

Department of Women's and Children's Health

Annual report 2015

Introduction Uppsala maj 2016

2015 was another successful year for the Women's and Children's Health (WCH) with numerous achievements in the areas of teaching and research by the staff of the Department of Women's and Children's Health. The vision is to reduce teachers and researchers administrative duties and enabling them to focus on their main duties. We can do so by the contributions of our highly proficient and qualitative administrative staff.

The WCH has extensive responsibilities in the teaching of nursing students at ground and advanced level, midwifery students, medical students, master of global health students and graduate students. The students generally give excellent evaluations and feedback on our educational programs. This would not have been possible without the extensive work and support from our teachers. It is however important for all teachers to stay involved in their scientific work, and we have launched several initiatives to facilitate this. In terms of exciting new developments, as we plan to start a new programme directed at the intensive care for children, it will be possible for nurses to specialise within their existing program at a more advanced level.

The research questions addressed within WCH sciences covers a broad spectrum of issues ranging from contemporary hot public health issues on the political agenda to pertinent issues of molecular biology related to important women's and children's health problems. They take advantage from a truly multidisciplinary collaboration, and involve cooperation with other departments of the university and other universities in Sweden and around the world.

The research activities are organized in fourtheen research groups. The number of PhD students continues to increase implying more publications and dissertations will be published in the coming years. From a research perspective, it is particularly satisfying to note the increasing number of students within caring sciences. The research has a multidisciplinary and multiprofessional perspective including preventive, supportive, and caring actions. The focus is on clinically relevant problems in the health care sector.

A number of recruitment efforts are under way which will further strengthen research and education at the department. During the year 2015, Andreas Mårtensson started his position as Professor in International Child Health, Ingegerd Hildingsson started her position as senior lecturer working with the Midwifery program, Hanna Taylor was recruited as an administrator, mainly responsible for foreign PhD students.

Three associate professors were promoted to Professors in November: Birgitta Essén was promoted in International maternity health and migration, Annelie Stavreus Evers in Biomedical laboratory science with a focus on reproductive medicine, myself in Reproductive health.

Other talent management-related developments included; Jan Gustafsson retired from his position as Professor in pediatrics, however he continues as a senior professor. Margareta Larsson retired from her position as senior lecturer in Reproductive health but will continue as part time deputy lecturer.

We feel fortunate to work within a very successful University in a well-organised institution in good economic standing. To help foster a collaborative work environment within the Department, the administration continues to focus on improving

communication across all levels. Example initiatives include the development of the Co-worker Portal ('Medarbetarportalen'), the Annual Calendar, the Head of Department coffee chats ('Prefekt fika') and the Head of Department blog ('Prefekt blog').

In addition, the WCH greatly values its relationships with the Obstetric Gynaecology Department and the Children's Hospital of Uppsala. The majority of our lecturers, professors and researchers work clinically across all levels of these institutions, further cementing these relationships.

Finally, during 2015 many discussions focused on the future location of the department. No permanent solution has been found yet, but we continue to search for an optimal new work location with the assistance of the Medical Faculty.

Finally, the year 2015 was successful from both a science and education perspective. An impressive number of scientific papers were produced: an annual production of 351 peer-review articles and 14 PhD dissertations in 2015 makes WCH a very productive department at Uppsala University. The attraction of external grants has gradually increased during the last decade, this year being no exception.

I would like to thank all teachers, researchers, administrators and laboratory technicians for their outstanding work during the past year.

Agneta Skoog Svanberg Chairman of the the department of Women's and Children's Health

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Gunnar Sjörs Nikolaos Tsolakis
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Organization

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Agneta Skoog Svanberg

Deputy Chairman

Matts Olovsson

Department board

(from July 2015)

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Birgitta Essén teacher representative
Lena Hellström-Westas teacher representative
Carina Källestål teacher representative
Stefan Swartling Peterson teacher representative

Gunn Engvall teacher representative, deputy
Matts Olovsson teacher representative, deputy

Martin Selinus representative for technical/adm. personnel

Karin Törnblom representative for technical/adm. personnel, deputy

Jessica Påfs graduate student representative

Cecilia Montgomery graduate student representative, deputy

Vacant student representative Vacant student representative

Vacant student representative, deputy

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Ove Axelsson
Mehari Gebre-Medhin
Jan Gustafsson
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
Marie Säve
Kerstin Ståhlberg
Hanna Taylor
Jenny Thor
Karin Törnblom

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Kristine Eklund Hans Lindgren

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Research Groups

Gynecological Endocrinology

Tord Naessén, MD, PhD, Professor

Obstetrical Research

Ulf Högberg, MD, PhD, Professor

Reproductive Biology

Matts Olovsson, MD, PhD, Professor

Reproductive Health

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

Margareta Larsson, PhD, Associate professor, Senior lecturer

Pediatric Endocrinology

Jan Gustafsson, MD, PhD, Professor

Perinatal, Neonatal and Pediatric Cardiology Research

Lena Hellström-Westas, MD, PhD, Professor

Pediatric Neurology

Gunnar Ahlsten, MD, PhD, Associate Professor

Pediatric Oncology

Gustaf Ljungman, MD, PhD, Associate Professor

Pediatric Surgery and Pediatric Urology

Rolf Christofferson, MD, PhD, Associate Professor

Paediatric Inflammation

Kjell Alving, PhD, Professor

Child Health and Parenting Research Group

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. Environmental pollutants in elderly and possible associations to age-related diseases 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), applied in many of the conditions mentioned 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: www.nck.uu.s

Members of the group during 2015

Tord Naessen Professor

Gun Heimer Professor (NCK)

Hannes Bohman Post doc.
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 2013-2015

- 1. Kristjansdottir J, Olsson GI, Sundelin C, Naessen T. Self-reported health in adolescent girls varies according to the season and its relation to medication and hormonal contraception--a descriptive study. Eur J Contracept Reprod Health Care. 2013 Oct;18(5):343-54.
- 2. Akhter T, Larsson A, Larsson M, Wikstrom AK, Naessen T. Artery wall layer dimensions during normal pregnancy: a longitudinal study using noninvasive high-frequency ultrasound. Am J Physiol Heart Circ Physiol. 2013 Jan 15;304(2):H229-34.
- 3. Akhter T, Wikstrom AK, Larsson M, Naessen T. Individual common carotid artery wall layer dimensions, but not carotid intima-media thickness, indicate increased cardiovascular risk in women with preeclampsia: an investigation using noninvasive high-frequency ultrasound. Circ Cardiovasc Imaging. 2013 Sep;6(5):762-8.

- 4. 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.
- 5. 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.
- 6. 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 Ster Biochem Mol Biol. 2015/09/22 (E date).

NCK publications

- 7. Redovisning av regeringsuppdraget "*Utvärdering av utbildningar* (U2011/5671/JÄM)", ISBN 978-91-978448-6-4, NCK-rapport 2013.
- 8. "Våld mot kvinnor med funktionsnedsättning", ISSN 1654-7195, NCK-rapport 2013:1.
- 9. 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.
- 10. 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.
- 11. "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)
- 12. Heimer G, Björck A, Kunosson C. *Våldsutsatta kvinnor samhällets ansvar*. Tredje upplagan av NCK:s lärobok, ISBN 978-91-44–09444-1. Studentlitteratur 2014.
- 13. Redovisning av regeringsuppdraget att "*Utveckla den nationella stödtelefonen Kvinnofridslinjen* (U2011/3939/JÄM)", ISBN 978-91-978448-8-8, NCK-rapport 2015.

Agencies that support the work

ALF, 930,000 SEK Selander's foundation, 150,000 SEK

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

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. Recently we found increased endogenous estrogen

levels in both men and women with prevalent CVD, and 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 etc.

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 some age-related changes/diseases.

2. Suggestion and evaluation of a new principle for non-invasive assessment of the artery wall with regard to arterial aging, based on very high-frequency ultrasound (22 – 50MHz).

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 erythematosos, 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, in monitoring effects of menopausal hormone therapy initiated soon after menopause, 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 analysis indicate that the method can monitor effects of intervention against arterial aging, even on the individual level.

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, e.g. statins, menopausal hormone therapy and life-style changes etc.

3. Pregnancy complications: signs of artery wall aging during and after pre-eclampsia and whether some pregnancy complication might in part be caused by the preexisting maternal vascular status.

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 artery 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-elampsia, intrauterine growth retardation etc.

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. preeclampsia.

4. 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 predefined brain regions, as assessed by Positron Emission Tomography (PET). Currently, we study the lateralization of serotoninergic activity in the frontal brain, in relation to PMS/PMDD symptoms.

The results might help to better 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.

5. Recurrent depressions in the adolescence and metabolic consequences later in life.

Prevalence of self-rated health in school children 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, has been followed up for 20 years. A pilot results indicated that subjects 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 form this cohort.

6. 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 are 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.

7. Violence against women (NCK project).

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

Obstetrical Research

Ulf Högberg

The overall research theme is human reproduction from conception to birth adding knowledge about adverse outcomes why, how and then. The research group is developing an integrative approach in a life course perspective from the womb to child and young adult's health with the ultimate aim to improve reproductive health. The research methods are translational, experimental clinical and reproductive epidemiology.

Members of the group during 2015

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Ulf Högberg Seniorprofessor
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Helena Åkerud¹ Professor (adj.)
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¹changed to Reproductive Health research group autumn 2015

Publications 2013-2015

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.
- 2. **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.
- 3. **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.
- 4. Dumitrescu B, **Axelsson O,** Strand R T. Sängläge vid tidig vattenavgång enligt evidens eller gammal vana? Läkartidningen. 2015;(112)
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Fou Uppsala/Örebro	670 000
Brottsofferfonden	480 000
AFA	2 000 000
VR	3 565 000
SIDA/ISP	500 000

Senior professor Ove Axelsson has research profile in perinatal, obstetrical and clinical research and head supervisor for Johanna Belachew. Professor Ulf Högberg, head of the research group, has a research profile is clinical and reproductive epidemiology integrating Swedish and low-income country research settings. Professor Helena Åkerud has a broad translational research profile in infertility, gynecology and obstetrics, but changed to the Research Group Reproductive Health during the autumn 2015. Associate professor Anna-Karin Wikström has a research profile in clinical and reproductive epidemiology and experimental design. Associate professor Maria Janson's research profile of clinical obstetric epidemiology address fetal and maternal and complications as asphyxia, metabolic acidosis and complications of abdominal delivery. Associate professor Ulf Hanson has a research profile in clinical and epidemiologic research.

The Obstetric research group has extensive collaboration with other research groups in the department: Reproductive Biology, Gynecological Endocrinology, Reproductive Health, International Child Health and Nutrition, International Maternal and Reproductive Health and Migration, Perinatal Neonatal and Pediatric Cardiology, Social Pediatrics.

One core theme in the research group is short- and long term follow-up of the child after fetal and birth exposure. Together with two research groups Reproductive Biology and Reproductive Health we are responsible for an ongoing collection of plasma and leucocyte samples from women pregnant at about I8 weeks. So far samples from about 80000 women have been collected. This unique blood bank is a research source for several on-going research projects and will be source for epigenetic studies. Helena Åkerud and Ulf Högberg are in the steering group of the BASIC- Biobank (Research Group Reproductive Health) collecting prospectively maternal blood samples, salivary cortisol and samples from placenta in association to maternal and child mental health. In 2014 a research database Uppsala Mother-Child Cohort has been created, with Ulf Högberg as principal investigator. It is comprising 35,000 mother-child pairs, with clinical information from birth, neonatal and child health care linked to the national Swedish Health Registries. Analysis of fetal exposure as preeclampsia, diabetes, maternal mental disease and psychotropic, to child growth deviations, visits to children's psychologists are in process. In 2013 Ulf Högberg principal investigator and in collaboration Neuroscience/Children psychiatry, pregnancy cohorts in Nicaragua (in collaboration with UNAN-Léon University) and Ethiopia (in collaboration with Addis Ababa University) have been revisited 9-10 years after birth addressing mental health among the mothers and their off-springs. Reporting is in process. In 2015 a data collection of follow up 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 is in collaboration with Professor Geir Jacobsen and co-workers at NTNU, Trondheim. Responsible researchers at Uppsala University are Ulf Högberg, Anna-Karin Wikström and Mia Ramklint, associate professor, children and adult psychiatrist. The objective of the study is to analyse the physical and mental health in the mothers and the offspring after being exposed to birth of a SGA infant, preterm birth and/or preeclampsia.

Especially the relation between the pregnancy complications and the development of Attention Deficit Hyperactivity Disorder (ADHD) and autism spectrum disorder (ASD) will be examined. The project includes follow up in the national registers. Ove Axelsson was head supervisor for Johanna Belachew, who defended her thesis in 2015. Her research focused on placental problems at delivery and included clinical as well as epidemiological studies. Ove Axelsson is also supervisor for Ellen Ternby whose research project deals with knowledge of Down syndrome among pregnant women, partners and professionals within antenatal care.

In 2014 Helena Åkerud was appointed as adj. professor. She is presently focusing to investigate if there are distinct biological mechanisms that are affected in relation to assisted reproduction. Mechanisms that might explain why there seem to be increased risks related to assisted reproduction, such as pregnancy complications, adverse perinatal outcome, as well as an increased risk of birth defects and rare disorders where imprinted genes are affected will furthermore be investigated. She was head supervisor for Helena Kaihola and Karin Lindgren, and deputy supervisor for Michaela Granfors defending their thesis in 2015. She is head supervisor of Lina Bergman, and deputy supervisor of Johanna Gunnarsdottir, Maria Nelander, and Margit Endler. She was head supervisor for Evangelia Elenis but changed to be deputy supervisor in 2015. Postdoc in her team is Karin Kårehed. She left as supervisor for Lena Liljeström in 2015. Helena Åkerud moved to the research group Reproductive Health during the autumn 2015.

Anna-Karin Wikström focuses her research on placental dysfunctional disorders, with preeclampsia as the main focus. Further, Anna-Karin is in the steering committee for the network on clinical studies in obstetrics and gynecology (SNAKS), member of the Board of Education Swedish Society for Obstetrics and Gynaecology (utbildningsnämnden), chairman of the evaluation board for ALF funding in obstetrics, gynaecology, neonatology and urology at KI and chairman for the obstetric part of the National Pregnancy Register. She has since her postdoc period at Clinical Epidemiological Unit at Karolinska Institutet developed a close collaboration with the unit, particularly with professor Sven Cnattingius and MD, PhD Olof Stephansson. Anna-Karin is tutoring a post doc at the unit, MD Marija Simic, who is working with a database including longitudinal collected blood pressure measurements from almost 200,000 pregnancies. Anna-Karin has international collaborators where manuscripts are in preparation within all collaborations: Professor Roly Skjaerven (Bergen University), Professor Eszter Vanky (NTNU), Professor Baskaran Thilaganathan (Kings Collage London) and Associated Professor Julia Simard (Stanford). In 2015 Anna-Karin was the principal supervisor of two PhD students who defended their thesis. Sara Sohlberg on placental function during preeclampsia and Michaela Granfors on hypothyreosis during pregnancy. She has three on going PhD-projects as principal supervisor: Preeclampsia and the brain (PhD-student Maria Nelander), Epidemiological studies of preeclampsia (PhD-student Johanna Gunnarsdottir) and Intrauterine Growth (PhD-student Linda Lindström), Anna-Karin Wikström is also deputy supervisor of Lena Liljeström (Fetal hypoxia), Katja Junus (Pro-BNP in preeclampsia) and Patricia Eckerdahl (Pregnancy complications and postpartum depression) at Uppsala University and Margit Endler (Placental retention) and Siavash Maghsoudlou (Pregnancy complications in Golestan) at Karolinska Institutet. During 2015 Siavash Maghsoudlou had a half-time seminar. Together with professor Inger Sundström-Poromaa (Reproductive Health, KBH) Anna-Karin has a new project on obesity and pregnancy complications. The main aim is improved risk assessments of obese women in obstetric care by development of 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. Further, by usage of actigraphs activity- and inactivity patterns will be evaluated in the pregnant population, with the goal to find the most beneficial pattern concerning maternal and fetal outcomes. Heiddis Valgeirsdottir and Heidrun Maak are planned PhD-students within the project.

Ulf Högberg is principal investigator of a study initiated in 2014 about second victim addressing posttraumatic symptoms among obstetricians and midwives after severe events in maternity care in

collaboration with department of Neuroscience /Psychiatry, Uppsala University, LIME/Medical Management Centre, Karolinska Institutet, Social medicine and global health, Lund University. Högberg is head supervisor of Susanne Hesselman, Anna Palm and Åsa Wahlberg, deputy supervisor at the departments of Clinical science/obstetrics & gynecology (thesis defended in 2015) and Public Health/Epidemiology & Global Health (planned thesis defended in 2015), Umeå University, and one PhD project exploring patient safety in perinatal care at Department of Clinical Science and Education, Unit of Obstetrics and Gynecology (Southern Hospital, KI (planned thesis defence in 2016. A new PhD candidate, Sibone Mocumbi, University Eduardo Mondlane (UEM), within SIDA-supported collaboration was registrated in 2015 with Ulf Högberg as main supervisor, and as deputy supervisor Anna Bergström (Research Group International Child Health and Nutrition), in collaboration with UEM and KI (co-supervisor associate professor Claudia Hanson). Ulf Högberg is principal investigator in a project started in 2015 "Shaken baby syndrome/abusive head trauma in Sweden - Diagnosis, occurrence, risk factors, societal consequences and perspectives." Ulf Högberg is co-investigator (PI Associate Professor Alkistis Skalkidou) of the project started in 2015 "EMBLA, an internet-based intervention as a supplement to clinical management for vulvodynia patients".

Maria Jonsson is main supervisor for Lena Liljeström, and deputy supervisor for Susanne Hesselman and Åsa Wahlberg. She is also principal investigator for two clinical multicenter RCT: s that are conducted at the delivery ward, Akademiska hospital, one national and one international trial.

PhD Ajlana Lutvica was deputy supervisor of Johanna Belachew and Sara Sohlberg.

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 and associate professor Solveig Norden Lindeberg has ongoing register studies regarding preeclampsia and malformations.

Reproductive biology

Matts Olovsson

Members of the group during 2015

Olovsson, Matts Professor Bourlev, Vladimir Professor Stavréus-Evers, Anneli Professor

Edelstam, Greta Associate professor
Lundkvist, Örjan Associate professor
Rezapour, Masoumeh Associate professor
Skirnisdottir, Ingridur Associate professor
Wånggren, Kjell Associate professor

MD, PhD Holte, Jan Wikström, Ingrid MD, PhD Lindström, Annika MD, PhD MD, PhD Brodin, Thomas Karypidis, Helena MD, PhD Sanner, Karin MD, PhD Shemer, Elisabeth Wikström MD, PhD Arnadottir, Ragnheidur PhD Bäcklin, Britt Marie PhD Hambiliki, Fredwell PhD Lindahl, Magnus PhD Ljunger, Elisabeth PhD PhD Lövkvist, Lena Rumman, Amani PhD Saha, Rama PhD Assefa, Nega MD Bredhult, Carolina MD Helmestam, Malin MD Hreinsson, Julius MD Karlström, Per-Olof MD Michos, Constantinos MD Murto, Tiina MD Nash, Peppi MD Persson, Pär MD

Gudmundsson, Johannes Medical doctor Jansson, Caroline PhD-student Junus, Katja PhD-student Kunovac Kallak, Theodora PhD-student Moberg, Christian PhD-student Arnio, Riina Research student Fatma Gulen, Yaldir Research student Iliasova, Natalia Research student Karlberg, Malin Research student Haroun, Sally Research student Hermansson, Ruth Research student

Norenhag, Johanna Research student Sandell, Petra Research student Spagnoli, Gabriel Research student

Davey, Eva Biomedical laboratory scientist

Båth, Ann-Sofie Study nurse

Publications 2013-2015

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Dissertations 2015

1. Theodora Kunovac Kallak, 150424.

Agencies that support the work/Funding

ALF, 1 873 000 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 have a large study where screening based on cytology is with HPV-testing. We will start a new study where we compare self-sampling wits sampling by a midwife, for the analysis of HR-HPV. We are studying the prevalence of HR-HPV in women aged 60-75 years. 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.

Reproduktiv hälsa

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 2015

Inger Sundström Poromaa, professor

Agneta Skoog Svanberg, professor

Dan Hellberg, adjunct professor

Helena Åkerud, adjunct professor

Alkistis Skalkidou, associate professor

Charlotte Hellgren, post doc

Erika Comasco, post doc (20%)

Jocelien Olivier, post doc

Juliane Schlenstedt, post doc

Elin Bannbers, PhD

Catrin Borneskog, PhD

Fatimah Dabo, PhD

Malin Gingnell, PhD

Kristiina Kask, PhD

Åsa Lindholm, PhD

Annika Lindström, PhD

Helena Lundgren, PhD

Karin Stålberg, PhD

Birgitta Segebladh, PhD

Jan Wesström, PhD

Inger Wallin Lundell, PhD

Helena Volgsten, PhD

Helena Kaihola, PhD

Miriam Hudecova, PhD

Theodora Kunovac Kallak, PhD

Raghad Samir, PhD

Sara Sylvén, PhD

Emma Håstad, PhD student

Kathrine Bjersand, PhD student

Patricia Eckerdal, PhD student

Åsa Edvinsson, PhD student

Cecilia Lundin, PhD student

Anna-Karin Hannerfors, PhD student

Sussy Hofmayer, PhD student

Stavros Iliadis, PhD student

Emma Bränn, PhD student

Hanna Henriksson, PhD student

Paridhi Jha, PhD student

Merit Kullinger, PhD student Gyula Pekar, PhD student Nada Hana, research ass Lena Moby, research nurse Kollia, Natasa, statistician

Publications 2013-2015

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Dissertations 2015

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The Swedish multicenter study on gamete donation.

Agneta Skoog Svanberg, Gunilla Sydsjö and Claudia Lampic, Evangelia Elenis

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 thesis 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, Thomas Parling, Maria Jonsson, Margareta Larsson, Alkistis Skalkidou, Inger Sundström Poromaa, Josefin Sjömark

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, Margareta Larsson, Kyllike Christensen, Paridhi Jha

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.

BASIC - Biology, Affect, Stress, Imaging and Cognition in Pregnancy and the Puerperium

Alkistis Skalkidou, Inger Sundström Poromaa, Sara Sylven, Stavros Iliadis, Patricia Eckerdal, Charlotte Hellgren, Malin Gingnell, Erika Comasco, Mia Ramklint, Carin Marziscko, Gustaf Gredebeck

This study is an attempt to further extend our knowledge on the pathophysiological processes underlying antenatal depression and postpartum depression (PPD) and also to find predictors of the diseases to improve early recognition. All women attending the routine ultrasound examination in gestational week 16-17 are asked to participate in this study. During pregnancy women are followed by web-based questionnaires (depression rating scales, personality inventory, early life stress, sleep disorders). Blood and tissue samples have been collected from all women at parturition, and a final assessment of all women will be made six months postpartum. The study has thus far included 4800 women and tissue sampling at delivery is obtained in more than 80% of cases. The number of papers

from the BASIC study has now exceeded 20 and more manuscripts are under way. Extensive genotyping of the population has been performed in 2014, which is expected to yield further publications. Thus far, two PhD student have graduated with studies emanating from BASIC. Additionally, five PhD students are working on information or bio samples from the study.

A follow-up study on the offspring of the cohorts UPPSAT (2006-7) and BASIC (2009-ongoing), trying to elucidate complex genetic and environmental interactions in shaping child psychopathology has been initiated (U-BIRTH study). The children at followed at 18 months, 6 years and 11 years with questionnaires and saliva sampling. Umbilical cord blood is also available for a large proportion of the BASIC paticipants. In addition, a study in collaboration with Uppsala Barn and Baby Labbet, Dept of Psychology, Uppsala University, in which children to healthy (n=100) and depressed mothers (n=20) from the BASIC cohort are subjected to a battery of elaborate psychological tests.

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. The database for the first aim of the study is, however, completed so preliminary analyses will take place during 2016.

International Child Health and Nutrition

Andreas Mårtensson

The research programme International Child Health and Nutrition focuses on health system strategies, and interventions and implementation research for improved child health and survival, on prevention and management of childhood malnutrition, improved understanding and management of childhood fever, and on equity in child health and survival.

Members of the group during 2015

Almblad, Ann-Charlotte, Doctoral student

Bergström, Anna, Researcher

Berhane Hanna, Doctoral student

Chopra, Mickey, Researcher

Doherty, Tanya, Professor

Duc, Duong, Doctoral student

KC, Ashish, Doctoral student

Eneroth, Hanna, PhD, Nutritionist

Eriksson, Leif, Lecturer

Ewald, Uwe, Professor emeritus

Granberg Caroline, Research assistant

Henriksson, Dorcus Kiwanuka, Doctoral student

Hofvander, Yngve, Professor emeritus

Ijumba, Petrida, Researcher

Johansson, Emily White, Doctoral student

Khan, Islam Ashraful, Researcher

Källestål, Carina, Researcher, associate professor

Lindström, Emma, Researcher

Moshfigur Rahman Syed, Researcher

Musafili, Aimable, Doctoral student, researcher

Målqvist, Mats, Researcher, associate professor

Mårtensson, Andreas, Professor, Research group leader

Nahar, Baitun, Doctoral student

Nguyen Thu Nga, Researcher

Pathak Ashish, Postdoctoral student

Pena, Rodolpho, Associate professor

Pérez, Wilton, Researcher

Persson, Lars-Åke, Senior Professor, Research group leader

Peterson, Stefan Swartling, Professor

Rahman, Anisur, Researcher

Rana Nisha, Research assistant

Selling, Katarina Ekholm, Researcher, associate professor

Shaheen, Rubina, Doctoral student

Sohel, Nazmul, Researcher

Svefors, Pernilla, Doctoral student

Tadesse, Amare, Doctoral student

Wrammert, Johan, Doctoral student

Ziaei, Shirin, Doctoral student

Åsling Monemi, Kajsa, Physician

Publications 2013-2015

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Project 1: Reducing neonatal mortality

K.C. Ashish, Anna Bergström, Leif Eriksson, Johan Wrammert, Uwe Ewald, Aimable Musafili, Mats Målqvist, Lars Åke Persson, Stefan Peterson

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 randomised 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. This project and linked initiatives have generated several papers on neonatal health, including three completed PhD theses (Mats Målqvist 2010, Leif Eriksson 2012 and Nguyen T Nga 2013). One more PhD student has ongoing studies related to the trial. Sida is the main funder of this project and Swedish Research Council has provided additional funds. 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. Currently we perform 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

The Uganda Newborn Study (UNEST) funded by Gates via Saving Newborn Lives demonstrated that community health worker (CHW) home visits in pregnancy and newborn period improves delivery and newborn practices. Christine Nalwadda further demonstrated in her articles and thesis that CHWs can identify sick newborns in need of referral from the home to health centres, and that referral compliance was high. However, the first level health facilities are largely unable to cater for the sick newborns for policy gaps, and lack of skills, drugs and equipment. Uganda Ministry of Health has adopted the UNEST home visiting counselling materials for national use. Dialogue

around policy changes to empower first level health units to cater for sick newborns is ongoing. A journal supplement on UNEST was published in 2015.

An EU-funded project EQUIP – essential quality improvement using information power – was 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.

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. A series of manuscripts were submitted during the year.

Private sector implementation of Integrated Community Case Management of Malaria and Pneumonia and Diarrhea (ICCM) was evaluated in Uganda. A publication by Phyllis Awor et al. attracted a lot of international interest and is now followed up by a WHO/Alliance and Swedish Science Council funded study in Uganda.

In Rwanda an analysis was performed of the development of child survival from the early 1990s, across the time of genocide and the period of impressive rebuilding of society. This study, together with hospital-based studies of perinatal mortality, and an evaluation of the "Helping Babies Breathe" (HBB) training program were presented in a PhD thesis in 2015.

In Nepal there is an on-going trial on the evaluation of delayed versus early cord clamping and its effects on the prevalence of anaemia when the newborn has reached the age of eight to twelve months. A total of 540 live births have been included in this randomized controlled trial. The study is conducted at the Paropakar Maternity and Women's Hospital, Nepal. Pregnant woman of gestational age 34-41 weeks, who deliver vaginally, have been included in the study. The interventions consist of delayed clamping of the umbilical cord (\geq 180 seconds after delivery) or early clamping of the umbilical cord (\leq 60 s). At 8 and 12 months of age, infant's iron status and developmental milestones will be measured.

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) is currently under way. This simple tool has shown promising results in reducing admittance to intensive care unit and reducing time to initiation of adequate treatment.

Project 2: Short- and long-term effects of improved prenatal nutrition.

Eva-Charlotte Ekström, Katarina Selling, Emma Lindström, Shirin Ziaiei, Pernilla Svefors, Lars Åke Persson, Stefan Peterson

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), 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 foetal life. The publications from MINIMat also include micronutrient status in pregnancy and infancy, risk factors for infant anaemia, 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 10-years follow-up of these children have been published. The 15-years follow-up in the stage of planning and grant application 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. The key collaborative institution in this project is icddr,b in Bangladesh, but we also collaborate with Karolinska Institutet, Lund University, Institute of Child Health, London, UK, 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 and the research partners have also received funding from several agencies.

A study of health system aspects of the rapidly increasing diabetes prevalence in low- and middle-income 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.

Project 3: Exclusive breastfeeding and HIV

Tanya Doherty, Mickey Chopra, Petrida Ijumba, Lars Åke Persson

Exclusive breastfeeding during the first six months of life is considered one of the most important means of preventing child deaths by infections. The dilemmas around exclusive infant feeding options when trying to prevent mother-to-child transmission of HIV are being studied by a series of PhD students in collaboration with University of Western Cape and MRC in South Africa. Swedish Research Council has financed the ongoing collaboration between our groups and Save the Children (US) has provided support to our collaborating partners.

Project 4: Children with fever

Stefan Peterson, Katarina Selling, Emily White Johansson, Freddy Kitutu, Andreas Mårtensson

In different studies in Uganda the diagnosis and management of children with fever are addressed. A research prioritization process with worldwide participants (so called CHNRI) is now the next step where we are core members. We have previously contributed to changing WHO/UNICEF and Uganda policy to integrated community case management (iCCM) of Malaria, Pneumonia and Diarrhoea by means of Community Health Workers, which is now expanding through Africa supported by UNICEF, USAID and others. We have shown that iCCM may also work in private sector drug shops in Uganda, where many sick Ugandan children get treated. This is of immediate policy relevance to, for example, the Global Fund's Affordable Medicine Facility Malaria, a major private sector initiative in nine countries. Together with Makerere University we have acquired funding for further trials from Swedish Research Council and the (WHO affiliated) Alliance for Health Policy and Systems Research.

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 student) uses new data recently collected from standardized national cross-sectional household and health facility surveys conducted in multiple sub-Saharan African countries to improve understanding of extent and determinants of diagnostic test use and adherence across

different contexts, including in different malaria risk settings in sub-Saharan Africa, whereas Freddy Kitutu (the first student enrolled in a double degree PhD programme between Makarere and Uppsala University) is focusing on the utility of mRDT use in private health sector in Uganda.

The "know-do gap" refers to the fact that 2 out of 3 children in the world die unnecessarily – we have the knowledge and resources to prevent or cure them, but it is not translated to action. We have two projects evaluating various forms of "implementation bottleneck analysis" and quality improvement as strategies to improve access to and quality of care. Funded by the European Union and Gates Foundation, respectively, these studies are implemented in Uganda and Tanzania in collaboration with Makerere University, Ifakara Health Institute, Karolinska Institutet and London School of Hygiene and Tropical Medicine. Several publications are foreseen with process and results from these studies in the coming years.

In addition 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 ethiology 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.

In a Swedish Research Council and 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 and assessment of antimalarial drug resistance in Tanzania, with a special focus on potential evolution and spread of artemisinin tolerance/resistance, a phenomenon that has recently been observed in South East Asia, using both standard in vivo studies and molecular surveillance of antimalarial drug resistance of Plasmodium falciparum.

Project 5: Implementation Science

Anna Bergström, Leif Eriksson, Emily White Johansson, Mats Målqvist, Stefan Peterson, Lars Åke Persson

Researchers at IMCH have an interest to advance in the field of implementation research. Since 2014 Anna Bergström and Leif Eriksson run a Master/PhD-level course in Implementation Science and projects such as the NeoKIP departs from the notion that there is need to develop understanding on how to translate knowledge into practice.

Health system contextual factors influence health workers ability to adopt new practices. Since 2010, we have together with international partners been involved in developing a questionnaire-based tool for assessment of the local health system context as perceived by the individual health worker. The development of the Context Assessment for Community Health (COACH) tool was undertaken with partners from Canada and in, and with partners from, Bangladesh, Vietnam, South Africa, Uganda

and Nicaragua. The main article was published in 2015. The validated tool measures eight dimensions of context: Organizational resources, Community engagement, Monitoring services for action, Sources of knowledge, Commitment to work, Work culture, Leadership, Informal payment. The COACH tool (© Bergström & Estabrooks) is now available in public domain and the research group is currently finalizing a manual on how to use it. The response from the global implementation science community has been very positive and the COACH tool was recently a part of 5 Horizon2020 proposals. Also, qualitative researchers find the dimensions useful in framework analysis. The tool is currently being used in Vietnam and Mozambique.

Weblink: http://www.kbh.uu.se/imch/coach

The PeriKIP project is an extension of the NeoKIP project but where the intervention of facilitated participatory groups applying PDSA is also implemented on district hospital level and at provincial hospital level. The project was launched in Cao Bang province in northern Vietnam in Sept 2015. The intervention was implemented from November 2015 and will run for 12 months. The intervention is implemented in 48 primary health units, 3 district hospitals and at the provincial hospital. The PeriKIP project is funded by the Swedish Research Council through Profars Wallin at Dalarna University. Anna Bergström, a co-investigator in the PeriKIP, has a three year financed post-doc from EU/FORTE 2015-2017 and lives in Vietnam as part of her post-doc.

Project 6: Assessing the context of the health system

Anna Bergström, Carina Källestål, Mats Målqvist, Katarina Selling, Lars Åke Persson, Stefan Peterson

Since 2010, we have together with international partners been involved in developing a questionnaire-based tool for assessment of the health system context and the individual health worker's perceptions of aspects regarding different building blocks of the system. The development of the Context Assessment for Community Health (COACH) tool has been undertaken in, and with partners from, Bangladesh, Vietnam, South Africa, Uganda and Nicaragua. Development of the tool including undertaking and statistical analysis was completed in November 2013. The COACH tool was integrated into the NeoKIP follow up project in 2014 whereby all health workers involved in maternal and neonatal health services and about half of the village health workers in the NeoKIP project study areas were invited to undertake the survey. Data on test-retest reliability has also been collected from Vietnam and response process with a smaller selection of health workers undertaken to analyse the cognitive validity of the Vietnamese COACH tool.

The main article from the project was published in 2015. The COACH project has been presented at a number of international conferences, e.g. at the Third Global Symposium on Health System Research in Cape Town, South Africa, at the BMC Health Service Research conference in London, and at the Knowledge Utilization Colloquia in Tällberg.

Project 7: Management of severe malnutrition

Eva-Charlotte Ekström, Baitun Nahar, Pia Olsson, Elazar Tadesse, Amare Worku, Lars Åke Persson

The development of effective and feasible strategies for prevention and management of severely malnourished children are addressed in studies in Ethiopia and Bangladesh. In Ethiopia results from the large study of the effectiveness of community-based rehabilitation of management of severe acute child malnutrition has been reported in scientific journals as well as in conferences. One of the PhD students will defend her thesis in mid-2016. Sida and Uppsala University have supported these studies.

Project 8: Gender-based violence and child health

Eva-Charlotte Ekström, Shirin Ziaiei, Lars Åke Pedrsson, 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 a paper on the association with child malnutrition was also published.

Project 9: Community development work and health effects

Carina Källestål, 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 analysed 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.

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.

Two doctoral students have defended their thesis successfully. One new post doc has been registered during the year.

Members of the group during 2015

Abdi Mohamed Zahra

Andrew Mgaya, Doctoral student

Anna Arvidsson, Doctoral student

Anna Wahlberg, Doctoral student

Asha Omar, Associate Professor

Barni Nor, RN, PhD

Bengt Haglund, Associate Professor

Birgitta Essén, Professor, Research group leader

Camilla Larsson, Research assistant

Christina Pedersen, Research assistant

Elin Larsson, PhD post doc

Erica Schytt, Senior lecturer

Eva-Britta Råssjö, PhD

Gunilla Aneblom, PhD

Helena Litorp, Doctoral student

Hussein Kidanto, MD, PhD

Jessica Påfs, Doctoral student

Jonna Arousell, Doctoral student

Kristina Bolme Kuhn

Magdalena Bjerneld, PhD

Mandira Paul, Doctoral student

Marie Klingberg-Allvin, Senior lecturer

Mattias Rööst, MD, PhD

Pauline Binder, PhD

Soheila Mohammadi, Doctoral student

Soorel Jose Puthoopparambil, Doctoral student

Ulrika Byrskog, PhD

William Ugarte, PhD

Viveca Odlind, Professor emeritus

Publications 2013-2015

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Dissertations 2015

- Helena Litorp
 "What about the Mother?": Rising Caesarean Section Rates and their Association with
 Maternal Near-Miss Morbidity and Death in a Low-resource Setting.
- Ulrika Byrskog
 "Moving On" and Transitional Bridges: Studies on migration, violence and wellbeing in
 encounters with Somali-born women and the maternity health care in Sweden

Agencies that support the work/Funding

ALF, 1 861 163 VR, 1 219 000 Forte, 950 000 Familjeplaneringsfonden, 223 000

Project 1: 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.

Project 2: 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.

Project 3: 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.

Project 4: Increased access to comprehensive abortion care – A Partner Driven Cooperation between Uppsala University and Ipas India, 2010-2015

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

Maternal mortality has decreased in India over the past decade and huge efforts have been put into promoting delivery in the hospital. However, less focus has been put on the deaths from abortions, estimated to account for 20% of the maternal deaths. The purpose of the Partner driven cooperation between the NGO Ipas India and Department of Women's and Children's Health, Uppsala University is to increase access to comprehensive abortion care in the public health system in the states of Maharashtra, Madhya Pradesh and Assam through strengthened partnership between India and Sweden.

The group has several on-going and completed community- and hospital-based projects but all have in common the use of interdisciplinary and mixed methods to define the complexity of reproductive ill-health covering biomedical, social, cultural, gender equality and legal aspects. Studies in the project are; exploring future physician's attitudes and perceptions towards abortion and contraception, health care providers' perceptions on pregnancy and comprehensive abortion care, women's and men's views and perceptions on sexual and reproductive health issues.

Outcomes are sharing of knowledge and experience by the faculty members of the two countries, which will help in enhancing the knowledge base and implementing best practices into the teaching systems. The joint research activities on evaluating attitudes can help to build on the on-going policy work made by Ipas within the country and developing a pool of advocates to influence policy on mid-level providers in abortion services. In the end of November/beginning of December 2013 a concluding meeting took place in Delhi with representatives from the Swedish Embassy and Sida.

Project 5: 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.

Project 6: 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.

International Sexual and Reproductive Health

Margareta Larsson

Our research group studies women's health and rights, youth health and nutrition 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 2015 and several 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 2015

Abeid Muzdalifat PhD

Ahlberg Beth Maina PhD, Adjunct Professor

Axemo Pia PhD, Associate Professor

Balla, Elazar Tadelech Tadesse, Doctoral student

Berglund Anna PhD

Blixt Ingrid Doctoral student

Bodin Maja Doctoral student

Cato Karin Doctoral student

Contreras Mariela PhD

Dari Elisabeth PhD, Guest Professor

Dickson Kim, Doctoral student

Ekstrand Maria PhD

Ekström Eva-Charlotte PhD, Professor

Eriksson Elisabet, PhD

Furaha August Doctoral student

Haines Helen PhD

Hildingsson Ingegerd PhD, Professor

Hoque Waheedul Doctoral student

Häggström-Nordin Elisabet PhD

Högberg Hjördis Doctoral student

Höglund Berit PhD

Jordal Malin PhD

Kaime-Atterhög Wanjiku PhD

Kidanto Hussein PhD

Larsson Birgitta Doctoral student

Larsson Margareta PhD, Associate Professor, Senior Lecturer

Lindmark Gunilla PhD, Professor emerita

Makenzius Marlene PhD

Malm Mari-Cristin Doctoral student

Mattebo Magdalena PhD

Mbekenga Kokusiima Colomba PhD

Muganyizi Projestine PhD

Olsson Pia RNM, PhD, Associate Professor, Senior Lecturer

Omer-Salim Amal PhD

Pallangyo Eunice Doctoral student

Pembe Andrea PhD

Ragnar Inga Doctoral student

Rubertsson Christine PhD, Associate Professor, Senior Lecturer

Salih Joelsson Lana Doctoral student

Svensson Liisa Doctoral student

Ternström Elin Doctoral student

Trenholm Jill PhD

Tydén Tanja Professor

Wickström Maria Doctoral student

Publications 2013-2015

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Dissertations 2015

- 1. Amal Omer Salim
- 2. Abeid Muzdalifat
- 3. Mariela Contreras

Agencies that support the work/Funding

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The Public Health Agency of Sweden	70 000
Curtain University	31 000
Other Funds	125 000

Reproductive Health and Healthcare

Project 1: 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.

Project 2: Dysfunctional labour in a National Hospital in Dar es Salaam

PI: Elisabeth Darj

In this project at Muhimbili National Hospital in Tanzania we will analyse lactate in amniotic fluid in 1000 women. The aim is 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 will also be investigated whether high levels of lactate indicate an increased risk of caesarean section.

Project 3: Home based lifesaving skill education within maternal and newborn care in Tanzania

PI: Elisabeth Darj and Pia Axemo

The study is 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, we will study the involvement of men during pregnancy and birth and the views of health care workers.

Project 4: Introducing and evaluating a Reproductive Life Plan

PI: Margareta Larsson and Tanja Tydén

Randomized controlled trials among women and men using the RLP are ongoing. A fertility awareness web page is developed and will be evaluated. A longitudinal survey on life style and health, the Swedish Pregnancy Planning Study (SWEPP) is on-going in collaboration with several partners in Sweden and Europe, the PrePreg Network. Parents' interests in Preconception Genetic Carrier Screening is investigated as well as satisfaction with the couple relationship after childbirth. Think-a-loud interviews about pregnancy planning are ongoing.

Project 5: 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 Salaam, Tanzania. The project is a collaboration with Aga Khan University, Tanzania.

Project 6: Sexual/reproductive health among young people with intellectual disability – the health of their children

PI: Margareta Larsson and Berit Höglund

Women with intellectual disability (ID) and their children are risk groups. This project investigates health risks among children born to mothers with ID. Interview studies regarding sexual health and reproduction among young adults with ID are ongoing. Parents, professionals and young people will 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.

Project 7: 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 are being performed.

Project 8: The midwife's dialogue about alcohol with parents-to-be

PI: Margareta Larsson

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

Sexual Health and Rights

Project 1: 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.

Project 2: 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 health behaviours. In the longitudinal analyses frequent use of pornography was more associated to psychosomatic symptoms compared with depressive symptoms.

Project 3: 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.

Project 4: 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.

Project 5: 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

Project 1: Nutrition and women's health in Bangladesh

PI: Eva Charlotte Ekström, in collaboration with LÅ Persson

Randomized trials in Bangladesh are evaluating the effects of nutrition interventions in early life on maternal and child health over time, currently analyses of data from the 10 years follow-up is ongoing. Planning for the 15 years of follow-up was started.

Project 2: 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.

Project 3: 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.

Project 4: 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.

Project 5: Use of skin-lightening cosmetics among immigrant women PI: Elisabeth Darj

The aim of this project is to increase knowledge around the potentially dangerous bleaching products used in Sweden by immigrant women. We investigate the market, patterns of use and views on skin bleaching among immigrant women from Africa, Asia and Caribbean. Furthermore we have analysed the content of the products bought in East-Africa and Sweden.

Pediatric Endocrinology

Jan Gustafsson

Research within pediatric endocrinology contributes to the understanding of hormonal influences on growth and metabolism during infancy, childhood and puberty.

We study conditions behind intrauterine growth retardation and increased fetal growth as well as energy substrate metabolism in newborn infants. Since fetal conditions are important for adult life we use Swedish registers to study relationships between conditions at birth and growth, intellectual performance and development of adult disease. Eating disorders are known to influence somatic development and studies of endocrine and metabolic consequences of anorexia nervosa are ongoing. Overweight and obesity during childhood represent an increasing problem globally. Within the research group a large cohort of obese children is followed within the two projects ULSCO and Beta JUDO. Several aspects of type 1 diabetes during childhood are also studied in the research group. Focus is particularly on neurodevelopmental problems and metabolic control as well as weight gain during treatment and remaining endogenous insulin production. During the year Fredrik Ahlsson and Ylva Tindberg were appointed associate professors.

Members of the group during 2015

Gustafsson, Jan, Professor
Ahlsson, Fredrik, MD, Associate professor
Ciba, Iris MD, Doctoral student
Diderholm, Barbro, MD, PhD
Dahlbom, Marie, Research nurse
Forslund, Anders MD, PhD
Gebre-Medhin, Mehari, Professor em.
Grönberg, Annika MD, Doctoral student
Halldin-Stenlid, Maria, MD, PhD
Hedberg Nykvist, Kerstin Associate professor
Heyman, Maria, MD
Jonsson, Björn*, PhD

Koltowska, Maria, MD, PhD Lundgren, Maria, MD, PhD Myrelid, Åsa MD, PhD

Nylander, Charlotte MD, Doctoral student

Proos, Lemm MD, PhD

Staaf, Johan, MD, Doctoral student

Strand-Brodd, Katarina, MD, PhD

Swenne, Ingemar, Senior lecturer, Associate professor

Söderberg, Elisabeth, laboratory technician

Tindberg, Ylva. MD, Associate professor

Tuvemo, Torsten. Professor em.

Wahlström Jonsson, Inger MD, Doctoral student

Wester Oxelgren, Ulrika MD, Doctoral student

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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 and also metabolic disease later in life. The research is directed on metabolism both in newborn infants, children and adults. A study on effects of hypothermia on glucose homeostasis and cerebral glucose consumption after perinatal asphyxia is ongoing as well as studies on metabolic effects in adult life of being born large for gestational age with regard to weight. In collaboration with professor Inger Sundström a study on gene expression in placentas from women giving birth to large for gestational age infants have been published. This line of research will continue with studies of epigenetic markers in umbilical cords in infants with high or normal birth weights. In collaboration with child psychiatry a study on blood glucose regulation in children with ADHD has recently been performed.

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, Department of Public Health and Caring Sciences and professor Fredrik Serenius in the 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 initiate beta-cell secretion, in some cases hypersecretion, of insulin in infancy and childhood, which in turn may contribute to 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 on a global level. The research group connected to the regional childhood obesity center at Uppsala University Hospital has continued working with the EU-project Beta-JUDO. During the year the study Combat-JUDO was started. This is a parallel, double-blinded, randomized, 6 months study with lifestyle intervention and exenatide or lifestyle intervention and placebo in adolescents with obesity. The aim is to explore differences between the groups with regard to changes in BMI. The study, which is part of the Beta-JUDO project, will end in august 2016. Within the project studies of hypersecretion of insulin as a possible mechanism behind childhood overweight and obesity are also ongoing together with professor Peter Bergsten at the 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 in epidemiological studies. The registers are the Medical Birth Register, the conscript register, the Inpatient Care Register, the Drug Register and the Causes of Death Register. Different circumstances during fetal life may influence morbidity during childhood and adult life. We have particularly studied effects of conditions during fetal life and childhood on growth, development of obesity and cognitive function. The results show an association between overweight/obesity and impaired intellectual performance in young adults, particularly those with a low birth weight. Together with researchers in Auckland several studies on the importance of the intrauterine milieu for later life have been performed or are ongoing. Thus, first-borns have been shown to be more likely to be overweight or obese than their siblings. In another project overweight and obesity were studied in women born post-term. During the year a study on school performance after preterm birth was published in collaboration with Stockholm University. Studies on the effect of being born large for gestational age have pointed out long term effects of a high birth weight, particularly a weight >3SD, on adult metabolic disease. An epidemiological project on development and health in children of mothers with intellectual disability is ongoing in collaboration with the research group of International Sexual and Reproductive Health.

Mechanisms behind precocious puberty

Lemm Proos, Maria Halldin and Jan Gustafsson

Precocious puberty has been a field of research within the group for several years. Precocious puberty occurs more frequently in girls than in boys. 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 case of myelomeningocele and hydrocephalus are being studied.

Down syndrome

Ulrika Wester Oxelgren, Åsa Myrelid and Jan Gustafsson

The pediatric endocrinology research group has studied endocrine disease in Down syndrome (DS) for many years in collaboration with professor Göran Annéren at Department of Immunology, Genetics and Pathology. Data on secretion of growth hormone and effects of growth hormone treatment on growth and psychomotor performance has been published and by use register data causes of death in DS have been studied. In a thesis project the association between DS and ADHD as well as ASD is presently investigated in collaboration with professor Elisabeth Fernell at the university of Gothenburg. Within the project the prevalences of ADHD and ASD are investigated and the effect of pharmacological treatment of ADHD in subjects with DS is studied.

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. Together with associate professor Per Frisk and the doctoral student Anders Öberg, both in the pediatric oncology research group, 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 teenagers with eating disorders are treated according to a protocol, which enables continuous evaluation of the course of the disease and the outcome of treatment. The somatic restitution is followed by measurements of growth and weight gain and by analyses of hormones and nutritional factors. 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 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

A project on energy homeostasis in subjects with defects of fatty acid oxidations represents a collaboration between our department and that of Clinical Science, Intervention and Technology, Division of Pediatrics at Karolinska Institute. Fatty acid oxidation disorders are diseases, which impairs energy production from β-oxidation of fatty acids. The patients risk hypoglycemia and brain damage. Within the project growth, energy balance, neurocognitive outcome and long term complications are studied in children with defects in oxidation of long chain and very long chain fatty acids. Further, metabolic studies of patients with defects in the urea cycle resulting in hyperammonemia are planned with particular focus on protein- and energy metabolism.

Diabetes

Charlotte Nylander, Ylva Tindberg, Annika Grönberg and Ingemar Swenne

The doctoral student Charlotte Nylander has finished the work with her her thesis during the year in which she has studied factors influencing treatment adherence in the care individuals with type 1 diabetes. She has particularly studied protective factors and risk factors behind development of risk behavior. Revealing disabilities, such as ADHD is essential, since such problems can influence treatment adherence. The project is performed together with professor Elisabeth Fernell, University of Gothenburg.

In another project on pediatric type 1 diabetes metabolic control, weight gain and remaining endogenous insulin production are studied in children and adolescents. The 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 as well as genetic predisposition.

Perinatal, Neonatal and Paediatric Cardiology Research

Lena Hellström-Westas

The perinatal, neonatal and paediatric cardiology research spans over a broad research field and includes perinatal epidemiology, umbilical cord clamping, and neonatal intensive care of term and preterm infants including neurocritical care and studies of brain and visual physiology, cardiology and lung physiology, pain and stress responses, skin-to-skin care, family-centred care and breast feeding.

Members of the group during 2015

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Eva-Lotta Funkquist

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Reviews 2013-2015

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- 2. van Rooij LG, **Hellström-Westas** L, de Vries LS. Treatment of neonatal seizures. *Semin Fetal Neonatal Med* 2013;18(4):209-15.

Dissertations 2015

There were no dissertations in the research group in 2015.

Agencies that support the work/Funding

ALF
Swedish Research Council
Födelsefonden
HRH Crown Princess Lovisa Foundation
Heart and Lung Foundation
Jerring Foundation
Lilla Barnets fond (The Small Child's Foundation)
Linnéa and Josef Carlsson Foundation
Swedish Medical Society

Project 1: Epidemiological research

Fredrik Serenius, Lena Hellström-Westas, Johan Ågren, Elisabet Mattsson, Gunnar Sjörs, Annika Öhman, Margareta Jennische, Cecilia Montgomery, Kristina Persson

This project includes long-term follow up of three cohorts of extremely preterm infants: the national EXPRESS study group including infants with gestational ages less than 27 weeks who were born during a three-year period (2004-2007), the "1000 gram study", i.e. infants born with a birth weight less than 1000 g (1992-93), and a regional Uppsala cohort of infants born 1986-89 who required neonatal intensive care. The project also includes register-based research on neonatal seizures and postnatal epilepsy.

Project 2: 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 brain monitoring (aEEG, EEG, NIRS), cerebral ultrasound, MRI, and measurement of various biomarkers.

Project 3: Maternal, neonatal and long-term effects of delayed, as compared to early, cord clamping in healthy term infants

Ola Andersson, Lena Hellström-Westas

In this project, infants of 400 healthy women with normal pregnancies were randomized to delayed or early cord clamping after delivery. Infants subjected to delayed cord clamping had higher ferritin and lower risk for iron deficiency at four months. At 12 months and four years, delayed cord clamping was associated with a modest, but significant positive effect on neurodevelopment in boys. A new randomized study is currently performed in Katmandu (Nepal), and a study comparing effects of different timing of umbilical cord clamping is performed in collaboration with Karolinska University Hospital/Karolinska Institutet.

Project 4: Early visual tracking performance and long-term outcome in very preterm infants

Lena Hellström-Westas, Ylva Fredriksson Kaul, Cecilia Montgomery, Nima Naseh, Katarina Strand-Brodd, Claes von Hofsten, Kerstin Rosander, Kristina Persson

A population-based cohort of very preterm infants born in Uppsala (2004-2007). The study group had repeated evaluation of motor function, neurological and cognitive assessments. In half of the infants MRI was performed at $2\frac{1}{2}$ -5 years. Visual tracking ability was tested at two and four months, and will be repeated at 12 years in conjunction with neurocognitive and psychological testing and cerebral MRI.

Project 5: Breastfeeding in term and preterm infants

Eva-Lotta Funkquist, Ylva Thernström Blomqvist, Paola Oras, Jenny Ericson, Lena Hellström-Westas

Breastfeeding rates are decreasing in Sweden, both among term and preterm infants, but the reasons for this drop 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.

Project 6: 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).

Project 7: 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.

Project 8: Early clinical predictors of response to pharmacological treatment of persistent ductus arteriosus in extremely preterm infants

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

Extremely preterm infants (gestational age less than 28 gestational weeks) have a high incidence of haemodynamically significant patent ductus arteriosus (PDA) which is associated with a lower survival rate and an increased incidence of intraventricular haemorrhage (IVH), necrotizing enterocolitis, and BPD. We have 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 closure of a PDA.

Project 9: Oxygenation, heat exchange and fluid balance in extremely preterm infants in the NICU and during surgery

Johan Ågren, Victoria Karlsson, Laszlo Markasz, Erik Normann

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.

Pediatric Neurology

Gunnar Ahlsten

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 Associate professor

Borgestig, Maria PhD Bratteby-Tollerz, Linda MSc

Dahl, MargaretaAssociate professorEeg-Olofsson, OrvarAssociate professorEhrstedt, ChristofferPostgraduate studentForsblad KPostgraduate student

Höglund, AnetteMScJonsson, PysseMed LicKimber, EvaPh.DKratz, ÅsaMSc

Kristiansen, Ingela Postgraduate student

Lidström, HelenePh DLiminga, GunnarPh.DLundberg, StaffanPh.DStrinnholm, MargaretaMSc

Strömberg, Bo Associate professor

Söderström, Helena MSc

Publications 2013-2015

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Dissertation 2015

No dissertation during 2015

Agencies that support the work/Funding

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 Oncology

Gustaf Ljungman

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.

Members of the group during 2015

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

Publications 2013-2015

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- 3. 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;

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- 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.
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BCF 300.000/year, 2 years (Frisk et al- insulinresistance)

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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 Hodgkins 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 will be presented 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".

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Neuroblastoma: Neuroendocrine markers in Neuroblastoma markers

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 safe and give enough material for diagnosis.

Functional and genetic studies of pediatric neural tumors

Pfeifer with collaborators Diaz de Ståhl, Johanna Sandgren, Chandrasekhar Kanduri .

Tumor specific genetic changes have been identified in several brain tumor types in children using array CGH and expression arrays, in a joint project with the Karolinska Institute. Using .global array and genome-wide sequencing-based analyses, we have found individual tumor-specific abberrations in many pediatric medulloblastomas, necessating possible individualized therapy in the future.

Studies on the role of noncoding RNA in neural tumors are ongoing, and suggest that nc RNA, originating from the large bulk of nontranscribed DNA, may have key regulatory functions in neuroblastoma and possibly other pediatric neural tumors.

National bio bank for pediatric solid tumors

Susan Pfeifer, coordinator.

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 2015material 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 Surgery and Pediatric Urology

Rolf Christofferson

Pediatric surgery and pediatric urology cover the surgical management of congenital malformations and acquired diseases of the gastrointestinal tract and urogenital systems in children under 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 only 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.

Members of the group

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 Ammar Farman, PhD-student 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, research nurse Maria Lindström Nilsson, RN, PhD-student Göran Läckgren, professor, MD, PhD Erik Sköldenberg, MD, PhD Anders Stenbäck, MD, PhD Arne Stenberg, associate professor, MD, PhD

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Dissertation 2015

1. Johan Danielson

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.

Basal metabolic rates in prematurely born babies during postnatal growth Gertrud Angsten, Roger Olsson, Stefan Branth

The basal metabolic rates in six prematurely born babies have been determined with indirect calorimetry and are correlated to their development in weight and height during their first 6 years of life. The project will give new information on whether the basal metabolic rate can predict the energy demands in prematurely born babies or not.

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 anorectal malformations and anal incontinence

Johan Danielson, Wilhelm Graf, Urban Karlbom, Tomas Wester

This project addresses the long term outcome of anorectal function and quality of life (QoL) in adult patients operated for anorectal malformations (ARM) in childhood. It also evaluates different strategies to reduce persistent anal incontinence after primary ARM surgery. The first study is of all ARM patients that have undergone primary surgical repair at the section of pediatric surgery between 1961 and 1993. The follow-up includes e.g. a validated QoL questionnaire, which also is answered by sex- and age-matched controls. A second study compares the functional outcome of ARM patients operated with the modern Peña procedure (posterior sagittal anorectoplasty) with that of patients operated with older types of surgery. The third study evaluates anorectal function and QoL in ARM patients subjected to dynamic graciloplasty due to anal incontinence in adulthood. The fourth study evaluates the effect on anorectal function and QoL two years after treatment with a new method against anal incontinence; anorectal submucosal injections of dextranomer particles suspended in non-animal hyaluronic acid (Solesta).

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. Primary outcome measure is the incidence of postoperative anastomotic stricture requiring dilatation. (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 2015 (~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 3-4, 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 ergo-spirometry. Blood test are also taken for analysis of inflammatory markers and IgE. (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.

Metabolic balance in children with short bowel syndrome and home parenteral nutrition

Helene Engstrand Lilja, Stefan Branth, Roger Olsson, Gertrud Angsten

A metabolic balance study in eight children with intestinal failure of different causes was performed. The children stayed 3 days in the hospital, and blood samples for analyses of liver function, acid-base-balance, thyroid function, hormones, glucose, lipids and amino acids were drawn. Loss of nitrogen, fatty acids and different ions were determined in urine and faecal samples. Measurements of bone mineral density was performed with Dual-energy X-ray absorptiometry (DEXA) and basal metabolic rate with indirect calorimetry. The study will give new data on the metabolic balance in children with home parental nutrition due to intestinal failure.

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

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

This project compares the enteral bacterial flora in infants with short bowel syndrome (SBS) and healthy infants. Bacterial overgrowth (BO) is a common problem in these infants but specific diagnostic methods of BO is missing. In this study we investigate which bacteria are involved with bacterial overgrowth in infants with SBS by analyzing bacterial-specific DNA in stool samples with the 454-pyrosequencing technique. Pyrosequencing is the method of choice to demonstrate bacterial diversity, but is not quantitative. Low bacterial diversity has previously been associated with IgE-associated eczema in children. Low bacterial diversity in infants with SBS may result in less stimulation of the immune system, that could cause BO. In this study we also want to investigate if a low and altered bacterial diversity in infants with SBS can be corrected with fecal transplantation from a healthy relative. Fecal transplantation has successfully been used in adults with e.g. refractory bacterial enteritis, but never in children with SBS.

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-1β and TNF-α 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 AB0-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, Helene Engstrand Lilja, Gunn Engvall

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. Long term follow-up requires a team-based working style and cooperation between the Children's hospital and the hospitals in the health care region. A process of value-based care was started in 2014 for these patient groups. The aim was to identify what is most valuable in the health care process for these children, youth and their parents.

The aim of this PhD-study is to explore the experiences concerning health care in 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. (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 autonomous nervous system responds to the presence of and interaction with a dog. The second study is of 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, Erik Sköldenberg

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 bladde 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=214) 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 214, thereby permitting a head-to-head comparison of Deflux therapy vs. Open surgery for the first time. In the fifth study, all the micturition cystograms of all the patients will be reviewed to determine whether the type of VUR or the bladder volume affects Deflux outcome or not. 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.

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. During 2015, Lillemor Berntson was appointed Associate Professor of Paediatric Rheumatology.

Members of the group during 2015

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 Tony Hansson, associate professor Charlotte Heijkenskjöld Rentzhog, PhD student Annika Hollsing, PhD Jennifer Johnsson, PhD student Johan Kaarme, PhD student Pia Kalm Stephens, research nurse Birgitta Karanikas, research nurse Hans Kollberg, associate professor Christina Krantz, PhD student Elisabet Lundmark, PhD student Andrei Malinovschi, associate professor Åsa Neuman, PhD Tryggve Nevéus, senior lecturer Lennart Nordvall, associate professor Britt-Inger Nyberg, research assistant Niklas Nyström, PhD student Christophe Pedroletti, PhD Inger Jönson Ring, PhD student Jörgen Syk, PhD Nikolaos Tsolakis, PhD student Anders Öman. PhD student

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Dissertations 2015

Maria Cederblad

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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, and Åsa Neuman, and PhD students are Charlotte Heijkenskjöld Rentzhog, 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 has been ongoing during 2015. Main research objectives in the group are:

- 1. Development of feasible biomarkers in preschool children. 2. Development and clinical evaluation of local and systemic biomarkers of Th2-driven inflammation, alone and in combination.
- 3. Characterization of non-atopic asthma in young subjects. 4. 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, 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 participates in an EU-sponsored double-blind study investigating egg yolk-derived immunoglobulin (IgY) as a promising prophylactic treatment of pseudomonas infections in CF. Since pseudomonas infections constitutes one of the most serious complications of CF, and is notoriously difficult to get rid of once established, this non-antibiotic treatment has the potential to greatly reduce morbidity, costs and antibiotic resistance. The group is also 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 perform multicentre research on CF. The concortium has focused on Staphylococcus aureus and aspergillus infections in CF. Planning has been undertaken for a study investigating the influence of different fatty acids on pulmonary function as well as for two 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). The 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) has started her PhD studies within this project during the year. The regional study on JIA is in progress. Anders Öman (paediatrician, Uppsala) has been registered as PhD student during the year. The aim of his 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 been developed to include studies of the microbiota in newly diagnosed children with JIA, in patients before and after EEN, and in patients on different medications. The group also have a collaboration with Per Hellström and Dominic-Luc Webb, Department of Medical Sciences, in studies on intestinal permeability in JIA. A pilot study has shown promising results. LB is also involved in a collaborative project with paediatric gastroenterologists, pathologists and paediatricians in Finland. The aim is to further develop analyses of mucosal biopsies immunohistochemically in children with JIA, collected in different stages of the disease. Samples from Swedish children with JIA are planned to be included. LB is also involved in two international review projects, one on microbiota in children with JIA and one on treatment of systemic JIA.

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. In international guidelines, three therapies are recommended as first-line treatment of enuresis: the antidiuretic drug desmopressin, the enuresis alarm and day-time bladder training – the latter called urotherapy. The first two of these methods are evidence-based, whereas urotherapy is not. In a prospective, randomised study the group has recently been able to provide evidence that urotherapy is in fact ineffective for this indication. These results, which have been provided by Tryggve Nevéus and Maria Cederblad, will have global impact. More than 25% of enuretic children do not respond to any of the standard therapies. In a double-blind, randomised, placebo-controlled, cross-over study, conducted by Tryggve Nevéus and 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. The results are about to be published. A prospective study on the treatment of therapy-resistant 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 Ingrid Jönson Ring.

Child Health and Parenting Research Group (CHAP)

Anna Sarkadi

The group is interdisciplinary and focuses on societal support to children and their families. Projects range from prevention through early intervention to specialised child protection. 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. 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 2015

PärBokströmPhD studentMariaCederbladRN, PhD student

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Dissertations 2015

- 1. Maria Cederblad
- Michael Wells

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Agencies that support the work/Funding

2012-2018		effects of population-	t for child and youth mental health based parenting interventions. 29 400 000 SEK
2015	ALF		1 236 500 SEK
2015	<i>Allmänna Barnhuset.</i> A validation study of the computer software In My Shoes		
			350 000 SEK
2015	Skandia Health problems in children	economic evaluation of	of prevention of mental health 800 000 SEK
2015	Gillberg Foundation		200 000 SEK

Project 1: 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. **Thomas Wallby**'s work concerns the equity and accessibility of the CHC preventive health services. The contents of the CHC services also need to become increasingly evidence-based. PhD students **Laleh Nayeb**, **Anna Fäldt** and **Kine Johansen** work directly on improving the evidence-base of child health services through developing better methods for screening of children with language (18 months), bilingual children (30 months) and motor developmental problems, respectively. Kine Johansen completed her half-time, showing that the structured tool for assessing motor development in infants, SOMP-I, was reliable in the hands of child health nurses who felt that it was a useful tool, also appreciated by parents, but that long-term implementation had a number of prerequisites.

One of the PhDs awarded in 2015 was written by **Maria Cederblad.** The thesis deals with a common issue at the top end of the CHC age-group: nocturnal enuresis where care at the CHC needs to improve to alleviate the social stigma of the condition and to provide children with evidence-based advice. In her thesis, she used an RCT to show that the current practice of basic bladder advice for several weeks before offering evidence-based therapies is not warranted.

Although child health services should address both mothers and fathers, the latter are often omitted in both research and child health care. **Michael Wells** showed in his PhD that father-friendly policies do not necessarily lead to father-friendly practices in the frontline services for children's healthcare.

An important question when reforming services is which interventions have effect on the long run. The BiF intervention was conducted in 2000-2004 by the research group and was initiated by Professor emeritus Claes Sundelin. It consisted of screening for postpartum depression, a sensitivity enhancing curriculum for everyday parent-child interaction (ICDP), language stimulation including three book gifts and materials promoting reading to the child, a booklet about motor development, support of social networks, and client-centred counselling. Dagmar Lagerberg and Margareta Magnusson are still busy publishing results from the trial – results that affect service provision.

The senior members of the group, **Monica Östberg and Monica Westerlund** are valuable resources and regularly visit the research seminars and participate in discussions on study design and PhD projects. Monica Westerlund is also co-supervisor for Laleh Nayeb.

Project 2: Effects, costs, and cost-effectiveness of parenting support 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' motives 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. 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 and Jenny Pitkänen are research assistant in the project, responsible for the sorting and scanning of more than 6000 questionnaires yearly. Elisabet Fält is a PhD student in the project, looking at how parents, nurses, and preschool teachers receive using the Strengths and Difficulties questionnaire – the main outcome measure in the study and the tool used at the child health visit for families in the study.

From the parenting literature we also know that harsh and over-reactive discipline correlates with difficulties in marital adjustment. PhD student **Natalie Engsheden** therefore focuses on evaluating preventive couple relationship education aiming to improve couple communication and conflict solving strategies.

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 PhD student **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. In 2015 **Richard Ssegonja**, health economist and MD joined the group and will be looking at adolescent depression and its costs and consequences.

Project 3: Child maltreatment and its consequences

The law forbidding corporal punishment passed 1979 reflects the Swedish values and ideologies that recognize children's rights and the importance of meeting their needs. However, the rates of severe forms of physical abuse have been stable since the early 1990s, and there has been an increase in mild forms of physical punishment, such as grabbing or shaking the child, especially in stressful situations, by "average" Swedish parents. **Steven Lucas**, chief medical officer of Child Health Services and **Gabriel Otterman** from the Child Protection Team both do important research on the correlates and consequences of violence exposure in the home, with special focus on bullying and the circumstances of child abuse in Swedish society, respectively. In an ongoing project the team will pilot the use of a questionnaire to assess psychosocial risk at the child health centres.

Preschool children are in an especially vulnerable situation when it comes to child maltreatment investigations, as their 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). Research assistant Anton Dahlberg, also a psychologist, assists the group 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.

Undergraduate Teaching

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

Inger Sundström Poromaa

During 2015, 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 have the opportunity to choose a course in nursing care of children and adolescents receiving intensiv care for autumn 2016. The web-based parts will also increase and new educational models to be introduced, such as flipped classroom. Approximately every third week the course also have seminars on campus. Students can often customize their clinical placement, which can be located in the hospital or outpatient. 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 been extensively revised. Women's and children's health are included in the first semester, whereas more ill health and severe conditions in gynecological, obstetric and pediatric care are included in the third and fourth semester. 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 ill health and promotion of health for women and children from a national and global perspective nursing will be started.

Obstetrics/Gynaecology and Paediatrics within the Registered Nurse Programme

The course in "Nursing and medical care in gynecological, obstetric and pediatric care", 12 ECTS, is a part of the fourth semester of the three-year Nursing programme, which involves several departments at Uppsala University. Both theoretical and practical education, as well as web-based seminars and seminars using problem-based learning methods are included, and the course is given every semester. The nursing programme is presently undergoing extensive restructuring, which also affects the courses within the program given by our Department. One consequence will be that an elective course on paediatric and gynaecologic nursing in a global perspective will be started.

The Biomedical Laboratory Science Programme

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

Obstetrics/Gynaecology and Paediatrics within the Medical Study programme

During 2015 the 10th semester of the medical program was reorganized such that students have Obstetrics/Gynecology, Pediatric and Infection/Microbiology during the same 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. This reorganization meant that parallel courses were given during the fall of 2015, which by all means was a relatively smooth process. For the medical students these changes will provide better access to clinical rotations. 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. The students' rating of the courses have been steadily improving during recent years: the paediatric course is rated highest of all clinical courses within the medical study program. Preparations for international exchange programs in Obstetrics/Gynecology and Pediatrics have started, as one of the rotations each semester, starting 2016, will be open to foreign students and given in English.

The International Health Master Programme

The International Health Master Programme 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. In 2015 27 students passed on their Master thesis.

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 2015 there were 118 registered doctoral students at the Department of Women's and Children's Health (Paediatrics 51; Obstetrics/Gynecology 38; IMCH 29), of which 20 were registered in 2015. During 2015 there were 14 dissertations (Paediatrics 2; Obstetrics/Gynecology 6; IMCH 6), 4 licentiate dissertations and 23 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 2015

The 2015 Gemzell scholarship - Helena Litorp, Md PhD