of metastatic disease may explain the declining trend in Swedish paediatric rhabdomyosarcoma survival rates. Acta Paediatrica 2016;105(1):74–81.
- 6. Cernvall M, Hovén E, Ljungman L, Ljungman G, Carlbring P, von Essen L. Posttraumatic stress and attentional bias towards cancer-related stimuli in parents of children recently diagnosed with cancer. PLoS ONE 2016;11(4).
- 7. Wikman A, Hovén E, Cernvall M, Ljungman G, Ljungman L, von Essen L. Parents of children diagnosed with cancer : work situation and sick leave, a five-year post end-of-treatment or a child's death follow-up study. Acta Oncologica 2016;55(9–10):1152–7.
- 8. Ljungman L, Cernvall M, Ghaderi A, Ljungman G, von Essen L, Ljotsson B. A Cognitive Behavioural Conceptualization of Psychological Distress in Parents of Children Previously Treated for Cancer. Psycho-Oncology 2016;25(SP. S3):65–65.
- Cernvall M, Ljungman L, Wikman A, Carlbring P, Ljungman G, von Essén L. Dimensions of Posttraumatic Stress Symptoms and their Relationships with Depression, Anxiety, and Quality of Life in Parents of Children Recently Diagnosed with Cancer. Psycho-Oncology 2016;25(SP. S3):76–76.
- Englund A, Molin D, Enblad G, Karlén J, Glimelius I, Ljungman G, et al. The role of tumourinfiltrating eosinophils, mast cells and macrophages in Classical and Nodular Lymphocyte Predominant Hodgkin Lymphoma in children. European Journal of Haematology 2016;97(5):430–8.
- 11. Thorsell-Cederberg J, Cernvall M, Dahl J, von Essen L, Ljungman G. Acceptance as a Mediator for Change in Acceptance and Commitment Therapy for Persons with Chronic Pain? International Journal of Behavioral Medicine 2016;23(1):21–9.
- Englund A, Glimelius B, Rostgaard K, Eloranta S, Molin D, Kuusk T, et al. Hodgkin Lymphoma In Children, Adolescents And Young Adults-A Comparative Study Of Clinical Presentation And Treatment Outcome. Haematologica 2016;101:36–36.
- 13. Oskarsson T, Söderhäll S, Arvidson J, Forestier E, Montgomery S, Bottai M, et al. Relapsed childhood acute lymphoblastic leukemia in the Nordic countries: prognostic factors, treatment and outcome. Haematologica 2016;101(1):68-76.
- 14. Engvall G, Ångstrom-Brännstrom C, Mullaney T, Nilsson K, Wickart-Johansson G, Svärd A-M, et al. It Is Tough and Tiring but It Works - Children's Experiences of Undergoing Radiotherapy. PLoS ONE 2016;11(4).
- Lindh V, Engvall G, Ångström-Brannström C, Nilsson K, Wickart-Johansson G, Lindh J. Children's Voices On Experiencing Radiotherapy. Oncology Nursing Forum 2016;43(2):134– 134.
- Almblad A-C, Målqvist M, Engvall G. Caring for the Acutely, Severely Ill Child-A Multifaceted Situation with Paradoxical Elements : Swedish Healthcare Professionals' Experiences. Journal of Pediatric Nursing 2016;31(5):E293–300.
- 17. Ångström-Brännström C, Engvall G, Mullaney T, Nilsson K, Wickart-Johansson G, Svärd AM, et al. Facilitating Radiotherapy for Children : Technique, Design and Professional Care in Synergy, a Multicenter Intervention Study. Pediatric Blood & Cancer 2016;63:S213–S213.
- 18. Maria C, Engsheden N, Gaderi A, Enebrink P, Engvall G, Nevéus T, et al. No difference in relationship satisfaction between parents of children with enuresis and normative data. Journal of Child and Family Studies 2016;25(4):1345–51.
- 19. Dalin F, Adamus G, Yang S, Landgren E, Palle J, Hallgren Å, et al. Aryl Hydrocarbon Receptor-Interacting Protein-Like 1 in Cancer-Associated Retinopathy. Ophthalmology (Rochester, Minn) 2016;123(6):1401–4.
- 20. Hedén L, Ahlström L. Individual response technology to promote active learning within the caring sciences : An experimental research study. Nurse Education Today 2016;36:202–6.
- 21. Marzouka N, Nordlund J, Bäcklin CL, Lönnerholm G, Syvänen A-C, Almlöf JC.

CopyNumber450kCancer : baseline correction for accurate copy number calling from the 450k methylation array. Bioinformatics 2016;32(7):1080–2.

- 22. Marincevic-Zuniga Y, Zachariadis V, Cavelier L, Castor A, Barbany G, Forestier E, et al. PAX5-ESRRB is a recurrent fusion gene in B-cell precursor pediatric acute lymphoblastic leukemia. Haematologica 2016;101(1):e20–3.
- 23. Wahlberg P, Lundmark A, Nordlund J, Busche S, Raine A, Tandre K, et al. DNA methylome analysis of acute lymphoblastic leukemia cells reveals stochastic de novo DNA methylation in CpG islands. Epigenomics 2016;8(10):1367–87.
- 24. Lindqvist CM, Lundmark A, Nordlund J, Freyhult E, Ekman D, Almlöf JC, et al. Deep targeted sequencing in pediatric acute lymphoblastic leukemia unveils distinct mutational patterns between genetic subtypes and novel relapse-associated genes. OncoTarget 2016;7(39):64071–88.
- 25. Wennstrom L, Edslev PW, Abrahamsson J, Norgaard JM, Floisand Y, Forestier E, et al. Acute Myeloid Leukemia in Adolescents and Young Adults Treated in Pediatric and Adult Departments in the Nordic Countries. Pediatric Blood & Cancer 2016;63(1):83–92.
- 26. Laursen ACL, Sandahl JD, Kjeldsen E, Abrahamsson J, Asdahl P, Ha S-Y, et al. Trisomy 8 in pediatric acute myeloid leukemia : A NOPHO-AML study. Genes, Chromosomes and Cancer 2016;55(9):719–26.
- Tierens A, Bjorklund E, Siitonen S, Marquart HV, Juergensen GW, Pelliniemi T-T, et al. Residual disease detected by flow cytometry is an independent predictor of survival in childhood acute myeloid leukaemia; results of the NOPHO-AML 2004 study. British Journal of Haematology 2016;174(4):600–9.
- Lohmann DJA, Abrahamsson J, Ha S-Y, Jonsson OG, Koskenvuo M, Lausen B, et al. Effect of age and body weight on toxicity and sur vival in pediatric acute myeloid leukemia : results from NOPHO-AML 2004. Haematologica 2016;101(11):1359–67
- 29. Ander M, Thorsell Cederberg J, Lindahl Norberg A, von Essen L. Losing your context Exploration of emotional suffering after cancer during adolescence. In 2016. p. 81–81.
- Jalmsell L, Lövgren M, Kreicbergs U, Henter JI, Frost BM. Children with cancer share their views: tell the truth but leave room for hope. <u>Acta Paediatr.</u> 2016 Sep;105(9):1094-9. doi: 10.1111/apa.13496. Epub 2016 Jul 3.

- 1. Mellgren K, Arvidson J, Toporski J, Winiarski J. Chimerism analysis in clinical practice and its relevance for the detection of graft rejection and malignant relapse in pediatric hematopoietic stem cell transplant patients. Pediatric Transplantation. 2015;19(7):758-766.
- Oskarsson T, Söderhäll S, Arvidson J, Forestier E, Montgomery S, Bottai M, Lausen B, Carlsen N, Hellebostad M, Lähteenmäki P, Saarinen-Pihkala UM, G Jónsson Ó, Heyman M; Nordic Society of Paediatric Haematology and Oncology (NOPHO) ALL relapse working group. Relapsed childhood acute lymphoblastic leukemia in the Nordic countries: prognostic factors, treatment and outcome. Haematologica. 2016 Jan;101(1):68-76. doi: 10.3324/haematol.2015.131680. Epub 2015 Oct 22. PMID: 26494838
- Cederblad M, Engsheden N, Ghaderi A, Enebrink P, Engvall G, Nevéus T, et al. No Difference in Relationship Satisfaction Between Parentsof Children with Enuresis and Normative Data. Journal of Child and Family Studies. 2015;
- 4. Cederblad M, Sarkadi A, Engvall G, Nevéus T. Infrequent enuresis, the uninvestigated majority comparisons between children with enuresis of varying severity.. Journal of Pediatric Urology. 2015;11(1):24.e1-24.e6.
- 5. Cederblad M, Sarkadi A, Engvall G, Nevéus T. No effect of basic bladder advice in enuresis : a randomised controlled trial. Journal of Pediatric Urology. 2015;11(3):153.e1.
- Ångström-Brännström C, Engvall G, Mullaney T, Nilsson K, Wickart-Johansson G, Svärd A, et al. Children Undergoing Radiotherapy : Swedish Parents' Experiences and Suggestions for Improvement.. PLoS ONE. 2015;10(10)

- Genberg-Andrén M, Öberg A, Andrén B, Hedenström H, Frisk P, Flachskampf F A. Cardiac Function After Hematopoietic Cell Transplantation : An Echocardiographic Cross-Sectional Study in Young Adults Treated in Childhood. Pediatric Blood & Cancer. 2015;62(1):143-147.
- Jalmsell L, Lovgren M, Hansson M G, Kreicbergs U, Frost B, Henter J I. They want the Truth while Still Being Allowed to Hope - An Interview Study with Severely Ill Children on Receiving Bad News. 47th Congress of the International Society of Paediatric Oncology (SIOP), October 8–11, 2015, Cape Town, South Africa. Pediatric Blood & Cancer. 2015;62(Suppl. 4):S347-S347.
- Lindqvist CM, Nordlund J, Ekman D, Johansson A, Moghadam BT, Raine A, Övernäs E, Dahlberg J, Wahlberg P, Henriksson N, Abrahamsson J, Frost BM, Grandér D, Heyman M, Larsson R, Palle J, Söderhäll S, Forestier E, Lönnerholm G, Syvänen AC, Berglund EC. The mutational landscape in pediatric acute lymphoblastic leukemia deciphered by whole genome sequencing.Hum Mutat. 2015 Jan;36(1):118-28. doi: 10.1002/humu.22719
- Ander M, Grönqvist H, Cernvall M, Engvall G, Hedström M, Ljungman G, et al. Development of health-related quality of life and symptoms of anxiety and depression among persons diagnosed with cancer during adolescence : a 10-year follow-up study. Psycho-Oncology. 2015 Sep 10. doi: 10.1002/pon.3965. [Epub ahead of print]
- Pritchard-Jones K, Bergeron C, de Camargo B, van den Heuvel-Eibrink MM, Acha T, Godzinski J, Oldenburger F, Boccon-Gibod L, Leuschner I, Vujanic G, Sandstedt B, de Kraker J, van Tinteren H, Graf N; SIOP Renal Tumours Study Group. Ljungman G collaborator. <u>Omission of doxorubicin from the treatment of stage II-III, intermediate-risk Wilms' tumour</u> (SIOP WT 2001): an open-label, non-inferiority, randomised controlled trial. Lancet. 2015 Sep 19;386(9999):1156-64. doi: 10.1016/S0140-6736(14)62395-3. Epub 2015 Jul 9.
- 12. Holm S, Ljungman G, Åsenlöf P, Linton SJ, Söderlund A. Treating youth in pain: comparing tailored behavioral medicine treatment provided by physical therapists in primary care with physical exercises. Eur J Pain 2015 Sep 24. doi: 10.1002/ejp.780. [Epub ahead of print].
- 13. Ander M, Norberg A L, Ljungman G, Ljotsson B, von Essen L. Identification of Cancer-related Psychological Suffering Experienced by Young People Diagnosed with Cancer During Adolescence and Development of a Psychological Treatment to Reduce This Suffering. 2015 World Congress of Psycho-Oncology (a joint conference of the International Psycho-Oncology Society and the American Psychosocial Oncology Society) 28 July – 1 August 2015 Washington, DC, USA. Psycho-Oncology. 2015;24(S2):114-115. :P1-21.
- Cernvall M, Carlbring P, Ljungman L, Ljungman G, von Essen L. Internet-based Guided Selfhelp for Parents of Children Diagnosed with Cancer: 1-year Follow-up of a Randomized Controlled Trial. In: 2015 World Congress of Psycho-Oncology. 2015.
- Cernvall M, Carlbring P, Ljungman L, Ljungman G, von Essen L. Internet-based Guided Selfhelp for Parents of Children Diagnosed with Cancer : 1-year Follow-up of a Randomized Controlled Trial. 2015 World Congress of Psycho-Oncology (a joint conference of the International Psycho-Oncology Society and the American Psychosocial Oncology Society) 28 July – 1 August 2015 Washington, DC, USA. Psycho-Oncology. 2015;24(S2):125-126. :P1-41.
- 16. Cernvall M, Carlbring P, Ljungman L, Ljungman G, von Essen L. Internet-based guided selfhelp for parents of children on cancer treatment : A randomized controlled trial. Psycho-Oncology. 2015;24(9):1152-1158.
- 17. Cernvall M, Hovén E, Ljungman L, Ljungman G, Carlbring P, von Essen L. Attentional bias towards cancer-related stimuli is related to symptoms of posttraumatic stress in parents of children recently diagnosed with cancer. Psycho-Oncology. 2015;24(S2):89-89. :V-1.
- Cernvall M, Skogseid E, Carlbring P, Ljungman L, Ljungman G, von Essen L. Experiential Avoidance and Rumination in Parents of Children on Cancer Treatment : Relationships with Posttraumatic Stress Symptoms and Symptoms of Depression. J Clin Psychol Med Settings. 2015 Oct 13. [Epub ahead of print]. PMID:26462676. Doi: 10.1007/s10880-015-9437-4.
- 19. Dantonello T M, Stark M, Timmermann B, Fuchs J, Selle B, Linderkamp C, et al. Tumour volume reduction after neoadjuvant chemotherapy impacts outcome in localised embryonal rhabdomyosarcoma. Pediatric Blood & Cancer. 2015;62(1):16-23.

- Englund A, Hopstadius C, Enblad G, Gustafsson G, Ljungman G. Hodgkin lymphoma a survey of children and adolescents treated in Sweden 1985-2009.. Acta Oncologica. 2015;54(1):41-8. Hedén L, von Essen L, Ljungman G. The relationship between fear and pain levels during needle procedures in children from the parents' perspective. European Journal of Pain. 2015; 2015 Apr 2. doi: 10.1002/ejp.711. [Epub ahead of print]
- Ljungman L, Hovén E, Ljungman G, Cernvall M, von Essen L. Does time heal all wounds? A longitudinal study of the development of posttraumatic stress symptoms in parents of survivors of childhood cancer and bereaved parents. Psycho-Oncology. 2015; Jun 4. doi: 10.1002/pon.3856. [Epub ahead of print]
- 22. Thorsell-Cederberg J, Cernvall M, Dahl J, von Essen L, Ljungman G. Acceptance as a Mediator for Change in Acceptance and Commitment Therapy for Persons with Chronic Pain?. International Journal of Behavioral Medicine Int J Behav Med. 2015 June 4. [Epub ahead of print]. 2015;:9494.
- 23. Nordlund J, Bäcklin C, Zachariadis V, Cavelier L, Dahlberg J, Öfverholm I, et al. DNA methylation-based subtype prediction for pediatric acute lymphoblastic leukemia. Clinical Epigenetics. 2015;7:11.
- 24. Lindqvist CM, Nordlund J, Ekman D, Johansson A, Moghadam BT, Raine A, Övernäs E, Dahlberg J, Wahlberg P, Henriksson N, Abrahamsson J, Frost BM, Grandér D, Heyman M, Larsson R, Palle J, Söderhäll S, Forestier E, Lönnerholm G, Syvänen AC, Berglund EC. The mutational landscape in pediatric acute lymphoblastic leukemia deciphered by whole genome sequencing. Hum Mutat. 2015 Jan;36(1):118-28. doi: 10.1002/humu.22719
- 25. Nordlund J, Bäcklin C, Zachariadis V, Cavelier L, Dahlberg J, Öfverholm I, et al. DNA methylation-based subtype prediction for pediatric acute lymphoblastic leukemia. Clinical Epigenetics. 2015;7:11.
- 26. Sandahl J D, Kjeldsen E, Abrahamsson J, Ha S, Heldrup J, Jahnukainen K, et al. The applicability of the WHO classification in paediatric AML. A NOPHO-AML study. British Journal of Haematology. 2015;169(6):859-867.

- Hedén L, von Essen L, Ljungman G. Effect of single-dose paracetamol for needle procedures in children with cancer - a RCT. Acta Paediatr. 2014 Mar;103(3):314-9. doi: 10.1111/apa.12509. Epub 2013 Dec 19.
- Dantonello T, Lochbühler H, Schuck A, Kube S, Godzinski J, Sköldenberg E, Ljungman G, Ladenstein R, Hallmen E, Wessalowski R, Franke M, Bielack, SS, Klingebiel T, Koscielniak E on behalf of the Cooperative Weichteilsarkom Studiengruppe (CWS). Challenges in the local treatment of large abdominal embryonal rhabdomyosarcoma. Ann Surg Oncol. 2014 Oct;21(11):3579-86. doi: 10.1245/s10434-014-3551-7. Epub 2014 Jul 22.
- Kamsvåg Maganusson T, Thorsell J, Svanberg A-C, Esssen von L, Arvidson J, Mellgren K, Toporski J, Ljungman G. Parents' and children's perceptions of distress related to oral mucositis during stem cell transplantation. Acta Paediatr. 2014 June; 103(6): 630-6. doi: 10.1111/apa.12627. [Epub ahead of print]
- Englund A, Hopstadius C, Gustafsson G, Enblad G, Ljungman G. Hodgkin lymphoma- a survey of children and adolescents treated in Sweden 1985-2009. Englund A, Hopstadius C, Gustafsson G, Enblad G, Ljungman G. Hodgkin lymphoma- a survey of children and adolescents treated in Sweden 1985-2009. Acta Oncol. 2015 Jan;54(1):41-8. doi: 10.3109/0284186X.2014.948058. Epub 2014 Sep 9.
- Ljungman L, Cernvall, M, Grönqvist H, Ljotsson B, Ljungman G, & von Essen L. Long-term Positive and Negative Psychological Late Effects for Parents of Childhood Cancer Survivors: A Systematic Review. PLoS One. 2014 Jul 24;9(7):e103340. doi: 10.1371/journal.pone.0103340. eCollection 2014.
- 6. Dantonello TM, Stark M, Timmermann B, Fuchs J, Selle B, Linderkamp C, Handgretinger R, Hagen R, Feuchtgruber S, Kube S, Kosztyla D, Kazanowska B, Ladenstein R, Niggli F, Ljungman G, Bielack SS, Klingebiel T, Koscielniak E; on behalf of the Cooperative Weichteilsarkom Studiengruppe [CWS]. Tumour volume reduction after neoadjuvant

chemotherapy impacts outcome in localised embryonal rhabdomyosarcoma. Pediatr Blood Cancer. 2015 Jan;62(1):16-23. doi: 10.1002/pbc.25207. Epub 2014 Sep 27.

- 7. Lehmann V, Gronqvist H, Engvall G, Ander M, Tuinman MA, Hagedoorn M, et al. Negative and positive consequences of adolescent cancer 10 years after diagnosis: an interview-based longitudinal study in Sweden. Psychooncology 2014;23(11):1229-35.
- Cederblad M, Sarkadi A, Engvall G, Neveus T (2014) Infrequent enuresis, the uninvestigated majority comparisons between children with enuresis of varying severity. J Pediatr Urol. doi:10.1016/j.jpurol.2014.06.026.
- 9. Genberg M, Öberg A, Andrén B, Hedenström H, Frisk P, Flachskamp FA. Cardiac function in young adults after hematopoietic cell transplantation. (Pediatric Blood and Cancer e-published 2014)
- Fogelstrand L, Staffas A, Wasslavik C, Sjögren H, Söderhäll S, Frost BM, Forestier E, Degerman S, Behrendtz M, Heldrup J, Karrman K, Johansson B, Heyman M, Abrahamsson J, Palmqvist L. Prognostic implications of mutations in NOTCH1 and FBXW7 in childhood T-ALL treated according to the NOPHO ALL-1992 and ALL-2000 protocols.Pediatr Blood Cancer. 2014 Mar;61(3):424-30. doi: 10.1002/pbc.24803. Epub 2013 Oct 8.
- Riva R, Forinder U, Arvidson J, Mellgren K, Toporski J, Winiarski J, Norberg AL. Patterns of psychological responses in parents of children that underwent stem cell transplantation. Psychooncology. 2014 Nov;23(11):1307-13
- Sandahl JD, Kjeldsen E, Abrahamsson J, Ha SY, Heldrup J, Jahnukainen K, Jónsson OG, Lausen B, Palle J, Zeller B, Forestier E, Hasle H. Ploidy and clinical characteristics of childhood acute myeloid leukemia: A NOPHO-AML study. Genes Chromosomes Cancer. 2014 Aug;53(8):667-75. doi: 10.1002/gcc.22177. Epub 2014 Apr 18.
- 13. Kumar Pandey G, Mitra S, Subhash S, Hertwig F, Kanduri M, Mishra K Fransson S, Ganeshram A, Mondal T, Bandaru S, Ostensson M, Akyürek LM, Abrahamsson J, Pfeifer S, Larsson E, Shi L, Peng Z, Fischer M, Martinsson T, Hedborg F, Kogner P, Kanduri C. The Risk-Associated Long Noncoding RNA NBAT-1Controls Neuroblastoma Progression by RegulatingCell Proliferation and Neuronal Differentiation. Cancer Cell. 2014;26(5):722-737.
- 14. Libard S, Popova S N, Amini R, Kärjä V, Pietiläinen T, Hämäläinen K M, Sundström C, Hesselager G, Bergqvist M, Ekman S, Zetterling M, Smits A, Nilsson P, Pfeifer S, de Ståhl TD, Enblad G, Ponten F, Alafuzoff I.. Human cytomegalovirus tegument protein pp65 is detected in all intra- and extra-axial brain tumours independent of the tumour type or grade. PLoS ONE. 2014;9(9):e108861-.
- 15. Lindqvist C M, Nordlund J, Ekman D, Johansson A, Moghadam B T, Raine A, Övernäs E, Dahlberg J, Wahlberg P, Henriksson N, Abrahamsson J, Frost BM, Grandér D, Heyman M, Larsson R, Palle J, Söderhäll S, Forestier E, Lönnerholm G, Syvänen AC, Berglund EC. The Mutational Landscape in Pediatric Acute Lymphoblastic Leukemia Deciphered by Whole Genome Sequencing. Human Mutation. 2014;36(1):118-128.

#### PhD dissertations

No dissertation 2016

#### Funding

ALF 1,1 milj to the research group 2016 CF 500.000/year, 3 years (Ljungman et al- oral mucositis) 2014-2016 BCF 500.000/year, 3 years (Ljungman et al- oral mucositis) 2014-2016 BCF 288 000/year, 2 years (Englund research time Hodgkin project) 2013-2014 BCF 345.000/year, 2 years (Englund research time Hodgkin project) 2015-2016 BCF 750.000/year, 6 years (Ljungman 50% senior research position) 2012-2017. BCF 300.000/year, 2 years (Frisk et al- insulinresistance) NovoNordisk 200.000 (Frisk et al- insulinresistance) BCF 400.000/year, 3 years (Frost et al- intersection of curative /palliative treatment) BCF 300.000/year, 2 years (Hedborg, Pfeifer - noncoding RNA in neural tumors) BCF 350.000/year, 3 year 2012-2014 (DiazdeSTåhl, Pfeifer et al)

### Childhood leukemia: biology, treatment, and consequences Targets and function of DNA methylation in acute childhood leukemia

#### Lönnerholm, Syvänen, Gustafsson, Frost, Palle et al.

Multidisciplinary study using patient leukemia cell specimens in the Scandinavian NOPHO biobank. The primary objective is to identify the most important genes or genomic loci that display variations in CpG methylation patterns and thus may be used as biomarkers for classification of childhood ALL and AML and for prognosis of the disease progression and response to treatment in individual patients. As DNA methylation is reversible, genes with methylated CpG sites are potential targets for novel therapies.

#### DNA methylation in pediatric acute myeloid leukemia.

#### Palle, Nordlund, Bäcklin, Syvänen.

The aim is to study the epigenetics in childhood AML with the Illumina 450 K analyses which gives information of the methylation status in 450.000 CpG sites over the AML cell genome. This data will be analysed comparing the methylation status in different subgroups of AML to outcome and we will also compare AML with ALL. These samples have before been analysed with in vitro drug resistance and the methylation status will also be correlated to this. All samples have been collected in collaboration with the Nordic Society for Pediatric Hematology and Oncology (NOPHO).

#### Late complications after treatment for childhood cancer

#### Johan Arvidson, Per Frisk.

A longstanding topic has been long term complications in a special cohort of survivors of autologous bone marrow transplantation for hematological malignancies. Studied complications have included both somatic function and quality of life. 1) Psychosocial functioning including sexual functioning 20 years after treatment with autologous bone marrow transplantation for lymphoid malignancies versus first line treatment without transplantation. 2) Insulin resistance in long-term survivors of allogeneic stem cell transplantation in childhood. 3) Retrospective study of interventions due to decreasing donor chimerism in patients after pediatric allogeneic SCT 4) Retrospective study on outcome after different conditioning regimens used in children with ALL who undergo HSCT. A Nordic study.5) Together with Lund (Cecilia Follin) and endocrinologist in Uppsala Britt Edén, we have started a study on patients with ALL who received cranial radiation before 6 years of age. The main investigation consists of measuring growth hormone response after insulin infusion.

### Insulin resistance and bone health in young adults who underwent stem cell transplantation for childhood leukemia

#### Per Frisk, Anders Öberg

The aim of this cross-sectional study is to investigate the prevalence of insulin resistance in young adults who underwent stem cell transplantation in childhood and to investigate their bone health. The patient group includes patients > 18 years of age who underwent stem cell transplantation in childhood (< 18 years) in Uppsala or Huddinge, Stockholm. Hitherto, 29 patients have been enrolled into the study and 10 patients have completed their investigations.

#### Vitamin D in children with cancer

#### Natalja Jackmann, Per Frisk, Outi Mäkitie, Arja Harila-Saari, Jan Gustafsson

Several epidemiological studies have demonstrated the importance of vitamin D for bone health, immune functions, infections, asthma and for prevention of metabolic syndrome, cardiovascular diseases and certain cancers. This study includes 2 separate projects assessing the prevalence, risk factors, and associating clinical features of vitamin D deficiency and longitudinal changes in vitamin D status during cancer therapy. These results and a pilot dose-response intervention study will be used as background data to design a larger vitamin D intervention study to evaluate potential health benefits of vitamin D supplementation in patients with childhood cancer.

# Treatment-related complications of childhood cancer and epidemiology of solid tumors, Hodgkin lymphoma in children and adolescents – etiological factors, epidemiology and late-effects of treatment Ljungman, Englund, et al.

This is a study of pediatric patients with Hodgkin lymphoma (HL). The aims are to: 1) Study if HL in children, adolescents and adults differ with respect to inflammatory micro-environment (eosinophils, macrophages, mast cells, regulatory T-cells and CD20-positive cells) and if the microenvironment has any implications for clinical outcome in children and adolescents (collaboration between Uppsala, Stockholm and Umeå). 2) Present a population-based epidemiological survey of all children and adolescents with HL in Sweden for a time period of 25 years (1985-2009). 3) Compare disease presentation and late effects of treatment in adolescents and young adults based on the hypothesis that they share the same disease characteristics but despite that receive different treatment (collaboration with Denmark).

### Interventions for procedural pain in children and adolescents with cancer Ljungman, Hedén, et al.

Pain is a major problem for children with cancer. Pain can be procedure-related, treatment- related pain (side-effects of treatments such as chemotherapy and radiotherapy), and cancer- related. In this project, we study procedure-related pain and its treatment. Needle insertion in a subcutaneous port can be regarded as a model where children's fear, distress, and pain in connection to procedures can be studied in a reasonably standardized way. Using this model we can learn about the effects of different pharmacological and psychological interventions in different randomized controlled trials.

#### Interventions for oral mucositis in children with cancer

#### Ljungman, Thorsell, Kamsvåg-Magnusson et al.

Oral mucositis is a painful condition with inflammation and ulceration of the mucous membranes in the mouth, caused by chemo- and radiotherapy and is particularly frequent in hematopoietic stem cell transplantation (HSCT). Pain intensity varies, but the pain is often so severe that the patient is unable to eat solid food (grade 3) or even to consume liquids (grade 4). In very severe cases the patient cannot talk, nor swallow saliva. Oral mucositis is reported by patients to be one of the most painful and debilitating side effects of cancer treatment.

Specific pharmacological and psychological interventions that can reduce oral mucositis symptoms are evaluated in randomized controlled trials. The studies are carried out on a national level at the different pediatric HSCT centers in Sweden.

### Psychosocial issues in children and adolescents with cancer and their parents

#### Ljungman, Engvall, et al.

In addition to being a part of the Pediatric Oncology research group at the Department of Women's and Children's Health, Uppsala University, Ljungman takes part in, and shares leadership of, the Psychosocial Oncology research group headed by Professor Louise von Essen. The projects have resulted in a number of publications and they can be categorized in either one of the two following main groups: 1. Cancer during adolescence - Psychosocial and health economic consequences and 2. Occurrence, development, and treatment of posttraumatic stress disorder (PTSD) among parents of children with cancer. Presently this has moved on to a multi-institutional collaboration in one part of a new strategic research proposal from Uppsala University, the U-Care program. The aim is to provide, and with scientific rigor evaluate, internet-based stepped-care treatment for parents of children with cancer with PTSD and for adolescents with cancer with psychosocial problems.

### Psychosocial functioning 20 years after hematological stem cell transplantation

#### Arvidson et al.

Follow up program of BMT in Uppsala, where all survivors of hematological bone marrow transplantation since 1985 are followed both somatically and psychologically. Focus is on quality of life as well as organ function.

### Design and evaluation of care environment and technical tools in pediatric radiotherapy

#### Engvall et al.

Umeå University, Karolinska Institutet Stockholm, and Uppsala University are included in a multicenter study. The Institute of Design, Umeå and Skandion Clinic are co-workers. The project started 2012, focusing on design and evaluation of care environment and technical tools in Pediatric radiotherapy. The aims are to develop methods and material for pre-treatment information and preparation, develop methods that enable contact between child and parents during treatment, and finally to evaluate these methods to identify which methods that should be implemented in Pediatric Radiotherapy and at the Skandion clinic.

### Implementing a Pediatric Early Warning Score for increased patient safety Engvall et al.

In order to increase patient safety, a pediatric early warning score (PEWS) was introduced in the daily routine at the medical, surgery, and orthopaedic wards, excluding neonatology, at the University Hospital of Pediatrics in Uppsala 2013. The aim is to determine the effect of the implementation of PEWS at the different wards at the hospital. The focus is on both process and outcome variables. The used implementation method is based on a participatory approach. The impact of PEWS on health outcomes among children admitted to the University Hospital of Pediatrics in Uppsala 2016-2017.

#### Effects of animal-assisted therapy in pediatric care

#### Engvall et al.

There is scientific literature describing the dog's positive effect on patients and staff in health care. The aim is to investigate the physiological and psychological effects of dog in pediatric care and to investigate whether there is evidence of increased prevalence of allergen and/or bacteria associated with the dog's presence at a pediatric and surgery wards.

## Health-related quality of life, function and experience of care for children and adolescents with esophageal atresia, imperforate anus and VACTERL

#### Engvall et al.

In 2014 a project started about value-based care for patients with esophageal atresia, imperforate anus and VACTERL association. The aim is to identify children's' and their parents' experiences of care, what

create the most value in the care process and their health-related quality of life and function. A second aim is to design a program for the screening of the child's functioning and need for support in child's everyday life and schooling before starting school by a "5-year-screening".

#### Neuroendocrine markers in Neuroblastoma

#### Georgantzi et al.

Neuroblastoma (NB) is the most frequent extracranial malignant tumor of childhood, originating from cells of the adrenal medulla or the sympathetic nervous system and exhibits a unique biological and clinical heterogeneity. In our study we want to: 1) to investigate the expression of different neuroendocrine markers in Neuroblastoma (NB), and to determine if these proteins are correlated to tumor stage, biological markers and outcome and 2) to explore if ultrasound-guided cutting needle biopsies are

#### Swedish childhood solid tumors biobank

#### Gustaf Ljungman, clinical leader and chairman of the board.

A collaborative effort since 2009 between the six universities in Sweden and the Childrens Cancer Foundation and its neural network NBCNS (neuroblastoma CNS tumors in children) with the goal of establishing a well-functioning national biobank of pediatric neural tumors., ie brain tumors and neuroblastoma. The biobank has started 2012. Yearly 60 brain tumor biopsies and 15 neuroblastoma biopsies are expected to be biobanked. The aim is to include all biopsied pediatric solid tumors (about 120/year). The purpose of the biobank is to facilitate research leading to improved diagnostics. estimation of prognosis, and the development of new therapeutic strategies. From autumn 2015 material from all pediatric solid tumors is collected nationwide

#### Difficult decisions and ethical aspects in pediatric oncology At the intersection of curative and palliative treatment in pediatric oncology

#### Frost et al.

The aim is to o examine to what extent there is a distinctive focus on palliative treatment in departments of pediatric oncology in Sweden, and how children in terminal care and their families perceive the meaning and importance of palliative care.

#### Experiences and ethics of sibling donors

#### Frost et al.

Uppsala collaborative study between the medical and philosophical faculty, which will in a later phase collaborate with international colleges. The study will concentrate on the impact of being used as a donor during childhood. Emphasis is put on psychological, social and ethical questions.

#### **Pediatric Neurology**

The research of the group deals with clinical neurological diseases and neurological dysfunctions. The researchers come from many different professions and their research comprise a wide range of scientific questions.

#### Members of the group

Ahlsten, Gunnar MD, Associate professor Borgestig, Maria PhD Bratteby-Tollerz, Linda MSc Dahl, Margareta MD, Associate professor Eeg-Olofsson, Orvar MD, Associate professor Ehrstedt, Christoffer, MD, PhD student Forsblad, Kristina, MD Höglund, Anette MSc Jonsson, Pysse Med Lic Kimber, Eva MD, PhD Kratz. Åsa MSc Kristiansen, Ingela MD, PhD student Lidström, Helene Ph D Liminga, Gunnar MD, PhD Lundberg, Staffan MD, PhD Strinnholm, Margareta MSc Strömberg, Bo MD, Associate professor

#### **Dissertation 2016**

No dissertation during 2016

#### List of publications 2014-2016 - original articles

- 1. Ehrstedt C, Kristiansen I, Ahlsten G, Casar-Borota O, Dahl M, Libard S, et al. Clinical characteristics and late effects in CNS tumours of childhood: Do not forget long term follow-up of the low grade tumours. European journal of paediatric neurology 2016;20(4):580-587.
- Borgestig M, Sandqvist J, Parsons R, Falkmer T, Hemmingsson H. Eye gaze performance for children with severe physical impairments using gaze-based assistive technology-A longitudinal study. Assistive technology 2016;28(2):93–102.
- 3. Rytterström P, Borgestig M, Hemmingsson H. Teachers' experiences of using eye gazecontrolled computers for pupils with severe motor impairments and without speech. European Journal of Special Needs Education 2016;31(4):506–19
- 4. Van't Hooft I, Norberg AL, Björklund A, Lönnerblad M, Strömberg B. Multiprofessional follow-up programmes are needed to address psychosocial, neurocognitive and educational issues in children with brain tumours. Acta Paediatrica 2016;105(6):676–83.
- Serenius F, Ewald U, Farooqi A, Fellman V, Hafström M, Hellgren K, et al. Neurodevelopmental Outcomes Among Extremely Preterm Infants 6.5 Years After Active Perinatal Care in Sweden. JAMA pediatrics 2016;170(10):954–63.
- 6. Serenius F, Farooqi A, Fellman V, Hafström M, Kallen K, Lindberg E, et al. Developmental problems in extremely preterm children with borderline intellectual functioning and free from neurosensory disabilities at 6.5 years in Sweden (the EXPRESS study). European Journal of Pediatrics 2016;175(11):1551–2.

- Ek I, Höglund A, Lidström H. An experience-based treatment model for children unwilling to eat : A Swedish study looks at ways of encouraging children to change their habits at mealtimes and helps parents adapt to these new approaches. Nursing Children and Young People 2016;28(5):22–8.
- 8. McKinlay A, Linden M, DePompei R, Jonsson CA, Anderson V, Braga L, et al. Service provision for children and young people with acquired brain injury : Practice recommendations. Brain Injury 2016;30(13–14):1656–64.

- 1. Källén K, Serenius F, Westgren M, Marsal K. Impact of obsteric factors on outcome of extremely preterm births in Sweden: prospective population-based observational study (EXPRESS). Acta Obstetrica et Gynecologica Scandinavica 2015;94(11):1203-14.
- 2. Lourenço Dos Santos S, Baraibar M A, Lundberg S, Eeg-Olofsson O, Larsson L, Friguet B. Oxidative proteome alterations during skeletal muscle ageing. Redox Biology 2015;5:267-74.
- 3. Serenius F, Blennow M, Marsal K, Sjörs G, Källén K. Intensity of Perinatal Care for Extremely Preterm Infants: Outcomes at 2,5 Years. Pediatrics 2015;135(5):E1163-E1172.
- 4. Tollerz L U, Forslund A H, Olsson R M, Lidström H, Holmbäck U. Children with cerbra palsy do not achieve healthy physical activity levels. Acta Paediatrica 2015;104(11):1125-29.
- Van`t Hooft I, Norberg Lindahl A, Björklund A, Lönnerblad M, Strömberg B. Multiprofessional follow-up programmes are needed to adress psychosocial, neurocognitive and educational issues in children with brain tumours. Acta Paediatrica 2105 Nov. 4, DOI: 10, 1111/apa 13207.

#### 2014

- 1. Jonsson P, Jonsson B, Eeg-Olofsson O. Psychological and social outcome of epilepsy in wellfunctioning children and adolescents.Eur J Paediatr Neurol 2014;18(3):381-90.
- Livingston JH, Mayer J, Jenkinson E, Kasher P, Stivaros S, Berger A et al. Leukoencephalopathy with Calcifications and Cysts: A Purely Neurological Disorder Distinct from Coats Plus. Neuropediatrics 2014;45(3):175-82.
- 3. Dahl M, Bergsten C, Hammarberg A, Sandström M. Autism spectrum disorders in severe cerebral palsy often discovered late. Retospective review of 10 years of medical records. Läkartidningen 2014;111:1296-8.
- 4. Ek I, Johansen J. Varför äter inte barnet. Läkartidningen 2014;111(11):464-6.

#### Agencies that support the work

ALF, research support to the University Hospital Regional research council Uppsala-Örebro region Reaearch grant from Uppsala county council Hedström foundation at Uppsala University Gillberg foundation Barncancerfonden Norrbacka-Eugenia foundation Margaretahemmet foundation Sunnerdahl foundation Josef and Linnea Carlsson foundation

#### Epilepsy

Rolandic epilepsy, the most common type of childhood epilepsies, has been studied from several aspects. A follow-up study to describe oromotor difficulties and dichotic listening test in this electroclinical syndrome is being prepared for publication.

A study evaluating the work-up and treatment of children with infantile spasms treated at our clinic during the last twenty years has been performed during 2015.

#### Spina bifida

Research on this group of children has been carried out for at least 15 years. Different medical factors especially the Chiari II-malformation and early puberty has been in focus in follow-up studies.

The global function of these children and adults is studied and its implications for what type and extent of support these individuals need at different ages has generated valuable new knowledge. A new study deals with children with spinal malformations who have an intact skin above the lesion.

We participate in the creation and start of a national quality register on children with spinal dysraphism and hydrocephalus. The registry will function as a secondary prevention programme for this group of children.

#### Follow-up studies of prematurely born infants

We participate in a national prospective longitudinal study on the neurological, ophthalmological and psychological development of infants born after less than 27 weeks of gestation between 2004 - 2007 in Sweden. 497 children survived until 1 year of age and these children have been followed - up at  $2\frac{1}{2}$  years corrected age and att 6  $\frac{1}{2}$  years chronological age. The results from the  $2\frac{1}{2}$  year examinations were published in JAMA May 2013. The results from the 6  $\frac{1}{2}$  year study are analysed and the manuscript will be submitted for publication in the beginning of 2016. Furthermore the follow-up of the same cohort of children at the age of 12 will start in the spring of 2016.

Another two studies were published during 2015 from the EXPRESS group in which we participate.

#### **Evaluation of motor function**

A follow-up study of children who underwent selective dorsal rhizotomy is under progress.

#### Brain tumours in children

Together with the Department of Paediatric Oncology at the Karolinska Institute in Stockholm a project with the aim to co-ordinate the psychological, neurocognitive and pedagogical long-term follow-up with the medical follow-up of children diagnosed with brain tumours in the Stockholm and Uppsala-Örebro healthcare regions in Sweden has been completed. The results were published in Acta Paediatrica in November 2015.

During 2011 two different doctorial projects were started dealing with brain tumours in children and adolescents diagnosed and treated in the Uppsala-Örebro health care region in Sweden. One part of the projects is to give a broad description of the initial presentation, clinical course and late effects for all children treated for brain tumours in the region 1995-2006. This part is now finished and a manuscript for publication is accepted for publication during 2016.

In the other parts two different kinds of brain tumours with low grade of malignancy according to the WHO classification will be studied.

1/ neuroglial tumours (gangliogliomas and dysembrionic neuroepithelial tumours (DNET) WHO grade I.

2/ astrocytomas WHO grade I in the posterior fossa.

The objectives are focused on medical, motor and cognitive late effects as well as possible methods for intervention. These projects are going on according to the time schedule and will end in two different dissertations.

#### Rehabilitation

Children with brain tumours, traumatic brain injuries or epilepsy nowadays, to a large extent, survive the injury or illness. Many children, however, demonstrate long-lasting difficulties affecting motor function, cognition and/or behaviour. The aim of the present project is to investigate incidence and prevalence, rehabilitation received, functioning level, as well as activities and limitations in daily life of children with acquired brain injury. Another aim is to create and evaluate a new model of rehabilitation focusing on the needs of children and families in a long perspective.

#### **Pediatric Surgery and Pediatric Urology**

#### Helene Engstrand Lilja

Pediatric surgery and pediatric urology cover the surgical management of congenital malformations and acquired diseases of the gastrointestinal tract and urogenital systems in children from the neonatal period until the age of 15. This field of research therefore spans from prenatal diagnosis in fetuses to long-term follow-up of functional outcomes in adolescents. Research in pediatric surgery and urology is performed in four centers in Sweden, and the complexity of the conditions often require multidisciplinary collaborations with e.g. pediatricians, neonatologists, adult surgeons and urologists, as well as basic scientists.

Two PhD students defended their thesis successfully during 2016

#### Members of the group during 2016

Ammar Al-Mashhadi, MD, PhD-student Gertrud Angsten, MD, PhD Gillian Barker, MD, PhD Rolf Christofferson, associate professor, MD, PhD Johan Danielson, MD, PhD-student Felipe Donoso, MD, PhD-student Helene Engstrand Lilja, associate professor, MD, PhD Peter Flacker, MD, PhD-student Fanny Fredriksson, MD, PhD-student Elisabet Gustafson, MD, PhD-student Niclas Högberg, MD, PhD Ann-Marie Kassa, RN, PhD-student Maria Lindström Nilsson, RN, PhD-student Göran Läckgren, professor, MD, PhD Staffan Meurling professor, MD, PhD Erik Sköldenberg, MD, PhD Anders Stenbäck, MD, PhD Arne Stenberg, associate professor, MD, PhD

#### Publications 2014-2016

- Asif S, Ekdahl KN, Fromell K, Gustafson E, Barbu A, Le Blanc K, Nilsson B, Teramura Y. Heparinization of cell surfaces with short peptide-conjugated PEG-lipid regulates thromboinflammation in transplantation of human MSCs and hepatocytes. Acta Biomater. 2016 Apr 15;35:194-205.
- Donoso F, Kassa AM, Gustafson E, Meurling S, Lilja HE. Outcome and management in infants with esophageal atresia- a single centre observational study. Journal of Pediatric Surgery. 2016;51(9):1421-1425.
- 3. Fredriksson F, Christofferson RH, Lilja HE. Adhesive small bowel obstruction after laparotomy during infancy. British Journal of Surgery 2016;103(3):284-289.

- 4. Högberg N, Carlsson PO, Hillered L, Stenbäck A, Larsson A, Lilja HE. Intestinal intraluminal glycerol and plasma I-FABP levels in preterm infants with necrotizing enterocolitis. Clinics in Surgery 26 augusti 2016; volume 1 Article 1085.
- 5. Lilja HE, Schulten D. Repair of giant omphalocele in a premature neonate with non crosslinked porcine acellular dermal matrix (Strattice Tissue Matrix). Journal of Pediatric Surgery Case Reports 2016 (12):27-30.
- 6. Peleli M, Al-Mashhadi A, Yang T, Larsson E, Wåhlin N, Jensen B L, et al. Renal denervation attenuates NADPH oxidase-mediated oxidative stress and hypertension in rats with hydronephrosis. American Journal of Physiology Renal Physiology. 2016 Jan 1;310(1):F43-56.
- Stenström P, Brautigam M, Lilja HE, Wester T. Patient-reported nationwide outcome of children and adolescents with total colonic aganglionosis. Journal of Pediatric Surgery 2016 Nov 17.

- 1. Al-Mashhadi A N, Nevéus T, Stenberg A, Karanikas B, Persson A E, Carlstrom M, et al. Surgical treatment reduces blood pressure in children with unilateral congenital hydronephrosis. Journal of Pediatric Urology. 2015;11(2):91.e1-91.e6.
- 2. Angsten G, Danielson J, Kassa A, Lilja H E. Outcome of laparoscopic versus open gastrostomy in children. Pediatric surgery international (Print). 2015;31(11):1067-1072.
- 3. Danielson J, Karlbom U, Graf W, Olsen L, Wester T. Posterior sagittal anorectoplasty results in better bowel function and quality of life in adulthood than pull-through procedures. Journal of Pediatric Surgery. 2015;50(9):1556-1559.
- Engstrand Lilja H, Wefer H, Nyström N, Finkel Y, Engstrand L. Intestinal dysbiosis in children with short bowel syndrome is associated with impaired outcome. Microbiome 2015 May; 4;3:18 DOI: 10.1186/s40168-015-0084-7.
- 5. Granstrom A L, Danielson J, Husberg B, Nordenskjold A, Wester T. Adult outcomes after surgery for Hirschsprung's disease : Evaluation of bowel function and quality of life. Journal of Pediatric Surgery. 2015;50(11):1865-1869.
- 6. Klar J, Raykova D, Gustafson E, Tóthová I, Ameur A, Wanders A, et al. Phenotypic expansion of visceral myopathy associated with ACTG2 tandem base substitution. European Journal of Human Genetics. 2015;23(12):1679-1683.
- 7. Korberg I B, Hofmeister W, Markljung E, Cao J, Nilsson D, Ludwig M, et al. WNT3 involvement in human bladder exstrophy and cloaca development in zebrafish. Human Molecular Genetics. 2015;24(18):5069-5078.

- 1. Dantonello T M, Lochbühler H, Schuck A, Kube S, Godzinski J, Sköldenberg E, et al. Challenges in the Local Treatment of Large Abdominal Embryonal Rhabdomyosarcoma. Annals of Surgical Oncology. 2014;21(11):3579-3586.
- Draaken M, Baudisch F, Timmermann B, Kuhl H, Kerick M, Proske J, et al. Classic bladder exstrophy : Frequent 22q11.21 duplications and definition of a 414 kb phenocritical region. Birth defects research. Clinical and molecular teratology. 2014;100(6)
- Fredriksson F, Christofferson R H, Carlsson P, Lilja H E. Locally increased concentrations of inflammatory cytokines in an experimental intraabdominal adhesion model. Journal of Pediatric Surgery. 2014;49(10):1480-1484.
- 4. Kirsch A J, Arlen A M, Läckgren G. Current Trends in Dextranomer Hyaluronic Acid Copolymer (Deflux) Injection Technique for Endoscopic Treatment of Vesicoureteral Reflux. Urology. 2014;84(2):462-468.
- 5. Reutter H, Draaken M, Pennimpede T, Wittler L, Brockschmidt F F, Ebert A, et al. Genomewide association study and mouse expression data identify a highly conserved 32 kb intergenic

region between WNT3 and WNT9b as possible susceptibility locus for isolated classic exstrophy of the bladder. Human Molecular Genetics. 2014;23(20):5536-5544.

- 6. Soderhall C, Lundin J, Lagerstedt-Robinson K, Grigelioniene G, Läckgren G, Kockum C C, et al. A Case with Bladder Exstrophy and Unbalanced X Chromosome Rearrangement. European journal of pediatric surgery. 2014;24(4):353-359.
- Wester T, Borg H, Naji H, Stenstrom P, Westbacke G, Lilja H E. Serial transverse enteroplasty to facilitate enteral autonomy in selected children with short bowel syndrome. British Journal of Surgery. 2014;101(10):1329-1333.

#### Reviews 2014-2016

#### 2016

1. Ekdahl KN, Teramura Y, Hamad OA, Asif S, Duehrkop C, Fromell K, Gustafson E, Hong J, Kozarcanin H, Magnusson PU, Huber-Lang M, Garred P, Nilsson B. Dangerous liaisons: complement, coagulation, and kallikrein/kinin cross-talk act as a linchpin in the events leading to thromboinflammation. Immunol Review 2016 Nov;274(1):245-269.

#### **Dissertations 2016**

- 1. Fanny Fredriksson. *Outcome and prevention strategies in peritoneal adhesion formation*. Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine 1217. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-554-9557-2.
- Elisabet Gustafson. *Thromboinflammation. in a Model of Hepatocyte Transplantation.* Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine 123. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-554-9592-3.

#### Agencies that support the work/Funding

ALF 671 860 SEK H.R.H. Crown Princess Lovisa's Association for Paediatric Health Care/Axel Tielman's Memorial Fund 200 000 SEK

#### High blood pressure in children with hydronephrosis

#### Ammar Al-Mashhadi, Arne Stenberg, Tryggve Nevéus, Mattias Carlström

Arterial hypertension a globally growing health problem, leading to e.g. myocardial infarction and stroke. Hypertension can be caused by renal dysfunction. Hydronephrosis is a relatively common (1%) condition after birth, and is characterized by dilation of the renal pelvis. Hydronephrosis is usually due to a partial ureteropelvic junction obstruction. Hydronephrosis may lead to progressive renal dysfunction. Although hydronephrosis is common, its pathophysiology is poorly understood and its clinical management is debated. Non-operative management of neonatal hydronephrosis is currently advocated, since the renal function can be rather well preserved for years. However, the long-term consequences of this new strategy are not known. We have recently discovered a strong

connection between hydronephrosis (experimental and congenital) and obstructive nephropathy and hypertension in later life. Increased oxidative stress and reduced nitric oxide (NO) bioavailability in the affected kidney(s) are thought to drive this process. In experimental hydronephrosis, we intend to determine if increased oxidative stress and reduced NO bioavailability in the macula densa cells can explain the arterial hypertension and the reduction of kidney function. The relative role of the systems can be determined by anti-oxidative therapy and/or NO-stimulatory therapy. We will also determine if relief of the obstruction, by either nephrectomy or pyeloplasty, reduces hypertension and salt-sensitivity in hydronephrosis. Also the roles of the renin-angiotensin system, reactive oxygen species, the renal sympathetic nerve activity, inflammatory molecules and infectious agents in hydronephrosis during early and adult age will be addressed. In children with hydronephrosis, we intend to determine if they have increased oxidative stress and/or decreased NO bioavailability and if they develop hypertension and renal disease in later life.

### A national, prospective study of children with disorders of sexual development (DSD)

#### Gillian Barker, Maria Halldin, Agneta Nordenskjöld et al.

Every year, approximately 40 children are born in Sweden with external genitalia that are not typically masculine or feminine. This disorder of sexual development (DSD) can be caused by a variety of alterations on the chromosomal, gonadal, or phenotypic levels. In this national, multicenter project, the parents of all children born in Sweden with DSD are asked to take part of a prospective study which will follow the treatment and development of the child. The four DSD centers in Sweden (Uppsala, Stockholm, Göteborg, and Lund) are involved in the study, Uppsala. The lead investigators are Agneta Nordensköld and Anna Nordenstam at the Astrid Lindgrens Barnsjukhus. This work has led to collaborative work between the centres. One of these is an application to the Ethical Committee has been submitted to carry out a randomized controlled trial of a free foreskin graft in hypospadias repair, which will also be run in 3 centres (Uppsala, Stockholm and Göteborg).

### Studies on long-term outcome of anorectal malformations and Hirschsprungs disease

#### Johan Danielson, Wilhelm Graf, Urban Karlbom, Tomas Wester

This project investigates the long-term outcome of anorectal function and quality of life (QoL) in adult patients with anorectal malformations (ARM) and Hirschsprungs disease (HSD). It also evaluates different strategies to reduce persistent anal incontinence after surgery.

The ongoing projects in this study group contain the following: (1) study of function and QoL in adult patients with HSD that previously underwent surgery for HSD at our clinic. (2) study of outcome in ARM-patients operated with dynamic graciloplasty. (3) study of what problems adult ARM patients with persistent anal incontinence have in the clinical setting. (4) study of an injectable device placed in the anal canal of adult patients with persistent anal incontinence. The three latter studies are currently being submitted for publication.

#### National prospective study of pediatric patients receiving a gastrostomy

Johan Danielson, Jan Rutqvist, Einar Arnbjörnsson, Gunnar Göthberg (pediatric surgeons responsible for the study at each pediatric surgical center, Danielson is the controler of the study)

This project is a prospective, multicenter, non-randomized study of pediatric patients receiving a gastrostomy. All four centers of pediatric surgery in Sweden are including patients. The patients are followed one year after surgery and complications and patients satisfaction are monitored and related to the underlying condition and surgical technique. The study has to date included over 500 patients and aims to include 1000 during a five-year period.

### Esophageal and respiratory morbidity and function in the growing child operated for esophageal atresia

#### Felipe Donoso Torres, Helene Engstrand Lilja

Approximately 30 children annually are born esophageal atresia (EA). The survival rate is around 90%, and many of these children experience e.g. gastrointestinal reflux, dysphagia, anastomotic stricture, recurrent respiratory tract infections, and impaired pulmonary function. This Ph.D.-project consists of four parts: (1) retrospective review of the hospital records of children operated for EA 1994-2004 and 2005-2013. The latter cohort received prophylactic proton pump inhibition, but the first one did not. We have found that prophylactic PPI-treatment does not reduce the rate of AS. Long gap EA, high birth weight and

anastomotic tension were found to be independent risk factors of AS. (2) Analysis of esophageal biopsies taken in children operated for EA at endoscopic control at 1 and 14-15 years of age between 2011 and 2017 (~40 children in each group). Outcome measure is incidence of esophagitis and esophageal metaplasia in relation to esophageal impedance findings and proton pump inhibition. (3) Prospective analysis of pulmonary function in children operated for EA at ages 7-8, and 14-15 (~40 children in each group). The testing includes dynamic and static spirometry, diffusion capacity of CO, exhaled NO, nitrogen wash-out, impulse oscillometry and forced oscillation, and ergospirometry. (4) Exploration of health-related quality of life in children operated for EA, and their parents, using a validated questionnaire (DISABKids). This questionnaire has not been applied in EA before.

### Intestinal microbial profiles of infants with short bowel syndrome using 454-pyrosequencing technique

#### Helene Engstrand Lilja, Niklas Nyström, Yigael Finkel, Lars Engstrand

The composition of the intestinal microbiota seems to be an important factor in determining the clinical outcome in children with short bowel syndrome (SBS). Alterations in the microbiota may result in serious complications such as small bowel bacterial overgrowth (SBBO) and intestinal mucosal inflammation that leads to prolonged parenteral nutrition (PN) dependency with subsequently increased risk of liver failure and sepsis. The study includes children diagnosed with SBS in the neonatal period. Healthy siblings served as controls. Faecal samples were collected and microbial profiles were analyzed by using 16S rRNA gene sequencing on the Illumina MiSeq platform. We observed a pronounced microbial dysbiosis in children with SBS on PN treatment with an increased and totally dominating relative abundance of *Enterobacteriacae* compared to children with SBS is consistent with intestinal microbiome mappings in inflammatory bowel diseases such as Crohns disease and necrotizing enterocolitis in preterm infants.

### Early reduced nephron number and development of hypertension and renal disease

#### Peter Flacker, Anders Stenbäck, Mattias Carlström, Tryggve Nevéus

The project aims at investigating the link, and the underlying mechanisms, between renal abnormalities during early life (e.g. reduced nephron number after nephrectomy) and later development of hypertension and renal disease. We hypothesize that virtually any renal complication that is associated with reduced nephron number can lead to excessive workload for the remaining nephrons, and cause oxidative stress in the JGA. Imbalance between reactive oxygen species and nitric oxide may impair important autoregulatory mechanisms including the TGF response, and subsequently lead to both hypertension and renal disease. This is modulated by salt intake. The mechanisms by which high salt intake exerts damaging effects on both renal and cardiovascular systems are still being debated, but interaction with the renin-angiotensin-aldosterone-system (RAAS) and renal sympathetic nerve (RSN) activity as well as modulation of nitric oxide and superoxide signalling have been proposed.

During the experimental part with rats we investigate the role of RSN activity, and the RAAS, in modulation of renal and cardiovascular functions in the uninephrectomy and high salt intake (UNX+HS) disease model. We also intend to have a look how UNX+HS influences renal microvascular function and to determine the specific contribution of different NADPH oxidase isoforms.

In the clinical part we are interested in the influence of early life reduction in renal mass (nephrectomy) on renal function, blood pressure, levels of oxidative stress and inflammation markers in plasma and urine.

We assume that the results of this project can help to give better recommendations regarding follow up, diet and potential prophylactic treatment in uninephrectomized patients.

#### Outcome and prevention strategies in peritoneal adhesion formation

#### Fanny Fredriksson, Rolf Christofferson, Helene Engstrand Lilja

Peritoneal adhesions occur in up to 93% of adults after peritoneal trauma during surgery. Most adhesions are asymptomatic but can cause female infertility, small bowel obstruction (SBO) and chronic abdominal pain. Adhesion prophylaxis is needed to reduce the significant morbidity and increased health care costs resulting from peritoneal adhesions. This thesis aims to establish a relevant and reproducible experimental adhesion model to simultaneously study the healing processs and adhesion formation and later to examine whether carbazate-activated polyvinyl alcohol (PVAC), an aldehyde-carbonyl scavenger, can reduce adhesion formation or not; and, in a long-term followup, to investigate the incidence of and identify risk factors for adhesive SBO requiring surgical treatment after laparotomy during infancy and to survey the prevalence of self-reported chronic abdominal pain and female infertility. Male Sprague-Dawley rats were subjected to laparotomy, cecal abrasion, and construction of a small bowel anastomosis and examined at various time points after surgery. Early elevation of IL-6, IL-1 $\beta$  and TNF- $\alpha$  concentrations in peritoneal fluid but not in plasma correlate to adhesion formation in this rodent adhesion model, indicating that anti-adhesion treatment should be early, local and not systemic. The animals were treated with either peritoneal instillation of PVAC, or the anastomosis was sutured with PVAC-impregnated resorbable polyglactin sutures. At day 7, bursting pressure of the anastomosis was measured and adhesions were blindly evaluated using Kennedy- and Nair scoring systems. PVAC-impregnated sutures reduced adhesion formation without reducing bursting pressure. Infants who underwent laparotomy between 1976 and 2011 were identified (n=1185) and 898 patients were included with a median follow-up time of 14.7 (range 0.0-36.0) years. The median age at first laparotomy was 6 (range 1.0365.0) days. There were 113 patients (12.6%) with adhesive SBO, with the highest incidence found in patients with Hirschsprung's disease (19 of 65, 29%), malrotation (13 of 45, 29%), intestinal atresia (11 of 40, 28%) and necrotizing enterocolitis (16 of 64, 25%). Lengthy duration of surgery (hazard ratio (HR) 1.25, 95% CI, 1.07 to 1.45), stoma formation (HR 1.72, 1.15 to 2.56) and postoperative complications (HR 1.81, 1.12 to 2.92) were independent risk factors. Chronic abdominal pain was reported in 180 (24.0%) of 750 patients, and 17 (13.8%) of 123 women reported infertility. The morbidity after laparotomy in neonates and infants is high. Awareness of the risk factors may promote changes in surgical practice.

#### Isolation and transplantation of hepatocytes

#### **Elisabet Gustafson**

In liver failure, regardless of cause, there is a clinical need for alternatives to liver transplantation. Hepatocyte transplantation is one option that has been held promising for a long time. The method has however been hampered by an early clearance of the transplanted cells by the innate immune system. We have established a method for isolation and culture of human hepatocytes from liver biopsies. The cells have been used for in vitro experiments analyzing the different aspects of innate immunity when the cells come in contact with ABO-compatible blood. Besides the inflammatory reactions from neutrophils and the complement system, there is also activation of several steps in the blood coagulation system. The study has outlined the basic background by which isolated hepatocytes are recognized by the innate immune system and identified a procoagulative phenotype of isolated hepatocytes. The project has included strategies to protect transplanted cells from recognition by systemic administration of inhibitors and surface modification of the cells. The aim of this project is to gain knowledge that may improve the short- and long-term survival of transplanted hepatocytes.

#### Microdialysis studies in experimental and clinical necrotizing enterocolitis

#### Niclas Högberg, Anders Stenbäck, Helene Engstrand Lilja

Necrotizing enterocolitis (NEC) is the most serious gastrointestinal disorder in newborn infants with an incidence of 10 to 15% in those with very low birth weight (VLBW; <1500 g). More than 90% of the infants who develop NEC are born prematurely. The risk of NEC is inversely related to gestational age and birth weight. The disease is characterized by inflammation of the bowel that can progress to bowel necrosis and multiple organ failure. Despite extensive research, NEC remains a major cause of death in neonates, with mortality rates approaching 40 % in VLBW infants. Intestinal ischemia is thought to be an important component of the pathogenesis of NEC, causing variable degrees of ischemia of the small and large intestine, ranging from mild ischemia of the intestinal mucosa to transmural necrosis of the gut wall. There is a need for a new, sensitive and specific diagnostic method for early identification of NEC in order to attenuate its course. We have recently shown that rectal intraluminal microdialysis in an animal model of NEC is a reproducible, sensitive and specific, non-invasive early diagnostic method to detect intestinal hypoxia. At present we are investigating if rectal intraluminal microdialysis is a useful early diagnostic method of intestinal hypoxia in infants suspected of suffering from NEC.

#### Health-related quality of life, function and experience of health care in children and youth with the diagnoses esophageal atresia, anorectal malformation and VACTERL association

#### Ann-Marie Kassa, Gunn Engvall, Helene Engstrand Lilja,

Esophageal atresia (EA) is a congenital malformation where the oral esophagus ends blindly and the aboral esophagus emerges as a tracheal fistula. In anorectal malformations (ARM) the anus is absent. These two malformations are often combined in VACTERL association. The VACTERL association includes congenital malformations in at least three of the following organ systems: Vertebral (V), anorectal (A), cardiac (C), tracheal and esophageal (TE), renal (R) and limb (L), most oftenly the forearm. Uppsala University Children's hospital admits 20-30 newborn children annually with the diagnoses EA, ARM and/or VACTERL.

The aim of this PhD-study is to explore the experiences concerning health care in these children, youth and their parents, as well as the patient's health-related quality of life and function. A second aim is to develop a programme for multi-professional screening of the child's functions and its need for support at school start. Four studies are included: (1) Computer-assisted qualitative interviews concerning health and hospital experiences in children 5-8 years old, including also interviews with their parents. In this first study the children described awareness of their health history and feelings of being proud but also of being different and not understood due to their physical dysfunction. They were happy to visit the hospital to meet familiar staff but expressed negative feelings about missing out on normal life. Various ways of coping with the difficult situations were stated and suggestions to improve hospital care were given.

(2) Qualitative interviews with youth and young adults 15- 20 years old concerning experiences of health and health care, focusing on the transfer to adult health care. (3) Quantitative study with postal questionnaires: Health related Quality of Life (DISABkids) for children 8 - 17 years old, and a proxy version for their parents. For identifying signs of depression and anxiety, Beck Youth scales are used for children and youth and Beck depression and Anxiety Inventory for the parents. (4) Pilot study including multi-professional screening of children for assessment of functions and need for support around school start.

#### Effects of a dog in pediatric care

#### Maria Lindström Nilsson, Helene Engstrand Lilja, Ann Edner

Previous research on dogs in health care (AAT, animal assisted therapy) demonstrate positive effects on both patients and staff. In Swedish pediatric health care, dogs are seldomly used despite that the UN child convention states that measurements should be taken to optimize the physical, psychological, social and existential well-being of children in need of health care. The aims of this Ph.D.-project are to explore physiological and psychological effects of AAT with a dog in pediatric care, and to investigate whether there is a risk of increased allergen exposure or bacterial colonization of the child in dog AAT. The project is approved by the ethical review board. A prospective, randomized cross-over study of 50 children, 3-18 years old (equal gender distribution) admitted to a tertiary center pediatric ward for a neurologic, surgical or orthopedic affliction. Half of the children first play at will for 20-30 min, followed by 20-30 min play with a dog according to the child's desire. The other half play in the reverse order. During play, data on heart rate variability, skin electric conductance, oxygen saturation, skin temperature, salivary cortisol, and bacterial cultures are collected. Questionnaires are filled in by children/parents and by staff. The first study is how the child's doin to how the child, its parents and the medical staff experience AAT through semi structured observation and a questionnaire. The third study is how the medical staff experiences having a dog at their workplace through a questionnaire. The fourth study is of whether the bacterial flora in dog or child changes during AAT or not, and if the allergens in the room air change from before, during or after dog AAT.

### Long-term effects of endoscopic treatment of high-grade vesicoureteral reflux

#### Göran Läckgren, Anders Stenbäck

Approximately 1% of all children have vesicoureteral reflux (VUR; back-flow of urine from the bladder to the ureter), and half of them develop clinical symptoms of urinary tract infections (UTI) of varying severity. The reflux is graded I-V. In 1993, endoscopic treatment of VUR with dextranomer particles in non-animal hyaluronic acid (Deflux) was introduced. Submucosal injection of Deflux below the ureteral orifice in the bladder reduces VUR and can be done on an out-patient basis. This project addresses the long-term effects of Deflux therapy in children with advanced VUR (grade IV-V) in two cohorts (1993-8 and 1998-2003). In the first study, the hospital records (in Uppsala and the local hospital) of patients 1993-2003 (n=208) are reviewed, and parameters such as documented UTI, cystometry findings, micturition cystograms, renal scintigraphies, as well as morbidity and intercurrent diseases, are extracted. In the second study, a questionnaire is filled in by, and telephone interview is performed with the parents or patients with focus on UTI and signs of bladder dysfunction. In the third study, a clinical assessment of the patients is performed at the local hospital, combined with MAG-3 renal scintigraphy to detect residual VUR, and ultrasonography of the kidneys and bladder. In the fourth study, the 52 patients that had residual,

symptomatic VUR despite Deflux therapy, and subsequently were subjected to open reimplantation of the ureter(s), will be reviewed and worked-up as the other 208, thereby permitting a head-to-head comparison of Deflux therapy vs. open surgery.

The project will reveal the long-term effects of Deflux in VUR, and identify risk factors for severe UTI, and thereby the possibility to avoid them. The rationale for comparing two cohorts regarding outcome and kidney function is to distinguish between children that need early, active treatment and children that may not need treatment for their VUR at all.

On two occasions (2006 and 2012) a questionnaire (QaA) has been sent out to all patients regarding urinary tract infections (UTI) and bladder dysfunction. The first investigation has been presented and published in J Urology 2007. The second QaA (2012) has shown a significant lower risk of new febrile UTI in men compared to women and therefore a third QaA (2017) combined with a new study of hospital charts is going to be performed. The purpose is to focus on the female population and investigate potential risks for new UTI with increasing age and also look at eventual risks for UTI in pregnancy.

### Implementation of the national follow-up program for anorectal malformations in a tertiary university hospital

#### Björn Sjöström, Rolf Christofferson

Anorectal malformations (ARM) means absence of a normal anus, most oftenly with a fistula from rectum to the perineum, vestibulum or urethra. Approximately forty children are born with anorectal malformations annually in Sweden, and of these, 10-14 children are operated at Akademiska sjukhuset. Up to 78% of children with ARM have associated malformations, e.g. genitourinary, spinal, cardiac or skeletal. Adults and adolescents that have been operated for ARM report impaired

anal continence and less quality of life than matched controls, which underlines the importance of a structured follow-up with early and aggressive treatment of e.g. constipation and soiling. In order to harmonize the follow-up, the Swedish Pediatric Surgical Association launched a national follow-up program in 2010. The aims of this study are to (1) to validate the implementation of the program at Uppsala University Children's hospital, (2) to classify the ARM according to the Krickenbeck classification, and (3) to analyze the functional outcome at 5 and 14 years, during the interval of 2010 to 2014.

#### **Paediatric Inflammation Research**

#### **Kjell Alving**

The group of Paediatric Inflammation Research covers a wide spectrum of paediatric specialties, roughly divided into five interrelated subgroups focusing on allergology, pulmonology, rheumatology, gastroenterology, and nephrology, respectively.

#### Members of the group during 2016

Kjell Alving, professor Lillemor Berntsson, associate professor Magnus Borres, adjunct professor Maria Cederblad, PhD Gianni Celsi, associate professor Ingrid Dahlbom, PhD Sten Dreborg, associate professor Maria Ekelund, PhD student Anna Fäldt, PhD student Tony Hansson, associate professor Charlotte Heijkenskjöld Rentzhog, PhD Annika Hollsing, PhD Jennifer Johnsson, PhD student Johan Kaarme, PhD student Pia Kalm Stephens, PhD student Birgitta Karanikas, research nurse Hans Kollberg, associate professor Christina Krantz, PhD student Elisabet Lundmark, PhD student Åsa Neuman, PhD Tryggve Nevéus, senior lecturer Lennart Nordvall, associate professor Britt-Inger Nyberg, technician Niklas Nyström, PhD student Christophe Pedroletti, PhD Inger Jönson Ring, PhD student Jörgen Syk, PhD Nikolaos Tsolakis, PhD student Anders Öman, PhD student

#### Publications 2014-2016

- 1. Al-Shamkhi N, Alving K, Dahlen SE, Hedlin G, Middelveld R, Bjerg A, Ekerljung L, Olin AC, Sommar J, Forsberg B, Janson C, and Malinovschi A, *Important non-disease-related determinants of exhaled nitric oxide levels in mild asthma results from the Swedish GA(2) LEN study*. Clin Exp Allergy, 2016. **46** (9): 1185-93.
- Arvonen M, Berntson L, Pokka T, Karttunen TJ, Vahasalo P, and Stoll ML, *Gut microbiota-host interactions and juvenile idiopathic arthritis*. Pediatr Rheumatol Online J, 2016. 14 (1): 44.
- 3. Bazargani F, Jonson-Ring I, and Neveus T, *Rapid maxillary expansion in therapy-resistant enuretic children: An orthodontic perspective.* Angle Orthod, 2016. **86** (3): 481-6.
- 4. Berntson L, Agback P, and Dicksved J, Changes in fecal microbiota and metabolomics in a

*child with juvenile idiopathic arthritis (JIA) responding to two treatment periods with exclusive enteral nutrition (EEN).* Clin Rheumatol, 2016. **35** (6): 1501-6.

- Berntson L, Hedlund-Treutiger I, and Alving K, Anti-inflammatory effect of exclusive enteral nutrition in patients with juvenile idiopathic arthritis. Clin Exp Rheumatol, 2016. 34 (5): 941-945.
- 6. Berntson L, Hedlund-Treutiger I, and Alving K, *Anti-inflammatory effect of exclusive enteral nutrition in patients with juvenile idiopathic arthritis.* Clin Exp Rheumatol, 2016. **34** (5): 941-945.
- Bjerg A, Ekerljung L, Eriksson J, Naslund J, Sjolander S, Ronmark E, Dahl A, Holmberg K, Wennergren G, Toren K, Borres MP, Lotvall J, and Lundback B, *Increase in pollen sensitization in Swedish adults and protective effect of keeping animals in childhood*. Clin Exp Allergy, 2016. 46 (10): 1328-36.
- Brandstrom J, Lilja G, Nilsson C, Ingemarsson N, Borres MP, Brostedt P, and Englund H, *IgE* to novel citrus seed allergens among cashew-allergic children. Pediatr Allergy Immunol, 2016. 27 (5): 550-3.
- 9. Cederblad M, Engsheden N, Ghaderi A, Enebrink P, Engvall G, Nevéus T, and Sarkadi A, *No difference in relationship satisfaction between parents of children with enuresis and normative data.* J Child Fam Stud, 2016. **25**: 1345-51.
- 10. Dahlbom I, Nyberg BI, Berntson L, and Hansson T, *Simultaneous detection of IgA and IgG antibodies against tissue transglutaminase: The preferred pre-biopsy test in childhood celiac disease.* Scand J Clin Lab Invest, 2016. **76** (3): 208-16.
- 11. Dahlin JS, Malinovschi A, Ohrvik H, Sandelin M, Janson C, Alving K, and Hallgren J, *Lin-CD34hi CD117int/hi FcepsilonRI+ cells in human blood constitute a rare population of mast cell progenitors.* Blood, 2016. **127** (4): 383-91.
- 12. Dreborg S, *Cow's milk protein allergy and common gastrointestinal symptoms in infants*. Acta Paediatr, 2016. **105** (3): 253-4.
- 13. Dreborg S, Basomba A, Löfkvist T, Holgersson M, and Möller C, Validation of methods for estimation of changes in skin reactivity and correlation to shock organ sensitivity. Immunotherapy: Open Access, 2016. **2**: 109.
- 14. Dreborg S, Holgersson M, and Möller C, *Evaluation of changes in skin reactivity by skin prick test titration*. Immunotherapy: Open Access, 2016. **2**: 116.
- 15. Dreborg S, Wen X, Kim L, Tsai G, Nevis I, Potts R, Chiu J, Dominic A, and Kim H, *Do epinephrine auto-injectors have an unsuitable needle length in children and adolescents at risk for anaphylaxis from food allergy?* Allergy Asthma Clin Immunol, 2016. **12**: 11.
- 16. Grandahl M, Rosenblad A, Stenhammar C, Tyden T, Westerling R, Larsson M, Oscarsson M, Andrae B, Dalianis T, and Neveus T, *School-based intervention for the prevention of HPV among adolescents: a cluster randomised controlled study.* BMJ Open, 2016. **6** (1): e009875.
- 17. Johansson H, Norlander K, Alving K, Hedenstrom H, Janson C, Malinovschi A, Nordang L, and Emtner M, *Exercise test using dry air in random adolescents: Temporal profile and predictors of bronchoconstriction.* Respirology, 2016. **21** (2): 289-96.
- Kaarme J, Hickman RA, Neveus T, Blomberg J, and Ohrmalm C, *Reassuringly low carriage of* enteropathogens among healthy Swedish children in day care centres. Public Health, 2016. 140: 221-227.
- 19. Lovstrom L, Emtner M, Alving K, Nordvall L, Borres MP, Janson C, and Malinovschi A, *High levels of physical activity are associated with poorer asthma control in young females but not in males.* Respirology, 2016. **21** (1): 79-87.
- 20. Lundmark E, Stenberg A, Hagglof B, and Neveus T, *Reboxetine in therapy-resistant enuresis: A randomized placebo-controlled study.* J Pediatr Urol, 2016. **12** (6): 397 e1-397 e5.
- Malinovschi A, Janson C, Borres M, and Alving K, Simultaneously increased fraction of exhaled nitric oxide levels and blood eosinophil counts relate to increased asthma morbidity. J Allergy Clin Immunol, 2016. 138 (5): 1301-1308 e2.
- 22. Maruyama N, Nakagawa T, Ito K, Cabanos C, Borres MP, Moverare R, Tanaka A, Sato S, and Ebisawa M, *Measurement of specific IgE antibodies to Ses i 1 improves the diagnosis of sesame allergy*. Clin Exp Allergy, 2016. **46** (1): 163-71.

- 23. Maruyama N, Sato S, Yanagida N, Cabanos C, Ito K, Borres MP, Moverare R, Tanaka A, and Ebisawa M, *Clinical utility of recombinant allergen components in diagnosing buckwheat allergy*. J Allergy Clin Immunol Pract, 2016. **4** (2): 322-3 e3.
- 24. Mew R, Borres M, Sjolander S, and du Toit G, *A retrospect study into the utility of allergen components in walnut allergy*. Pediatr Allergy Immunol, 2016. **27** (7): 750-752.
- 25. Mogensen I, Alving K, Bjerg A, Borres MP, Hedlin G, Sommar J, Dahlen SE, Janson C, and Malinovschi A, *Simultaneously elevated exhaled nitric oxide and serum-eosinophil cationic protein relate to recent asthma events in asthmatics in a cross-sectional population-based study.* Clin Exp Allergy, 2016. **46** (12): 1540-1548.
- 26. Ohrmalm L, Malinovschi A, Wong M, Levinson P, Janson C, Broliden K, and Alving K, *Presence of rhinovirus in the respiratory tract of adolescents and young adults with asthma without symptoms of infection.* Respir Med, 2016. **115**: 1-6.
- Patelis A, Dosanjh A, Gunnbjornsdottir M, Borres MP, Hogman M, Alving K, Janson C, and Malinovschi A, *New data analysis in a population study raises the hypothesis that particle size contributes to the pro-asthmatic potential of small pet animal allergens*. Ups J Med Sci, 2016. 121 (1): 25-32.
- 28. Patelis A, Gunnbjornsdottir M, Alving K, Borres MP, Hogman M, Janson C, and Malinovschi A, *Allergen extract vs. component sensitization and airway inflammation, responsiveness and new-onset respiratory disease.* Clin Exp Allergy, 2016. **46** (5): 730-40.
- 29. Peterson CG, Lampinen M, Hansson T, Liden M, Hallgren R, and Carlson M, *Evaluation of biomarkers for ulcerative colitis comparing two sampling methods: fecal markers reflect colorectal inflammation both macroscopically and on a cellular level.* Scand J Clin Lab Invest, 2016. **76** (5): 393-401.
- Sundbom F, Malinovschi A, Lindberg E, Alving K, and Janson C, *Effects of poor asthma control, insomnia, anxiety and depression on quality of life in young asthmatics*. J Asthma, 2016. 53 (4): 398-403.
- 31. Syk J, Malinovschi A, Borres MP, Unden AL, Andreasson A, Lekander M, and Alving K, *Parallel reductions of IgE and exhaled nitric oxide after optimized anti-inflammatory asthma treatment*. Immun Inflamm Dis, 2016. **4** (2): 182-190.
- 32. Thacher JD, Gruzieva O, Pershagen G, Neuman A, van Hage M, Wickman M, Kull I, Melen E, and Bergstrom A, *Parental smoking and development of allergic sensitization from birth to adolescence*. Allergy, 2016. **71** (2): 239-48.
- 33. Villalta D, Pantarotto L, Da Re M, Conte M, Sjolander S, Borres MP, and Martelli P, *High prevalence of sIgE to Galactose-alpha-1,3-galactose in rural pre-Alps area: a cross-sectional study.* Clin Exp Allergy, 2016. **46** (2): 377-80.

- 1. Qvist T, Gilljam M, Jonsson B, Taylor-Robinson D, Jensen-Fangel S, Wang M, Svahn A, Kotz K, Hansson L, Hollsing A, Hansen CR, Finstad PL, Pressler T, Hoiby N, Katzenstein TL, and Scandinavian Cystic Fibrosis Study C, Epidemiology of nontuberculous mycobacteria among patients with cystic fibrosis in Scandinavia. J Cyst Fibros, 2015. 14 (1): 46-52.
- 2. Hansson T, Dahlbom I, Tuvemo T, and Frisk G, Silent coeliac disease is over-represented in children with type 1 diabetes and their siblings. Acta Paediatr, 2015. 104 (2): 185-91.
- 3. Norlander K, Johansson H, Jansson C, Nordvall L, and Nordang L, Surgical treatment is effective in severe cases of exercise-induced laryngeal obstruction: A follow-up study. Acta Otolaryngol, 2015. 135 (11): 1152-9.
- 4. Johansson H, Norlander K, Berglund L, Janson C, Malinovschi A, Nordvall L, Nordang L, and Emtner M, Prevalence of exercise-induced bronchoconstriction and exercise-induced laryngeal obstruction in a general adolescent population. Thorax, 2015. 70 (1): 57-63.
- Ahlgrim C, Gutermuth J, Onell A, Borres MP, Schaffner I, Darsow U, Pfab F, Brockow K, Ring J, Behrendt H, Jakob T, and Huss-Marp J, Comparison of Molecular Multiplex and Singleplex Analysis of IgE to Grass Pollen Allergens in Untreated German Grass Pollen-Allergic Patients. J Investig Allergol Clin Immunol, 2015. 25 (3): 190-5.

- 6. Benhamou Senouf AH, Borres MP, and Eigenmann PA, Native and denatured egg white protein IgE tests discriminate hen's egg allergic from egg-tolerant children. Pediatr Allergy Immunol, 2015. 26 (1): 12-7.
- 7. Bjerg A, Winberg A, Berthold M, Mattsson L, Borres MP, and Ronmark E, A population-based study of animal component sensitization, asthma, and rhinitis in schoolchildren. Pediatr Allergy Immunol, 2015. 26 (6): 557-63.
- 8. Brandstrom J, Nopp A, Johansson SG, Lilja G, Sundqvist AC, Borres MP, and Nilsson C, Basophil allergen threshold sensitivity and component-resolved diagnostics improve hazelnut allergy diagnosis. Clin Exp Allergy, 2015. 45 (9): 1412-8.
- 9. Ebisawa M, Moverare R, Sato S, Borres MP, and Ito K, The predictive relationship between peanut- and Ara h 2-specific serum IgE concentrations and peanut allergy. J Allergy Clin Immunol Pract, 2015. 3 (1): 131-2 e1.
- 10. Fiocchi A, Pecora V, Petersson CJ, Dahdah L, Borres MP, Amengual MJ, Huss-Marp J, Mazzina O, and Di Girolamo F, Sensitization pattern to inhalant and food allergens in symptomatic children at first evaluation. Ital J Pediatr, 2015. 41: 96.
- 11. Glaumann S, Nilsson C, Asarnoj A, Moverare R, Johansson SG, Borres MP, Lilja G, and Nopp A, IgG4 antibodies and peanut challenge outcome in children IgE-sensitized to peanut. Pediatr Allergy Immunol, 2015. 26 (4): 386-9.
- 12. Glaumann S, Nilsson C, Johansson SG, Asarnoj A, Wickman M, Borres MP, and Nopp A, Evaluation of basophil allergen threshold sensitivity (CD-sens) to peanut and Ara h 8 in children IgE-sensitized to Ara h 8. Clin Mol Allergy, 2015. 13 (1): 5.
- 13. Kuitunen M, Englund H, Remes S, Moverare R, Pelkonen A, Borres MP, and Makela MJ, High IgE levels to alpha-lactalbumin, beta-lactoglobulin and casein predict less successful cow's milk oral immunotherapy. Allergy, 2015. 70 (8): 955-62.
- Nilsson C, Brostedt P, Hidman J, van Odijk J, Borres MP, Sjolander S, and Englund H, Recognition pattern of kiwi seed storage proteins in kiwifruit-allergic children. Pediatr Allergy Immunol, 2015. 26 (8): 817-20.
- 15. Nilsson N, Sjolander S, Baar A, Berthold M, Pahr S, Vrtala S, Valenta R, Morita E, Hedlin G, Borres MP, and Nilsson C, Wheat allergy in children evaluated with challenge and IgE antibodies to wheat components. Pediatr Allergy Immunol, 2015. 26 (2): 119-25.
- Savvatianos S, Konstantinopoulos AP, Borga A, Stavroulakis G, Lidholm J, Borres MP, Manousakis E, and Papadopoulos NG, Sensitization to cashew nut 2S albumin, Ana o 3, is highly predictive of cashew and pistachio allergy in Greek children. J Allergy Clin Immunol, 2015. 136 (1): 192-4.
- 17. Heijkenskjold-Rentzhog C, Kalm-Stephens P, Nordvall L, Malinovschi A, and Alving K, New method for single-breath fraction of exhaled nitric oxide measurement with improved feasibility in preschool children with asthma. Pediatr Allergy Immunol, 2015. 26 (7): 662-7.
- 18. Jacinto T, Malinovschi A, Janson C, Fonseca J, and Alving K, Evolution of exhaled nitric oxide levels throughout development and aging of healthy humans. J Breath Res, 2015. 9 (3): 036005.
- 19. Johnson J, Borres MP, Nordvall L, Lidholm J, Janson C, Alving K, and Malinovschi A, Perceived food hypersensitivity relates to poor asthma control and quality of life in young non-atopic asthmatics. PLoS One, 2015. 10 (4): e0124675.
- 20. Konradsen JR, Skantz E, Nordlund B, Lidegran M, James A, Ono J, Ohta S, Izuhara K, Dahlen SE, Alving K, and Hedlin G, Predicting asthma morbidity in children using proposed markers of Th2-type inflammation. Pediatr Allergy Immunol, 2015. 26 (8): 772-9.
- 21. Dreborg S, Allergen skin prick test should be adjusted by the histamine reactivity. Int Arch Allergy Immunol, 2015. 166 (1): 77-80.
- 22. Dreborg S and Holgersson M, Evaluation of methods for the estimation of threshold concentrations by the skin prick test. Int Arch Allergy Immunol, 2015. 166 (1): 71-6.
- Cederblad M, Sarkadi A, Engvall G, Nevéus T. Infrequent enuresis, the uninvestigated majority. Comparisons between children with enuresis of varying severity. J Pediatr Urol. 2015;11:24.e1-.e6.

- Al-Mashhadi A, Nevéus T, Stenberg A, Karanikas B, Persson AEG, Carlström M, et al. Surgical treatment reduces blood pressure in children with unilateral congenital hydronephrosis. J Ped Urol. 2015;11(2):91.e1-6.
- 25. Cederblad M, Engvall G, Sarkadi A, Nevéus T. No effect of basic bladder advice in enuresis a randomised controlled trial. J Ped Urol. 2015;11(3):153e1-5.
- 26. Kaarme J, Hasan B, Rashid M, Olsen B. Zero prevalence of vancomycin-resistant enterococci among Swedish preschool children. Microb Drug Resist. 2015;21(1):65-8.
- Esbjornsson AC, Aalto K, Brostrom EW, Fasth A, Herlin T, Nielsen S, Nordal E, Peltoniemi S, Rygg M, Zak M, Berntson L, and Nordic Study Group of Paediatric R, Ankle arthritis predicts polyarticular disease course and unfavourable outcome in children with juvenile idiopathic arthritis. Clin Exp Rheumatol, 2015. 33 (5): 751-7.
- Engstrand Lilja H, Wefer H, Nystrom N, Finkel Y, and Engstrand L, Intestinal dysbiosis in children with short bowel syndrome is associated with impaired outcome. Microbiome, 2015. 3: 18.

- 1. Darsow U, Brockow K, Pfab F, Jakob T, Petersson CJ, Borres MP, Ring J, Behrendt H, and Huss-Marp J, Allergens. Heterogeneity of molecular sensitization profiles in grass pollen allergy--implications for immunotherapy? Clin Exp Allergy, 2014. 44 (5): 778-86.
- 2. Heijkenskjold-Rentzhog C, Nordvall L, Janson C, Borres MP, Alving K, and Malinovschi A, Alveolar and exhaled NO in relation to asthma characteristics--effects of correction for axial diffusion. Allergy, 2014. 69 (8): 1102-11.
- 3. Irander K, Borres MP, and Ghafouri B, The effects of physical exercise and smoking habits on the expression of SPLUNC1 in nasal lavage fluids from allergic rhinitis subjects. Int J Pediatr Otorhinolaryngol, 2014. 78 (4): 618-22.
- 4. Johansson H, Norlander K, Hedenstrom H, Janson C, Nordang L, Nordvall L, and Emtner M, Exercise-induced dyspnea is a problem among the general adolescent population. Respir Med, 2014. 108 (6): 852-8.
- Johnson J, Malinovschi A, Alving K, Lidholm J, Borres MP, and Nordvall L, Ten-year review reveals changing trends and severity of allergic reactions to nuts and other foods. Acta Paediatr, 2014. 103 (8): 862-7.
- 6. Kalm-Stephens P, Sterner T, Kronholm Diab K, and Smedje G, Hypersensitivity and the working environment for allergy nurses in sweden. J Allergy (Cairo), 2014. 2014: 681934.
- 7. Katelaris CH, Kurosawa M, Moon HB, Borres M, Florvaag E, and Johansson SG, Pholcodine consumption and immunoglobulin E-sensitization in atopics from Australia, Korea, and Japan. Asia Pac Allergy, 2014. 4 (2): 86-90.
- 8. Konradsen JR, Nordlund B, Onell A, Borres MP, Gronlund H, and Hedlin G, Severe childhood asthma and allergy to furry animals: refined assessment using molecular-based allergy diagnostics. Pediatr Allergy Immunol, 2014. 25 (2): 187-92.
- 9. Krantz C, Janson C, Borres MP, Nordvall L, Alving K, and Malinovschi A, Nasal nitric oxide is associated with exhaled NO, bronchial responsiveness and poor asthma control. J Breath Res, 2014. 8 (2): 026002.
- Neuman A, Bergstrom A, Gustafsson P, Thunqvist P, Andersson N, Nordvall L, Kull I, and Wickman M, Infant wheeze, comorbidities and school age asthma. Pediatr Allergy Immunol, 2014. 25 (4): 380-6.
- Nilsson C, Nordvall L, Johansson SG, and Nopp A, Successful management of severe cow's milk allergy with omalizumab treatment and CD-sens monitoring. Asia Pac Allergy, 2014. 4 (4): 257-60.
- 12. Nozawa A, Okamoto Y, Moverare R, Borres MP, and Kurihara K, Monitoring Ara h 1, 2 and 3sIgE and sIgG4 antibodies in peanut allergic children receiving oral rush immunotherapy. Pediatr Allergy Immunol, 2014. 25 (4): 323-8.
- 13. Olen O, Neuman A, Koopmann B, Ludvigsson JF, Ballardini N, Westman M, Melen E, Kull I, Simren M, and Bergstrom A, Allergy-related diseases and recurrent abdominal pain during childhood a birth cohort study. Aliment Pharmacol Ther, 2014. 40 (11-12): 1349-58.

- 14. Patelis A, Gunnbjornsdottir M, Borres MP, Burney P, Gislason T, Toren K, Forsberg B, Alving K, Malinovschi A, and Janson C, Natural history of perceived food hypersensitivity and IgE sensitisation to food allergens in a cohort of adults. PLoS One, 2014. 9 (1): e85333.
- Patelis A, Janson C, Borres MP, Nordvall L, Alving K, and Malinovschi A, Aeroallergen and food IgE sensitization and local and systemic inflammation in asthma. Allergy, 2014. 69 (3): 380-7.
- 16. Stenberg Hammar K, Hedlin G, Konradsen JR, Nordlund B, Kull I, Giske CG, Pedroletti C, Soderhall C, and Melen E, Subnormal levels of vitamin D are associated with acute wheeze in young children. Acta Paediatr, 2014. 103 (8): 856-61.
- 17. Thacher JD, Gruzieva O, Pershagen G, Neuman A, Wickman M, Kull I, Melen E, and Bergstrom A, Pre- and postnatal exposure to parental smoking and allergic disease through adolescence. Pediatrics, 2014. 134 (3): 428-34.
- 18. Berntson L, Nordal E, Fasth A, Aalto K, Herlin T, Nielsen S, et al. Anti-type II collagen antibodies, anti-CCP, IgA RF and IgM RF are associated with joint damage, assessed eight years after onset of juvenile idiopathic arthritis (JIA). Pediatr Rheumatol Online J. 2014 Jun 11;12:22.
- Kazamia K, Holmquist L, Fagerlund A, Berntson L. Children with juvenile idiopathic arthritis frequently experience interruptions to their medical therapy. Acta Paediatrica. 2014;103(5):529-536.
- Cedstromer A, Ahlqwist M, Andlin-Sobocki A, Berntson L, Hedenberg-Magnusson B, Dahlstrom L. Temporomandibular condylar alterations in juvenile idiopathic arthritis most common in longitudinally severe disease despite medical treatment. Pediatr Rheumatol Online J. 2014 Sep 14;12:43.
- 21. Berntson L. Anti-inflammatory effect by exclusive enteral nutrition (EEN) in a patient with juvenile idiopathic arthritis (JIA): brief report. Clinical Rheumatology. 2014;33(8):1173-1175.
- 22. Cederblad M, Nevéus T, Åhman A, Österlund Efraimsson E, Sarkadi A. "Nobody asked us if we needed help" Swedish parents' experiences of enuresis. J Ped Urol. 2014;10(1):74-9.
- 23. Grandahl M, Oscarsson M, Stenhammar C, Nevéus T, Westerling R, Tydén T. Not the right time: why parents refuse to let their daughters have the human papillomavirus vaccination. Acta Paediatr. 2014;103(4):436-41.
- 24. Nevéus T, Leissner L, Rudblad S, Bazargani F. Respiration during sleep in children with therapy-resistant enuresis. Acta Paediatr. 2014;103(3):300-4.
- Grandahl M, Tydén T, Rosenblad A, Oscarsson M, Nevéus T, Stenhammar C. School nurses' attitudes and experiences regarding the human papillomavirus vaccination programme in Sweden: A population-based survey. BMC Public Health. 2014;14:540.
- 26. Neveus T, Leissner L, Rudblad S, and Bazargani F, Orthodontic widening of the palate may provide a cure for selected children with therapy-resistant enuresis. Acta Paediatr, 2014. 103 (11): 1187-91.

#### Reviews etc 2014-2016

- Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, Rittig S, Walle JV, von Gontard A, Wright A, Yang SS, and Neveus T, *The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the International Children's Continence Society.* Neurourol Urodyn, 2016. **35** (4): 471-81.
- 2. Borres MP, Maruyama N, Sato S, and Ebisawa M, *Recent advances in component resolved diagnosis in food allergy*. Allergol Int, 2016. **65** (4): 378-387.
- 3. Dreborg S, Ahlgren L, Erikson A, and Klasson U, *Den första svenska Gregoryboxen*. Barnläkaren, 2016. 1: 23-25.

- Malinovschi A, Ludviksdottir D, Tufvesson E, Rolla G, Bjermer L, Alving K, and Diamant Z, Application of nitric oxide measurements in clinical conditions beyond asthma. Eur Clin Respir J, 2015. 2: 28517.
- 2. Dreborg S, *Evaluation of allergen immunotherapy*. J Allergy Clin Immunol Pract, 2015. **3** (2): 267-8.
- 3. Dreborg S, *Debates in allergy medicine: food intolerance does not exist.* World Allergy Organ J, 2015. **8**: 37.
- 4. Borres MP, Sato S, and Ebisawa M, *IgE-related examination in food allergy with focus on allergen components*. Chem Immunol Allergy, 2015. **101**: 68-78.
- 5. Nevéus T. Evaluation of the enuretic child. In: Franco I, Austin P, Bauer S, von Gontard A, Homsy Y, editors. Pediatric incontinence: evaluation and clinical management. Chichester, West Sussex, UK: Wiley Blackwell; 2015. p. 221-6.

#### 2014

- 1. Bjermer L, Alving K, Diamant Z, Magnussen H, Pavord I, Piacentini G, Price D, Roche N, Sastre J, Thomas M, and Usmani O, *Current evidence and future research needs for FeNO measurement in respiratory diseases*. Respir Med, 2014. **108** (6): 830-41.
- Austin P, Bauer S, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: update report from the standardization committee of the International Children's Continence Society. J Urol. 2014;191(6):1863-5.

#### **Dissertations 2016**

Charlotte Heijkenskjöld Rentzhog

#### Agencies that support the work/Funding

Swedish Asthma and Allergy Association's Research Foundation (SEK 200,000) Swedish Foundation for Strategic Research (SEK 500,000)

#### Allergy

The allergological research is focused on the characterization (phenotyping) of children and young adults with asthma with the help of biomarkers. Senior researchers in this subgroup are Kjell Alving, Magnus Borres, Lennart Nordvall, Christophe Pedroletti, Sten Dreborg, Åsa Neuman, and Charlotte Heijkenskjöld Rentzhog. PhD students are Pia Kalm Stephens, Jennifer Johnson and Nikos Tsolakis. The research is mainly based on large patient cohorts where clinical data and biobank material are collected. For example, the MIDAS cohort (532 asthma patients and controls, age 10-35 years at baseline survey), the SPAIS cohort (959 children, age 13-14 years at baseline survey), and the NOAK cohort (187 adults with asthma participating in an interventional study over one year) are utilized in our research. A three-year follow up of the MIDAS cohort and a 15-year follow up of the SPAIS cohort was concluded during 2016. In October 2016, a Paediatric Allergy Centre was inaugurated, and the development of facilities and procedures enabling real-life clinical research on children and adolescents with asthma was initiated. Main research objectives in the group are:

 Development of feasible biomarkers in preschool children.
Development and clinical evaluation of local and systemic biomarkers of Th2-driven inflammation, alone and in combination.
Characterization of non-atopic asthma in young subjects.
The influence of IgE sensitisation pattern on inflammation and astma morbidity. For the development of clinical biomarkers in asthma, our group collaborates closely with several groups at Karolinska Institutet as well as with diagnostic companies, for example Thermo Fisher Scientific, Hemocue, Olink, and Circassia.

#### Pulmonology

The group's pulmonological research is focused on cystic fibrosis (CF) and the related disorder primary ciliary dysfunction (PCD) and involves Annika Hollsing, Christina Krantz and Hans Kollberg. The group is conducting a prospective 5-year study on the evaluation of novel lung function tests and non-invasive exhalation tests, to enable the early detection of decline in lung function, signs of upcoming exacerbations, and bacterial colonisation in CF. The group is specifically looking at the clinical utility of exhaled and nasal nitric oxide in CF and PCD. The group is also part of a Nordic research consortium that performs a multicentre research on CF. The concortium has during recent years focused on Staphylococcus aureus and Aspergillus infections in CF. The group also participates in two multi-centre pharmaceutical studies on gene modification and potentiation in patients with CF.

#### Rheumatology

The main focus of rheumatological research is on patients with juvenile idiopathic arthritis (JIA). A Nordic multicenter study, including a 15-year follow-up of 500 Nordic patients is ongoing. Lillemor Berntson (LB) continues as the Swedish coordinator and supervisor, and Maria Ekelund (paediatrician, Jönköping) is doing her PhD studies within this project. A regional study on JIA is in progress, and Anders Öman (paediatrician, Uppsala), is a PhD student in the project. The aim of the latter project is to study the role of the gastrointestinal canal in JIA. Our group has been first to publish on the clinical effect of exclusive enteral nutrition (EEN) in JIA. In cooperation with Lars Engstrand, Karolinska Institutet, and Johan Dicksved, SLU, this project has developed to include studies of the microbiota in newly-diagnosed children with JIA, in patients before and after EEN, and in patients on different anti-rheumatic medications. In parallel, faecal samples are now analysed for short-chain fatty acids, to assess the functional role of current microbiota. The group also collaborates with Per Hellström and Dominic-Luc Webb, Department of Medical Sciences, in studies on intestinal permeability in JIA. LB is also involved in a collaborative project with paediatric gastroenterologists, pathologists and paediatricians in Finland. Mucosal biopsies from Swedish children with JIA are now included in this study and immunohistochemical analyses in different stages of the disease are made. Two international review projects, one on microbiota in children with JIA and one on treatment of systemic JIA have been finished during the year.

#### Gastroenterology

Much of the group's gastroenterological research is focused on paediatric Crohn's disease. A translational research group with preclinical and clinical researchers from Uppsala University and Karolinska Institutet work on a hypothesis based on the potential role of RNA viruses as a pathogenic factor in Crohn's disease. Two retrospective studies have been finished and a large prospective cohort of paediatric Crohn's disease patients is now ready for further examination. In a subcohort, the effect of EEN on intestinal virome and microbiome is studied. Together with colorectal surgeons, a prospective cohort of Crohn's disease patients who need surgical treatment

with ileocecal resection is being developed. A collaboration with SciLifeLab is under development. In a pilot project, EEN is tested against obesity. In collaboration with paediatric surgeons, the treatment of enteral dysbiosis is evaluated in children with short bowel syndrome.

#### Nephrology

Uppsala University Children's Hospital is a recognized international centre of expertise in research on paediatric lower urinary tract function. Tryggve Nevéus, who leads these activities, is since 2014 President of the International Children's Continence Society (ICCS), which is the relevant global research organisation in this field. The main focus of the research by the Uppsala group is enuresis (bedwetting). More than 25% of enuretic children do not respond to the available first-line therapies. In a double-blind, randomised, placebo-controlled, cross-over study, conducted by Tryggve Nevéus and PhD student Elisabet Lundmark, it has been evaluated whether noradrenergic medication, influencing arousal mechanisms, is useful in therapy-resistant enuretic children. We found that active treatment is indeed better than placebo. A prospective study on the treatment of therapyresistant enuresis with an orthodontic device that widens the nasal airways during sleep has been started, and approximately two thirds of the patients have been evaluated. This study is performed by Tryggve Nevéus and PhD student (dentist) Ingrid Jönson Ring. Furthermore, paediatrician and PhD student Johan Kaarme has investigated the microbiota of normal toddlers in daycare, and an alarming increase in the carriage rate of multiresistant gut bacteria was found.

#### Social medicine/ Child Health and Parenting Research Group (CHAP)

#### Anna Sarkadi

#### Child health and parenting

The group is interdisciplinary and focuses on societal support to children and their families. Projects range from prevention through early intervention to attending to the needs of vulnerable populations, such as asylum-seekers. Our special area of interest is parenting support, including both universal child health and early education services and parenting programmes. We specifically deal with effectiveness studies as well as implementation and improvement research, translating research results into practice. We also develop methods to interview preschool children reliably. All trials we conduct include a health economic evaluation of the intervention as well as qualitative studies with different stakeholders, including users.

#### Members of the group during 2016

Pär Bokström, PhD student Anton Dahlberg, PhD student Natalie Engsheden, RN, PhD student (parental leave) Helena Fabian, Research fellow Inna Feldman, Associate professor Elisabet Fält, RN, PhD student Karin Fängström, Clinical Psychologist, PhD student Kirsten Holmberg, Associate professor, associated member Laleh Nayeb, Licensed Speach Therapist, PhD student Camilla Nystrand, Research Assistant Raziye Salari, Research fellow Filipa Sampaio, Postdoc Anna Sarkadi, M.D., PhD, Professor Richard Ssegonja, PhD student Antónia Tökés, Research Assistant

#### Publications 2014-2016

- Johansen, K. Lucas, S. Persson, K. Sonnander, K. Magnusson, M. Sarkadi, A. Now I use words like asymmetry and unstable". Nurses' experiences in using a standardized assessment for motor performance within routine child healthcare" *J Evaluation in Clinical Practice* 2016;22(2):227-34
- Bokström, P. Fängström, K. Calam, R. Lucas, S. Sarkadi, A. Feasibility of the In My Shoes software for talking to preschoolers about their routine health visit. *Child Care Health Dev*. 2016;42(1):87-97.
- 3. Cederblad, M, Engsheden, N. Ghaderi, A. Enebrink, P. Englund, G. Nevéus, T. Sarkadi, A. No difference in relationship satisfaction between parents of children with enuresis and normative data *In press J Child & Family Studies*
- 4. Wells, MB and Sarkadi, A. Salari, R. Mothers' and fathers' attendance in a community-based universally offered parenting program in Sweden. *Scandinavian Journal of Public Health*, *44*, 274-280.

- Fransson, E. Sarkadi, A. Hjern, A. Bergström M. Why should they live more with one of us when they are children to us both? *Children and Youth Services Review (2016)*, doi: 10.1016/j.childyouth.2016.05.011
- 6. Fängström, K. Bokström, P. Dahlberg, A. Calam, R. Sarkadi, A. In My Shoes validation of a computer-assisted method for interviewing children. *Child Abuse Negl*. 2016 Aug;58:160-72.
- 7. Ha N.D Le, Alisha Gulenc, Lisa Gold, Sarkadi, A., Obioha C Ukoumunne, Jordana Bayer, Melissa Wake, Hariet Hiscock. Utility-based quality of life in mothers of children with behaviour problems: A population-based study.J *Paediatr Child Health.* 2016 Sep 6.
- Åhman, A. Sarkadi, A. Lindgren, P, Rubertsson, C. 'It made you think about your opinion'-Women's perception of a web-based decision aid concerning screening for fetal anomalies. *BMC Pregnancy and Childbirth* 2016 Sep 13;16:267
- 9. Salari, R., & Backman, A. (2016). Direct-to-consumer marketing of parenting programs: Comparing a promotion-focused and a prevention-focused strategy. *European Journal of Public Health*.
- 10. Salari, R., Bohlin, G., Rydell, A.-M., & Thorell, L. B. (2016). Neuropsychological functioning and attachment representations in early school age as predictors of ADHD symptoms in late adolescence. *Child Psychiatry & Human Development*, 1-15
- 11. Lindkvist M, Feldman I: Assessing outcomes for cost-utility analysis in mental health interventions: mapping mental health specific outcome measure GHQ-12 onto EQ-5D-3L. *Health and quality of life outcomes* 2016, 14(1):134.
- 12. Sampaio F, Enebrink P, Mihalopoulos C, Feldman I: Cost-effectiveness of four parenting programs and bibliotherapy for parents of children with conduct problems: a multicenter randomized controlled trial. *The journal of mental health policy and economics* 2016, 19(4):201-212.
- 13. Wellander L, Wells MB, Feldman I: Does Prevention Pay? Costs and Potential Cost-savings of School Interventions Targeting Children with Mental Health Problems. *The journal of mental health policy and economics* 2016, 19(2):91-101.
- 14. Feldman I, Eurenius E, Häggström J, Sampaio F, Lindkvist M, Pulkki-Brännström A-M, Ivarsson A: Effectiveness and cost-effectiveness of the Salut Programme: a universal health promotion intervention for parents and children—protocol of a register-based retrospective observational study. *BMJ open* 2016, 6(8).

- 1. Sarkadi, A., Alisha Gulenc, and Harriet Hiscock. Maternal- and child health nurses' selfperceived confidence in dealing with child behaviour problems. *Child: Care, Health and Development* 2015 Mar;41(2):324-8.
- 2. Laleh Nayeb, Thomas Wallby, Monica Westerlund, Eva-Kristina Salameh, Sarkadi, A. Child health nurses' perceptions about bilingual children's language development are associated with inadequate screening practices. *Acta Paediatr.* 2015 Feb;104(2):198-205.
- 3. Wells, M. Engman, J. Sarkadi, A. Gender equality in Swedish child health centers: An analysis of their physical environments and parental behaviors. *Semiotica* 2015; 204: 1 20
- 4. Cederblad, M, Englund, G. Sarkadi, A. Nevéus, T. No effect of basic bladder advice in enuresis: a randomised controlled trial. J Pediatr Urol. 2015 Apr 16.
- Sampaio, F., Sarkadi, A., Salari, R., Zethraeus, N., & Feldman, I. (2015). Cost and effects of a universal parenting programme delivered to parents of preschoolers. *European Journal of Public Health*, 25, 1035-1042.
- 6. Johansen, K. Persson, K. Sarkadi, A. Sonnander, K. Magnusson, M. Lucas, S. Can nurses be key players in assessing early motor development using a structured method in the child health setting? *J Evaluation in Clinical Practice* 2015 Aug;21(4):681-7.
- 7. Fabian, H. Sarkadi, A. Åhman, A. Challenges and benefits of conducting parental classes in Sweden midwives' perspectives. *Sex Reprod Health*. 2015 Dec;6(4):236-42.
- 8. Sarkadi, A. Goldfeld, S. Efron, D. How the system failed Dylan: About the effects of fragmented community child health care services on patient safety *Journal of Paediatrics and Child Health* 2015 Dec;51(12):1148-51.
- Johansen, K. Lucas, S. Persson, K. Sonnander, K. Magnusson, M. Sarkadi, A. Now I use words like asymmetry and unstable". Nurses' experiences in using a standardized assessment for motor performance within routine child healthcare" *J Evaluation in Clinical Practice* 2015 Oct 22.
- Bokström, P. Fängström, K. Calam, R. Lucas, S. Sarkadi, A. Feasibility of the In My Shoes software for talking to preschoolers about their routine health visit. *Child Care Health Dev.* 2015 Nov 12.
- 11. Cederblad, M, Engsheden, N. Ghaderi, A. Enebrink, P. Englund, G. Nevéus, T. Sarkadi, A. No difference in relationship satisfaction between parents of children with enuresis and normative *J Child & Family Studies* 2015 pp1-7
- Titova OE, Hogenkamp PS, Jacobsson JA, Feldman I, Schioth HB, Benedict C: Associations of self-reported sleep disturbance and duration with academic failure in community-dwelling Swedish adolescents: sleep and academic performance at school. *Sleep medicine* 2015, 16(1):87-93
- 13. Granstrom F, Molarius A, Garvin P, Elo S, Feldman I, Kristenson M: Exploring trends in and determinants of educational inequalities in self-rated health. *Scandinavian journal of public health* 2015, 43(7):677-686.
- 14. Salari, R., & Thorell, L. (2015). Parental monitoring in late adolescence: Relations to ADHD symptoms and longitudinal predictors. *Journal of Adolescence*, 40: 24-33.
- 15. Holmberg K, Lundholm C, Anckarsäter H, Larsson H, Almqvist C. <u>Impact of asthma</u> <u>medication and familial factors on the association between childhood asthma and attention-</u> <u>deficit/hyperactivity disorder: a combined twin- and register-based study: Epidemiology of</u> <u>Allergic Disease.</u> Clin Exp Allergy. 2015 May;45(5):964-73. doi: 10.1111/cea.12529.

#### 2014

- 1. Rahmqvist, J. Wells, M. and Sarkadi, A. Conscious parenting: A qualitative study on Swedish parents' motives to participate in Triple P, the Positive Parenting Program. *J Child and Family Studies* 2014;23(5): 934-944
- 2. Åhman, A. Maras, G, Axelsson, O. Rubertsson, C. Sarkadi, A. Lindgren, P, Ultrasonographic fetal soft markers in an unselected population: incidence and association to trisomies and invasive tests *Acta Obstretrica et Gynecologica Scandinavica* 2014 Apr;93(4):367-73.
- 3. Sarkadi, A. Filipa Sampaio, Michael P Kelly, and Inna Feldman<sup>-</sup>A novel approach using outcome distribution curves could be used to estimate the population-level impact of a public health intervention *Journal of Clinical Epidemiology* 2014 Jul;67(7):785-92.
- 4. Sarkadi, A. THE INVISIBLE FATHER. How can we help fathers feel less alienated in child health care services? Editorial. *Acta Paediatrica* 2014. 103 (3), 234-235
- 5. Salari, R. Wells, MB and Sarkadi, A. Child behavioural problems, parenting behaviours and parental adjustment in mothers and fathers in Sweden. *Scandinavian Journal of Public Health* 2014 Nov;42(7):547-53.
- Feldman, I. Sarkadi, A. Sampaio, F and Kelly, MP. Response to Invited Commentary: Methods to address control for confounding and nonperfect randomization when using outcome distribution curves to estimate the population-level impact of a public health intervention. *Journal of Clinical Epidemiology* 2014 Nov;67(11):1286-8.
- Cederblad, M, Englund, G. Sarkadi, A. Nevéus, T. Infrequent enuresis, the uninvestigated majority comparisons between children with enuresis of varying severity. *J Pediatr Urol.* 2014 Sep
- 8. Cederblad, M. Nevéus, T. Åhman. A. Efraimsson, E.Ö. Sarkadi, A. "Nobody ever asked us if we needed help!" Swedish parents' experience of enuresis in their child. *J Pediatric Urology* 2014 Feb;10(1):74-9.
- 9. Molarius A, Simonsson B, Lindén-Boström M, Kalander-Blomqvist M, Feldman I, Eriksson HG. "Social inequalities in self-reported refraining from health care due to financial reasons in Sweden: health care on equal terms?" *BMC Health Serv Res.* 2014 14:605.
- 10. Holmberg K, Bölte S. Do symptoms of ADHD at ages 7 and 10 predict academic outcome at

age 16 in the general population? J Atten Disord. 2014 Nov;18(8):635-45.

11. Salari, R., Ralph, A., & Sanders, M. R. (2014). An efficacy trial: Positive Parenting Program for parents of teenagers. *Behaviour Change*, 31(1) 34-52.

#### **Dissertations 2016**

- 1. Maria Cederblad
- 2. Filipa Sampaio

#### Agencies that support the work/Funding

2012-2018	FORMAS, FAS, VINNOVA, VR common grant for child and youth mental healthresearch. Long-term effects of population-based parenting interventions. Outcomes,costs and benefits29 400 000 SEK			
2012	HFS-network	"Hälsokalkylator" (2012-2016)	1 500 000 SEK	
2013	Regional Canc	er Centre, Uppsala – Örebro " CancerPrevent"	(2014-2015) 500 000 SEK	
2016	<i>Skandia</i> in children	Health economic evaluation of prevention of	mental health problems 1 300 000 SEK	
2014	Forte	Health and Economic Impact of a Population Based Health		
2014	Promotion Programme for Children and Parents (2015-2017) 5,100,000 SEK			
2014	VR (C/A)	Analyzing causal long-term socio-economic e	effects of prevention and	
	early interventions for children and adolescents in Sweden (2015-2017)			
			3,110,000 SEK	
2014	VR (C/A) Health Economics Analyses of Intervention Targeting Internalising			
	Problems in Children and Adolescents: Translating Evidence into Policy and Practice			
	(2015-2018)		4,611,000 SEK	
2015	ALF		1 236 500 SEK	
2015	Allmänna Barnhuset. A validation study of the computer software In My Shoe 350 000 SEK			
2015	<i>Skandia</i> in children	Health economic evaluation of prevention of	mental health problems 800 000 SEK	
2015	Gillberg Found	lation	200 000 SEK	

#### **Child Health Centres service development**

Sweden is in the international forefront both in terms of children's rights and the equity of welfare services. For almost three decades there was no apparent need to change service delivery within the child health services. However, society structures as well as macroeconomic and political circumstances imply a need to develop more effective and equitable services. PhD students Laleh Nayeb and Kine Johansen (Anna Sarkadi co-supervises) work directly on improving the evidence-

base of child health services through developing better methods for screening bilingual children (at 30 months) and motor developmental problems, respectively. Our largest project, the Parents and Childreni Focus trial (see below) involves a new method of information transfer between the preschools and child health centres, using the Strengths and Difficulties questionnaire. Elisabet Fält is a PhD student in the project, looking at how parents, nurses, and preschool teachers perceive the information transfer, how it is implemented and with what clinical effects, and how parent and teacher scores correlate.

#### Effects, costs, and cost-effectiveness of preventive interventions

Research has shown that there is a strong association between parental behaviour and developmental outcomes in children. Previous studies have shown that when parents are taught strategies that are more consistent, warm, authoritative, moderate and firm in the context of parenting programs, children's rates of problematic behaviours decrease. Several research project in our group therefore concern parenting programs. Raziye Salari is looking at factors that influence parents' motivation to participate in parenting programs and how that might be influenced. We received major funding for a project on long-term effects of parenting programs as preventive interventions, where Helena Fabian is project leader and researcher. The study is a cluster-randomised controlled trial with three arms: two intervention arms and a comparison condition. The aim of the project is to determine what mix of parenting support interventions will lead to best outcomes on children's mental health on the population level. The intervention is Triple P (Positive Parenting Program) and the two intervention types are universal and universal plus selected intervention, where the latter is more intense and involves identification of vulnerable groups/individuals. To evaluate the intervention, all children 3, 4 and 5 years of age are sent a questionnaire before their annual visit to the CHC. Results from these questionnaires are also used to describe the physical and mental health of this population of children. Antónia Tökés is research assistant in the project, responsible for the sorting and scanning of more than 6000 questionnaires yearly. Anton Dahlberg is also PhD student in the project, looking at the effects of the parenting program Triple P on population outcomes as well as effects on those participating in the intervention.

In parenting program research the extent of health economic evaluations is limited, nationally as well as internationally. An important focus of our group is therefore to conduct such analyses. Inna Feldman leads this research and Filipa Sampaio and research assistant Camilla Nygren are involved in this quite ground-braking effort to model long-term effects of early interventions and thus provide decision-makers tools to base investment decisions on. Filipa Sampaio completed her dissertation in 2016 and currently works as a postdoc in the group. Richard Ssegonja, health economist and MD is a PhD student looking at adolescent depression and its costs and consequences.

#### The voices of young children

Preschool children's capacity to communicate their experiences in unaided face-to-face interviews is limited. Two PhD students in the group, Karin Fängström and Pär Bokström are therefore working on validating a computer-assisted interview called In My Shoes, for use with preschool children. They have conducted 54 interviews with preschool children after their visit at the child health clinic (which was video-recorded). PhD student Anton Dahlberg, also a psychologist, assists them with important work rating the interviews to ensure that there is an objective observer, not involved in the project that rates accuracy of children's accounts in relation to a video-recorded child health visit. Karin Fängström finished her half-time in 2015 and showed that In My Shoes is feasible with preschool children and that it is as efficient as a standard verbal interview in terms of accuracy and completeness. In 2016 we published an article showing that In My Shoes is not inferior to the standard interview method routinely used by the police and is in fact more accurate in identifying

people involved in the situation the child is interviewed about (using the video recordings).

## Service development for unaccompanied refugee minors with symptoms of PTSD

In 2015, a total of 35 369 unaccompanied refugee minors (URMs) sought asylum in Sweden. Unaccompanied refugee minors (URMs) are a particularly vulnerable group. In a previous study of 208 URM, we found that 76% screened positive for PTSD on the Children's Revised Impact of Event Scale; CRIES-8. To address this magnitude of mental health problems with potential later consequences, an indicated prevention program, Teaching Recovery Techniques, was translated to Swedish and piloted in a number of different settings in Uppsala County, Sweden. The pilot study included seven sites (health centre, NGO, school, 3 municipality group homes, and university) running a total of 10 groups.

Baseline measures are available for 67 participants: 85% reported moderate or severe depression and 42% suicidal ideation or plans. Preliminary results indicate that depression scores decreased significantly, whereas PTSD scores remained stable. More than half (60%) of participants reported negative life events during the study. In qualitative interviews, the participants reported feeling more in control of their own body and reactions and to cope better with crises. The "carers" appreciated the program contents but acknowledged the difficulties in supporting the participants in their home practices. Overall, results indicate that Teaching Recovery Techniques is a promising indicated preventive intervention for URM with PTSD symptoms. The TrT program can be delivered by staff without previous therapeutic experience in the Swedish context. This successful pilot study needs to be followed up with a controlled design and moderation. Anna Sarkadi and Raziye Salari are responsible for the project, financed by the National Public Health Agency and Skandia ideas for Life.

## Undergraduate Teaching

#### Education at the Department of Women's and Children's Health

#### **Tryggve Nevéus**

During 2016, as in previous years, a large number of students have participated in the broad range of programmes available at the Department. We continuously educate medical and nursing students in paediatrics and gynecology/obstetrics during their pregraduate study programs. The number of medical students is steadily increasing – presently around 180 students per year. We have a crucial role in the education of biomedical laboratory scientists. The Department also gives the postgraduate Registered Midwife course, the postgraduate course in Specialist Paediatric Nursing as well as the International Health Masters program.

#### The postgraduate Registered Midwife Programme

The registered Midwife Programme is a 90 ECTS degree program. The cornerstones of the education are reproductive health and midwifery, and the students are prepared for independent work within the fields of maternal health, youth health (contraceptive counselling), and infertility. The programme provides theoretical as well as clinical education and has a profile in global reproductive health and violence against women because of excellent resources at the department. Within the program it is possible to obtain a Master's degree, which in turn is a prerequisite for future PhD studies.

#### The postgraduate Specialist Paediatric Nursing Programme

The postgraduate education in paediatric nursing has been extensively revised during 2016. As part of the program, students now have the opportunity to choose a course in nursing care of children and adolescents receiving intensive care. The web-based parts of the courses have increased and new educational models, such as flipped classroom, has been introduced. Approximately every third week the course also have seminars on campus. Students can often customize their clinical assignments, which can be located in the hospital or in primary care. As these programs are available on an advanced level, students are given the opportunity to obtain a Master's degree.

#### Women's and Childrens Health within the Registered Nurse Programme

The Nursing Programme has recently been extensively revised. Women's and children's health are included in the first semester, whereas more in-depth education in gynecological, obstetric and paediatric care are included in the third and fourth semesters. Both theoretical and practical education, as well as web-based seminars and seminars using problem-based learning methods, are included. The department has 11 ECTS of the three-year Nursing programme, which involves several departments at Uppsala University. Furthermore, an elective course on promotion of health for women and children from a national and global perspective nursing has been be started.

#### The Biomedical Laboratory Science Programme

Students attend their first course, Basic Biomedical Laboratory Science, during their first semester, and complete their project work during their last semester, both at our Department. The students from Mittuniversitetet are also examined here. Collaboration with Ghent and Dublin within the Erasmus programme include several students each year.

# Obstetrics/Gynaecology and Paediatrics within the Medical Study programme

The medical study program at Uppsala University was recently reorganized so that students have

Obstetrics/Gynecology (10 ECTS), Paediatrics (10 ECTS) and Infection/Microbiology during the 9<sup>th</sup> semester. Students come to the department in three rows during the semester and have a final exam in all subjects at the end of the term. As previously, the studies comprise lectures, seminars (including problem-based learning) and auscultation at the hospital's various in- and outpatient wards. The department also cooperates with several hospitals outside Uppsala for parts of the students' clinical education. During 2016 international exchange programs in Obstetrics/Gynecology and Paediatrics have started, as one of the rotations each semester, is open to foreign students and given in English.

Finally, an elective course in Global Medicine, open to both medical and nursing students, is given by the Department during the 11<sup>th</sup> semester of the Medical Study Program.

#### Master programme in Global Health

The Master programme in Global Health is a 120 ECTS degree program that yields a M.Sc. in International Health. The programme starts with a course on basic Global Health, which is followed by courses in research methods, global nutrition, sexual and reproductive health and rights, public health in humanitarian action and child health. The studies end with a 30 ECTS thesis on a global health issue.

### **Research Education**

#### Lena Hellström Westas

The department has extensive PhD education within Paediatrics (including paediatric nursing), Paediatric Surgery, Obstetrics/Gynecology (including midwifery) and International Maternal and Child Health (IMCH). During the last years there has been a steady increase in the number of doctoral students at the department which is now steadily around 115. At the end of 2016 there were 116 registered doctoral students at the Department of Women's and Children's Health (Paediatrics 50; Obstetrics/Gynecology 35; IMCH 20), of which 20 were registered in 2016. During 2016 there were 19 dissertations (Paediatrics 6; Obstetrics/Gynecology 4; IMCH 9), 2 licentiate dissertations and 13 half-time seminars. A majority of the doctoral students are clinicians (obstetricians/gynaecologists, paediatricians, pediatric surgeons, midwives, nurses, physiotherapists, and psychologists). International doctoral students constitute a substantial proportion of the doctoral students and the projects are often performed as collaborative projects with other universities and institutions.

### Awards and Appointments 2016

- Poster Award in the cathegory "Engaging Power and Politics in Promoting Health and Public Value", Fourth Global Symposium on Health Systems Research 2016, Vancouver, Canada – Freddy Kitutu
- 2. For our work CHAP received the Children's Rights Prize 2016 awarded by the Children's Ombudsman in Uppsala County.
- Josephine Neimans stipendium

   Victoria Karlsson "Projektet rörande optimerad syrgaskoncentration under generell anestesi av barn i neonatalperioden"
   Maria Jonsson "Projekt rörande obstetriska riskfaktorer för neonatala kramper"

4. Födelsefondens tre stipendier

-Annika Esscher "Projekt i syfte att beskriva vad som karakteriserar kvinnor med ADHD och skiljer dem från kvinnor utan ADHD vad gäller faktorer rörande graviditet, förlossning och amning"

-Ola Andersson "Projekt gällande uppföljning med avseende järnbrist och anemi på 540 barn i Nepal"

-Inger Wahlström Johnsson "Projekt för att studera förekomst av riskfaktorer för fetma, diabetes och hjärt-kärlsjukdom hos en grupp 35-40-åringar med hög födelsevikt jämfört med en kontrollgrupp med genomsnittlig födelsevikt"

5. Lions stipendium

-Maria Nelander "Projekt för att skapa ett bättre kunskapsunderlag (bla med hjälp av MRT) för att underlätta bedömningen av gravida kvinnor med preeklampsi"

6. Gunnar Sedins resestipendium

-Liisa Svensson "Projektet handlar om att undersöka öka barnmorskekontinuitet som behandling för kvinnor med förlossningsrädsla; studiebesök till Danmark samt vetenskaplig konferens i Toronto"

7. Stiftelsen Familjeplaneringsfonden

-Karin Lindgren "Infertilitet med focus på: mekanismer, diagnos och behandling" -Evangelina Elenis "The Portrait of a Pregnancy through oocyte donation from a clinical perspective"

-Caroline Jansson "Upplevelser av missfall"

-Helena Kaihola "Biologiska markörer för ökad lyckandefrekvens vid IVF-behandling" -Lana Salih Joelsson "Livsstil och reproduktiv hälsa i Sverige – en prospektiv studie av kvinnor som söker hjälp för infertilitet"

-Stavros I Iliadis "Women undergoing In Vitro Fertilization and Peripartum Depression" -Maria Ekstrand Ragnar "Never too early: Evaluation of the Reproductive Life Plan (RLP) to increase reproductive and preconception health awareness among adolescents"

-Maja Bodin "Från graviditetsplanering till föräldraskap – en genusfråga"

-Elin Larsson "MIGPREV-projektet"

-Jenny Stern "Nyckeln till framgång – En kvalitativ studie om kvinnans och barnmorskans perspektiv på god preventivmedelsrådgivning"

-Anna Arvidsson "Transnationellt surrogatmoderskap med fokus på Sverige och Indien" -Katarina Kebbon Vaegter "Prediction Models in IVF"

-Cecilia Lundin "How common are mood and sexual side effects from combined oral contraceptives?"

-Helena Volgsten "Improving Post-abortion care: Healthy facility based on studies in Tanzania" -Jessica Påfs "Paradoxical barriers in the strive towards improved reproductive health in Rwanda"

-Maria Wickström "Sexuell och reproduktiv hälsa bland unga/vuxna med utvecklingstörning" -Joanna Arousell "Abort- och preventivmedelsrådgivning i det mångkulturella Sverige"

-Elin Ternström "Stärka genusaspekten i SRHR forskning på Uppsala Universitet"

-Jennifer Drevin "Vill du ha barn i ditt liv? Reproduktiv Livsplan som underlag för

hälsofrämjande preventivmedelsrådgivning" -Jóna Kristjánsdóttir "Ungas hälsa" -Anneli Stavreus Evers "Studier av endometriet efter hormonstimulering"