Oslo Diabetes Research Centre



ANNUAL REPORT 2013

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Steering Committee for Oslo Diabetes Research Centre

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- Kristian F. Hanssen, Professor dr.med.
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- Reidun Mosand, Diabetes nurse, Dep of Endocrinology
- Anders Hartmann, Professor, Dep of Nephrology
- Ludvig Sollid, MD Professor, Institute of Immunology
- Siri Vangen, Consultant dr.med., Centre for Women's health
- Haakon Stensæth, MD, Dep of Radiology
- Frode Lars Jahnsen, MD, PhD, Dep of Pathology
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- Lene Frost Andersen, Professor dr.philos.
- Christian A. Drevon, Professor dr.med.
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- Svein Olav Kolset, Professor dr.philos.
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- Margareta Wandel, Professor
- Lena Grønning-Wang, PhD

Asker and Bærum Hospital

• Odd Erik Johansen, dr.med.

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- Sidsel Graff-Iversen, Researcher PhD
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Institute of Health and Society, University of Oslo

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- Bjørgulf Clausen, Professor dr.med.
- Akthar Hussain, Professor dr.philos.

Norwegian School of Sports Science

- Roald Bahr, Professor dr.med.
- Sigmund Andersen, Professor dr.philos

Lillehammer University College

• Finn Skårderud, Professor PhD

Helseundersøkelsen i Nord-Trøndelag (HUNT)

• Kristian Midthjell, Professor dr.med.

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- Rolv Terje Lie, Professor, Medical Birth Registry
- Pål Rasmus Njølstad, Professor dr.med., Dep of Pediatrics
- Oddmund Søvik, Professor dr.med. (Em), Dep of Pediatrics

 Trond Markestad, Professor dr.med., Dep of Pediatrics

Bergen University College

• Marit Graue, PhD, Assoc. Professor

University of Northern Norway

 Svein Ivar Mellgren, Professor dr.med., Dep of Neurology

Sunnås sykehus

• Nils Hjeltnes, Consultant dr.med.

Others

• Jakob R. Larsen, MD, PhD

International Collaborators

- Prof Vincent Monnier, CWRU, Cleveland, Ohio, USA
- Prof Timothy Lyons, Queens University, Belfast, Northern Ireland
- Prof Alicia Jenkins, University of Sydney, Australia
- Prof Johnny Ludvigsson, Linköping University, Sweden
- Prof Mikael Knip, Helsinki University, Finland
- Prof Heikki Hyöty, University of Tampere, Finland
- Prof John Todd, University of Cambridge, UK
- Prof Flemming Poicot, Copenhagen, Denmark
- Jim McGuire PhD, Steno Diabetes Centre, Copenhagen, Denmark
- Prof John Gerich, Rochester NY, USA
- Prof Michael Stumvoll, Tübingen, Germany
- Prof Ashimina Mitrakou, Athens, Greece
- Prof Timon van Haeften, Holland
- Prof Ole Schmitz, Aarhus, Denmark
- Prof Allan Flyvbjerg, Aarhus, Denmark
- Prof Steve Chadban, Sydney, Australia
- Prof Olle Korsgren, Uppsala, Sweden
- Prof Gun Frisk, University of Uppsala, Sweden
- Prof Bart Roep, Leiden University, Holland
- Prof Chittaranjan Yajnik; KIM Hospital, Pune, India

Diabetes in a life-course perspective

The importance of our work is illustrated by some facts: Today 285 million people in the world have diabetes and it is expected to increase to 500 million in the next generation. 12.000 Norwegians get diabetes every year. In Norway approximately 200.000 know that they have diabetes, but around 170.000 do still not know. Diabetes is a serious disease. In Norway three out of four have at least one complication, one of five get serious eye complications, 500 suffer amputation and 150 need kidney transplantation every year. The risk for life threatening myocardial infarction and stroke is three fold increased. Research to prevent this is extremely important both for people and society.

This center has a strong clinical basis and is the only center in Norway covering the whole life-span of diabetes, from the fetus, through childhood and adolescence, early and late adult life. This lifecourse approach to diabetes attempts to capture the complex influence of factors operating at different points in life integrating both early-life and adult lifestyle models into a wider framework through an extensive collaboration between our ten established research groups and their internal and external collaborators. In the life-course perspective to diabetes we aim to assess how the effect of factors operating at different stages of life, from in utero to late adulthood, might accumulate and interact to determine development of diabetes and its complications later in life. Our high aim is to contribute substantially to prevent diabetes - and in the meantime - its complications.

Our center have 10 research groups spread throughout the Oslo University Hospital and Faculty of Medicine - in the Institute of Clinical Medicine (Clinic of Medicine, Clinic of Women and Child, Clinic of Laboratories and Imaging), Institute of Health and Society and Institute of Basic Medical Sciences. In this annual report you may count nearly hundred persons involved. It covers nearly all diabetes related research in these institutions. This year the Aker and Ullevål Diabetes Research Foundation has moved its financial activities to UNIFOR, and thereby strengthened the basis of the center within the University of Oslo. This foundation mainly covers the cost of our secretariat.

The center has the potential to attract more resources. Lars Christian Stene has been awarded

a large grant from the Norwegian Research Foundation. For the first time we were funded from the Novo Nordisk Foundation. We have been funded as an important research center of The Health Region South East and we steadily attract funding for PhD and postdoctoral fellowships. We are also an important international partner of the EU Seventh Framework for the study of viruses in the etiology of diabetes. In addition we get funding from Faculty of Medicine, Health and Rehabilitation Extra Foundation and the Norwegian Diabetes Association.

2013 was again a successful year for the Oslo Diabetes Research Centre. The center is steadily improving its' international reputation. The prestigious ISPAD Prize 2013 was honored the Chairman from the International Society for Pediatric and Adolescent Diabetes. We produced more than 50 international publications. In this year's annual report you may notice many publications in the highest ranked diabetes related scientific journals.

Some highlights: Jørn Petter Lindahl et.al. reported improved patient survival with simultaneous pancreas and kidney transplantation in recipients with diabetic end-stage renal disease. Kari Anne Sveen et.al. described increased small- and largefiber neuropathy after 40 years of type 1 diabetes and the associations with glycemic control and advanced protein glycation by follow up of the Oslo Study. Line Wisting found a high incidence of disturbed eating behavior and omission of insulin in adolescents receiving intensified insulin treatment in a nationwide population-based study. Lars Christian Stene published an excellent review of the influence of the prenatal environment and development of type 1 diabetes. Camilla Friis et.al. reported newborn body fat mass and the associations with maternal metabolic state and placental size. Cecilie Wium et.al. characterized the glucose metabolism in Nordic and South Asian subjects with type 2 diabetes. Christine Sommer et.al. described that ethnic differences in maternal dietary patterns are largely explained by socio-economic score and integration score in a population-based study. Lars Krogvold et.al. detected enteroviruses in the endocrine pancreas at diagnosis of type 1 diabetes. Certainly a broad spectrum of highly interesting results.

In 2013 we had seven PhD dissertations. We never had more in one year.

- Per Thorsby. Studies of candidate genes in overweight and diabetes mellitus.
- Camilla Margrethe Friis. Maternal Body Mass index and fetal growth.
- Dag Helge Frøisland. Children and adolescents with diabetes, -present state and future possibilities – A study of factors affecting competences and treatment results in children and adolescents with type 1 diabetes.
- Sara Salehi Hammerstad. Virus and Autoimmunity in Thyroiditis.
- Unni Mette Stamnes Köpp. Pathways contributing to childhood weight development and overweight in Norway.
- Kjersti Mørkrid. Gestational diabetes A study of prevalence and risk factors in a multi-ethnic population.
- Anh Thi Tran. Cardiovascular disease, diabetes and ethnicity.

We thank and acknowledge them, and are looking forward to include many of them for further research within our center.

The last annual two-day "Solstua Seminar" was arranged in March and forty participants and invited speakers gathered for exchange of knowledge. One topic was vascular anatomy and function, even in the fetus, and cardiovascular disease in diabetes. In addition ten selected young fellows presented their work. This seminar is crucial for networking and collaboration within our center.

We need to expand and we hope now to proceed in the organizational development of the center. The fusion of our hospitals has in many ways been contradictive to our center. However a process has started within the Faculty of Medicine and the Oslo University Hospital to improve the infrastructure of the center. This will be an important step forward for diabetes research.

Wall - Jorgans

Knut Dahl-Jørgensen Chairman Professor dr.med.

Leader	Work place	Research Area	Email
Knut Dahl-Jørgensen (Chairman)	Pediatric Department, Oslo University Hospital	Diabetes in children and adolescents Etiology of type 1 diabetes, complications	knut.dahl-jorgensen@medisin.uio.no
Kåre I. Birkeland (Vice chairman)	Department of Endocrinology, Oslo University Hospital	Prevention and treatment of type 2 diabetes	k.i.birkeland@medisin.uio.no
Kristian F. Hanssen/ Tore Julsrud Berg	Department of Endocrinology, Oslo University Hospital	Diabetic late complications	k.f.hanssen@medisin.uio.no t.j.berg@medisin.uio.no
Geir Joner	Pediatric Department, Oslo University Hospital	Epidemiology and etiology of type 1 diabetes, complications, mortality	geir.joner@medisin.uio.no
Benedicte Lie/ Dag Undlien	Department of Medical Genetics, Oslo University Hospital	Genetics and epigenetics of type 1 diabetes	b.a.lie@medisin.uio.no d.e.undlien@medisin.uio.no
Anne Karen Jenum	Department of General Practice, UiO	Diabetes and primary health issues in primary care	a.k.jenum@medisin.uio.no
Tore Henriksen/ Jens Bollerslev	Department of Endocrinology and Obstetrics, Oslo University Hospital,	Diabetes and pregnancy	tore.henriksen@rikshospitalet.no jens.bollerslev@rikshospitalet.no
Trond Jenssen	Department of Nephrology, Oslo University Hospital	Diabetic nephropathy	trond.jenssen@rikshospitalet.no
Jens Petter Berg	Department of Biochemistry, Oslo University Hospital	Metabolomics of hyperglycemia	j.p.berg@medisin.uio.no



Group leaders: Kristian F. Hanssen/ Tore Julsrud Berg

Group name: Diabetic late complications

Research focus:

Epidemiology and mechanisms of late complications. The mechanism by which hyperglycaemia is so deleterious to large and small blood vessels is basically unknown. A leading hypothesis is that glycation (the chemical reaction between glucose or intracellular metabolites of glucose and proteins) and subsequent rearrangements (Advanced Glycation Endproducts AGE's) is a main culprit. We have developed unique assays for different AGE's (CML, Hydroimidazolone and Glucosepane) in blood.

We have previously shown that serum AGE is associated with and predicts coronary heart disease in type 2 diabetes. Furthermore, that serum AGE is associated with micro-vascular complications.

Projects:

1. 30 years prospective study of late complications in type 1 diabetes (The Oslo Study):

A. Prospective study:

We have studied the progression of vascular changes, especially coronary vascular changes as measured by intravascular ultrasound (IVUS) and coronary angiography in the prospective Oslo Study and identified predictive parameters for this progression, especially AGE parameters.

B. Cross-sectional study:

Assess both macro and micro vascular status of the patients and associate with skin (measured in Dr. Monnier's lab Cleveland, USA) and serum AGE. A number of parameters have been followed prospectively over 25 years, and have given valuable data for our cross-sectional study (together with many groups within OUS, especially Dr. Brekke, Department of cardio-vascular radiology and Dr. Fosmark, Department of Ophtalmology).

Specific aims:

- To study cardiac events; sub endpoints will be the vessel area stenosis, significant plaque (>0.5 mm) progression both on IVUS, and coronary artery stenosis on coronary angiography.
- Serum and skin AGE, oxidative and inflammatory markers in relationship to complication status.

There are few studies that have examined long term complications and intensive diabetes treatment with such a long duration of the disease, and it is a unique opportunity to study the relationship between complications and biochemical markers of complications.

2. Glycation in the arterial wall:

We are studying glycation modification in the arterial wall in atherosclerosis with and without diabetes by western analysis, immunohistochemistry and LC MS/MS (mass spectrometry). We have already discovered some modifications in the wall that might be involved in the increased propensity to atherosclerosis in diabetes.

3. Advanced glycation of proteins and vascular complications in childhood diabetes:

(together with Dahl-Jørgensens group): Prospective study of early markers of atherosclerosis in a large group of adolescents with type 1 diabetes and controls - its relationship to glycation.

4. Coronary and glomerular morphology in kidney transplants - Long term study in two contrasting groups:

PI: Trond G. Jenssen (together with Svein Kolset, Institute of Nutrition)

- Study the effect of long-term normoglycaemia vs. hyperglycaemia on changes in the coronary arteries and the renal function and structure in type 1 diabetes patients. Two groups of patients with type 1 diabetes are studied, one group transplanted with a single kidney (HbA1c 8-8.5%), the other who received combined kidney-pancreas grafts and has obtained perfect normoglycaemia over the same period of time (HbA1c 4.5-5.5%).
- To investigate proteoglycans and

glycosaminoglycans which are important components of the filter network of the basement membrane.

- To explore proteoglycans (syndecan-1) and macrophage transcription factors (Id-1) in blood samples as markers of early kidney changes.
- Advanced Glycation Endproducts (AGE, CML,hydroimidazolone) by immunohistochemistry in the glomerulus and in serum samples to test the hypothesis that glycation markers can predict the development and progression of late complication (specifically early diabetic nephropathy and coronary heart disease).

5. DIALONG:

A study of long term survivors with more than 40 years of type 1 diabetes. A large clinical and biochemical study especially on macro-vascular disease and skin and joint complications. Collaborators within Oslo University Hospital and in Sweden, Denmark and US.

6. Prospective study of pre-eclampsia in pregnant type 1 diabetes:

In collaboration with research groups in Australia and US.

Group members:

- Kristian F. Hanssen MD,PhD, Professor of Medicine (Endocrinology) (Em)
- Tore Julsrud Berg MD, PhD, Associate Professor of Medicine
- Kari Anne Sveen, PhD student
- Bente K. Kilhovd, Consultant dr.med.
- Dag Fosmark, Consultant PhD (Department of Ophthalmology)
- Peter Torjesen, PhD
- Martin Heier, PhD student (together with Dahl-Jørgensens group)
- Lars Krogvold, PhD student (together with Dahl-Jørgensens group)
- Miliam Pepaj, PhD
- Kristine B. Holte, PhD student



Group Leader Knut Dahl-Jørgensen

Group name: Childhood Diabetes

Research focus:

The group has four main research areas. The first is the ethiology and prevention of type 1 diabetes and autoimmune diseases, especially focusing on the role of viruses and the interaction with the immune system in pancreatic and thyroid tissue samples. The second area is diabetes late complications. We have long term clinical studies on microvascular complications and the influence of glycemic control and advanced glycation. Recently the risk of early atherosclerosis in type 1 diabetes has been the focus in several of our studies, with measurement of vessel wall thickness (IVUS, IMT, MRI) and vessel elasticity, and biochemical markers, as well as clinical data and risk factors. In our large, nationwide clinical studies, now as part of the Childhood Diabetes Registry, we focus on important issues as intensified insulin treatment and pumps, diabetic nephropathy, diet, physical activity, quality of life and psychosocial problems and eating disturbances.

Projects:

Ethiology and prevention of type 1 diabetes and autoimmune diseases:

- 1. Diabetes Virus Detection Project
- Genetic studies of the importance of copynumber polymorphism in the development of type 1 diabetes
- 3. Viruses, genetics and autoimmunity in thyroiditis. A biopsy study

Diabetes late complications:

- 4. Atherosclerosis in Childhood Diabetes
- Long term vascular changes in type 1 diabetes

 Clinical aspects and biological markers 30 years follow-up of the Oslo Study
- 6. Advanced glycation of proteins and vascular complications in childhood diabetes
- Diabetic nephropathy: Hypertension and microalbuminuria in Norwegian children with type 1 diabetes

Clinical diabetes:

 Collaboration with the Norwegian Childhood Diabetes Registry (see page 14). A nationwide prospective population-based study for research and quality improvement by means of benchmarking

- Dietary intake, meal pattern and physical activity in children and adolescents with type 1 diabeteS
- 10. Diabetes in body and mind. The theory of the specific psychological processes in type 1 diabetes
- 11. Children and adolescents with diabetes

 present state and future possibilities
 a population-based study of factors affecting competences and treatment results in children and adolescents with type 1 diabetes
- 12. Eating disturbances in childhood diabetes
- Childhood diabetes and celiac disease
 A population based study

Obesity and type 2 diabetes:

 Pathways contributing to childhood weight development and overweight in Norway, substudy of The Mother and Child National Cohort.

Group members:

PhD students:

- Lars Krogvold, MD, Pediatrician
- Kari Anne Sveen, MD, Physician (together with Kristian Hanssens Group)
- Dag Helge Frøisland, MD, Pediatrician
- Martin Heier, MD, Pediatrician
- Sara Hammerstad, MD, Endocrinologist
- Unni Mette Køpp, MD, Pediatrician
- Line Wisting, Master Degree Psychology

Master students:

- Siv Janne Kummernes, RN, Diabetes specialist nurse
- Ingvild Ellingsrud, MD
- Marie D. Tonga, MD

Senior Independent Investigators:

- Hans Jacob Bangstad, MD, PhD, Professor
- Jon Haug, Dr.Philos, Clinical psychologist
- Torild Skrivarhaug, MD, PhD, Norwegian Childhood Diabetes Registry
- Hanna Dis Margeirsdottir, MD, Pediatrician



Group leader: Geir Joner

Group name: Childhood diabetes and diabetes epidemiology

Research focus:

Main focus is on diabetes epidemiology and causes of type1 diabetes and prevention. Special emphasis is on studies of nutritional factors and viral infections as risk factors and the role of gene-environmental interaction in the pathogenesis of type 1 diabetes. Research to prevent complications and premature death is also central to the group's work. The purpose of our research is to reduce the morbidity and complications of diabetes in children and adolescents, and it is achieved through the study of the causes and risk factors for complications and death. At present the most important tool for research are the Norwegian Childhood Diabetes Registry with biobank and the Norwegian Mother and Child Cohort Study.

Projects:

- Prediction of Autoimmune diabetes and celiac disease in childhood by Genes and perinatal Environment (PAGE): Data and biological samples from The mother and child-study (Norwegian Institute of Public Health) linked to the Norwegian Childhood Diabetes registry to study the effect of genetic and non-genetic risk factors for t1d and celiac disease.
- 2. A population based epidemiological study of diabetes complications, mortality and cause of death in Norway 1956-2011: Clinical and register-based follow-up of several cohorts of subjects with t1d from childhood for complications and death.
- 3. Biomarkers for intrauterine environment and risk of childhood type 1 diabetes: Data and biobank samples from 30000 pregnant women 1992-1994 linked to the Medical Birth Defect Registry of Norway and The Norwegian Childhood Diabetes Registry to study the effect of vitamin d-status and serum omega-3 fatty acids in pregnant women mothers on the risk of type 1 diabetes in the offspring.
- 4. Outcome of diabetes pregnancies: A study of outcome of pregnancies in women

with pregestational type 1 diabetes (intrauterine death, premature birth and malformations).

Group members:

- Group leader: Geir Joner, MD, PhD, senior consultant, Oslo University Hospital and Professor, Faculty of Medicine, University of Oslo
- Lars Chr. Stene, PhD, senior researcher
- Torild Skrivarhaug, MD, PhD, senior consultant and Director, Norwegian Childhood Diabetes Registry
- Vibeke Gagnum, MD, consultant and research fellow
- Magnhild P. Kolsgaard, cand.scient, research fellow
- Ingvild Menes Sørensen, MD, research fellow
- Ingvild Eidem, MD, research fellow
- Siv-Janne Kummernes, RN, Diabetes nurse, Masterstudent
- Ann Kristin Drivvoll, MSc



Group leaders: Benedicte Lie/ Dag E. Undlien

Group name: Immunogenetics and epigenetics of autoimmune diseases

Research focus:

Our main research focus is to identify and characterize genetic factors that predispose to type 1 diabetes and other autoimmune diseases. We also explore the functional relevance of risk variants primarily through their influence of gene expression. The interaction between genetic and environmental risk factors, as well as their clinical relevance on disease subphenotypes and disease progression is also addressed.

Projects:

- Correlation between genetic risk variants for type 1 diabetes and other autoimmune diseases and their gene expression in the immunologically important thymus.
- 2. Exploring and characterizing the HLA complex,

the most important genetic contributor to type 1 diabetes and other autoimmune diseases.

- 3. Differences and similarities between HLA risk profile to type 1 diabetes and celiac diseases for individuals with both diagnosis.
- 4. Exploring genetic and environmental risk factors, and their interactions, in rheumatoid arthritis, an autoimmune disease sharing many risk factors with type 1 diabetes.

Group members:

- Marte K. Viken, post doc
- Hanna Helgeland, post doc
- Fatemeh Kaveh, post doc
- Ingvild Gabrielsen, PhD student
- Kari Guderud, PhD student
- Maria Dehli Vigeland, Master student
- Siri Flåm, Medical Laboratory Scientist



Group leader: Kåre I. Birkeland

Group name: Type 2 diabetes and metabolism

Research focus:

Our main focus is on clinical epidemiological studies, observational studies and randomized clinical trials in subjects with obesity, prediabetes, metabolic syndrome and type 2 diabetes. We initiate and conduct our own studies, but participate also in international multi-center studies. These may be researcher initiated studies or clinical trials of new pharmacological agents for diabetes and related disorders (phase II-IV clinical studies) sponsored by pharmaceutical companies. Several of our researchers are also engaged in mechanistic studies and translational research in collaboration with different laboratories.

Our long-term goal is to contribute to prevention and better treatment of diseases related to overweight and physical inactivity, primarily type 2 diabetes and its complications. To achieve this, we search for etiological factors in disease development through hypothesis-generating epidemiological and observational studies and seek to test the hypotheses in mechanistic and randomized, controlled clinical trials. We aim to publish our results in internationally well recognized scientific journals and in relevant national and international meetings. We also engage ourselves in popular scientific publishing to increase knowledge about ours and others' research to the public. We collaborate closely and partly overlap with Anne Karen Jenum's group on the STORK-Goruddalen studies.

Ongoing studies:

- 1. The STORK-Groruddalen cohort study of 823 pregnant women (see Annual report from Anne Karen Jenum's group).
- 2. The DIVINE-study A randomized, placebocontrolled intervention with high-dose vitamin D in type 2 diabetes.
- 3. The MyoGlu-study A controlled, intervention study of high-intensive exercise training in subjects with abnormal glucose tolerance and controls.
- 4. The HypoGlu-study An observational study with hypo- and euglycaemic glucose clamp investigations of subjects with type 1 diabetes.
- 5. The ORIGINALE study. An international, multicenter, follow-up, observational study of 12 000 participants in the ORIGIN study.

Several multi-center phase II, III and IV clinical trials in collaboration with the pharmaceutical industry.

Group members:

- Kåre I. Birkeland, MD, PhD, Professor II, group leader
- Anne Karen Jenum, MD, PhD, Professor at Institute for Health and Society, Department of General Practice, UiO and Professor II at University College of Oslo
- Anne-Marie Aas, PhD, Assistant Professor II, Department of Nutrition,
- Hanne Løvdal Gulseth, MD, PhD, post doc •
- Cecilie Wium, MD, PhD student •
- Kirsti Bjerkan, PhD student •
- Line Sletner, MD, PhD student •
- Kjersti Mørkrid, M.Phil, PhD •
- Christine Sommer, MSc, PhD student •
- Anne Pernille Ofstad, MD, PhD student •
- Torgrim Langleite, MSc, PhD student •

- Susanna Hanvold, MSc, PhD student •
- •
- •

Ole Elvebakk, MD, PhD student

Hilde Risstad, MD, PhD student

Ingvild Høgestøl, Med., PhD student •

Research nurses:

Åse Halsne and Gøril Vinje

Medical students:

Tuva Wyller, Sara K. Fidjeland, Hildegunn Grødal, Thea Drivnes, Nina Marie Aamodt and Hanna Jervell Heyerdahl.



Group leader: Anne Karen Jenum

Group name: Diabetes and related health issues in primary care

Research focus:

We apply a life course approach in our research into the causation, care and prevention of type 2 diabetes and cardiovascular complications, especially when studying social and ethnic differences in health. The group members have a diverse professional background, facilitating synergies and convergence in research. Our group has two main areas of research, both originating from observations in primary care of the epidemic of diabetes, its different faces and the need to develop culturally sensitive interventions due to the demographic transition in Norway to a multiethnic country:

- The epidemic of type 2 diabetes and its complication and the quality of diabetes care in a multiethnic society – The Diabetes Care group.
- The developmental origin of health and disease, not least type 2 diabetes, studied in a mother, father and child multiethnic cohort. - The Mother and Child Health group.

We have performed and are involved in crosssectional studies, cohort studies, qualitative studies, one RCT using new technology, and are involved in developing culturally sensitive interventions in primary care. We are now including new members and collaborative partners, increasing the number of subprojects and reorganizing the structure into two separate groups, working in synergy.

Projects:

1. The STORK-Groruddalen cohort study of 823 pregnant women from multiethnic women and investigates the effect of ethnicity and a

range of environmental determinants on the prevalence and development of gestational diabetes (GDM), intrauterine growth and development and neonatal birth weight and anthropometric measures, http://www.med. uio.no/helsam/forskning/prosjekter/storkgroruddalen/. This project has so far developed 10 PhD projects, covering gestational diabetes and related maternal health issues, as well as neonatal body composition and fetal and childhood growth. Two PhD students using data from this cohort have finished their dissertations, and one has submitted her thesis and become a post-doc researcher. Four PhD projects for general practitioners are funded by the Norwegian Medical Association. Further, two more PhD students will use our data for one paper.

- Cardiovascular disease, diabetes and ethnicity, and the quality of diabetes care in a multiethnic general practice population in Oslo. One PhD student defended her thesis on this subject in 2013, and is now applying for a postdoc grant.
- The Norwegian study in Renewing Health: Stimulating self-management in patients with type 2 diabetes mellitus through tele-care with the Few Touch application and health counseling – A randomized controlled trial, is an EU-funded project with the Norwegian study developed by 6Faculty of Health Sciences, Oslo and Akershus University College of Applied Sciences, The Oslo and Akershus University College.
- A qualitative study about the need for drug information about diabetes among Pakistani and other non-western women in Norway, originating from School of Pharmacy, Faculty of Mathematics and Natural Sciences.

Senior researchers:

- Kjersti Mørkrid
- Anh Tran
- Per Lagerløv

Research fellows:

- Line Sletner
- Christine Sommer
- Nilam Shakeel
- Åse-Ruth Eggemoen
- Christin Wiegels Waage
- Ingun Toftemo
- Marthe-Lise Næss-Andresen
- Astrid Torbjørnsen

- Kåre Rønn-Richardsen
- Walaa Metwally Ali Abdalaah Abuelmagd

Master student:

- Anam Shakil (UiO)
- Annemette Estrup Risgaard (UMB)



Group leaders: Tore Henriksen/ Jens Bollerslev

Group name: Diabetes and Pregnancy

Research focus:

It is known that nutrition and other environment factors during fetal development may have long term effects on future health of the newborn baby. Insufficient or wrong nutrition during fetal life may increase the risk of development of cardio-vascular disease, diabetes, overweight and some cancers. Several international studies conclude that the most effective method for prevention of these diseases is optimizing the conditions for development during fetal life and early childhood. The association between the developmental conditions of the fetus and the newborn baby's future health is described as DOHaD- (Developmental Origins of Health and Disease) or the Barker-hypothesis.

Important factors for fetal development are e.g. overweight in the mother (BMI > 30 kg/m2) and other nutritional defects, infections, pre-eclampsia and expositions for toxic substances. 20 % of young women and future mothers in Norway are overweight and has surpassed smoking as a risk factor during pregnancy. It looks like that it is not the high BMI in itself which is deleterious but rather the inflammation and the extensive metabolic and endocrine changes linked to obesity. The purpose of our research is to understand how nutritional, metabolic, vascular and other developmental conditions influence the fetus in order to give preventive advice and treatment.

Ongoing studies:

STORK-Rikshospitalet.

STORK cohort study focuses on nutritional, metabolic, neuron-endocrine and vascular aspects of the interplay between the mother and child with regard to the growth and development of the fetus. The mother's metabolic status is investigated by different parameters: Overweight/obesity endocrine and inflammatory parameters, and plasma levels of lipids and glucose.

STORK placenta-study.

Placenta is the most important organ of the pregnancy and directs both maternal physiology and fetal development. Human in vivo-studies of placenta function has been difficult to perform due to serious methodological limitations. We have recently established a method ("The 4 vessel sampling method") which makes it possible to perform such investigations in the STORK placenta-project. We are here studying transfer of nutrition (glucose, lipids and amino acids) from mother to fetus.

Neogenesis of capillaries and growth of placenta.

Normal growth of placenta is dependent on angiogenesis. There are some indications that the fetus in itself in part directs this process and thus influences the nutritional supply to itself. We are studying this in an in vitro model for angiogenesis.

Pre-eclampsia - factors in placenta affecting the function of vascular endothelial cells. This project is linked to subprojects of STORK placenta-study. "The 4 vessel sampling method" is investigating factors from placenta which interfers with endothelial cell function in the mother. Disturbances in endothelial function may lead to high blood pressure in the mother and negative influences on placenta function and the development of the fetus.

Fit for delivery - study of the importance of exercise and nutrition for pregnancy outcome.

A randomized clinical intervention study in which the participants receive exercise and nutrition advice (Kristiansand). The end points: Maternell weight gain, body composition, birth weight and details of delivery are registered to evaluate the effect of intervention.

SOFUS (Stress experience of the parents by ultrasound investigation during pregnancy). The cohorte study investigates psychological stress in expecting parents in which fetuses have fetal abnormalities and compare to a control group. We measure psychometric and endocrine variables in the pregnant woman and circulatory data in the fetus by ultrasound.

STORK-3

The fetal liver has a central role in energy and nutritional metabolism. The aim of this study is to learn how the blood flow from placenta distributes to the liver and heart (ducus venosus) of the fetus in different stages of the fetal life and relationship to the mother's nutritional intake.

Most important national and international collaboration:

- Section of Endocrinology, OUS RH
- Dep. of Nutrition, UiO
- Dep. of Biostatistics, UiO
- Dep. of Medical Genetics, OUS Ullevål
- National competence center for Women Health, OUS RH
- Womens Health, Haukeland University Hospital and UiB
- Dep. of Obstetrics and Gynecology, Sørlandet hospital, Kristiansand
- Dep. of Neuropsychiatry and Psycho-somatic medicine, OUS RH
- Section of pediatric surgery, OUS
- Harold Hamm Diabetes Center and Section of Endocrinology and Diabetes, University of Oklahoma, USA
- Nofima mat, Ås and University of Copenhagen, DK
- Southampton University, UK
- University of Texas Health Science Center, San Antonio,
- Center for Pregnancy and Newborn Research, Dep. of Obstetrics and Gynecology, USA

Group members:

- Tore Henriksen, leder
- Jens Bollerslev
- Guttorm Haugen
- Thomas Åbyholm
- Svein Olav Kolset
- Elisabeth Qvigstad
- Bjørg Lorentzen
- Trond Michelsen
- Nanna Voldner
- Thor Ueland
- Kathrine Frey Frøslie
- Marie Cecilie Paasche Roland
- Camilla Friis
- Ane Moe Holme

- Kristin Godang
- Maia Blomhoff Holm
- Hildegunn Horne
- Anne Kaasen
- Gun Lisbeth Opheim
- Anne Helbig
- Linda Sagedal
- Ingvild Vistad



Group leader: Trond Jenssen

Group name: Diabetic Nephropathy

Research focus:

Cardiovascular risk factors and diabetes after organ transplantation. Pancreas and islet cell transplantation. Molecular and morphological changes in the diabetic Kidney.

Projects:

- New onset diabetes after transplantation (NODAT). Occurrence, Pathogenesis, Risk factors, Follow-up and Treatment. Studies on the role of glucagons in NODAT. Studies on endothelial function and dysfunction in posttransplant diabetes, and after normalization of glycemia with pancreas transplantation.
- Pancreas transplantation. Long-term development of diabetic and non-diabetic complications
- Islet cell transplantation clinical outcome.
 Treatment modalities including cotransplantation with mesenchymal stem cells.
- Metabolic risk factors for graft and patient survival in renal transplant patients.
- Molecular changes in transplanted kidneys, with emphasis on morphometry, basement membrane and proteoglycans.

At present 5 PhD candidates are directly involved in the projects.

Parts of our work (follow-up of pancreas transplantation) were presented at the annual meetings of the American Society of Transplantation and also at the European Association for the Study of Diabetes in 2013.

Group members:

- Trond Jenssen, Professor OUS RH
- Jørn Petter Lindahl, MD, OUS RH
- Anders Hartmann, Professor, OUS RH
- Karsten Midtvedt, MD PhD, OUS RH
- Ivar Eide, MD, OUS RH
- Finn Reinholt, Professor, OUS RH
- Ole Øyen, MD PhD, OUS RH
- Rune Horneland, MD, OUS RH
- Marit Elizabeth von Düring, OUS RH
- Svein O Kolset, Professor, University of Oslo
- Trine Reine, PhD, University of Oslo
- Annicke Stranda, PhD, University of Oslo
- Thea Anine Strøm Halden, PhD student, University of Oslo



Group leader: Jens P. Berg

Group name: Biomarkers in endocrinology and metabolism

Research focus:

One of the research aims in our group is to increase our understanding of the mechanisms leading to and the metabolic consequences of increased blood glucose by studies of small molecule metabolite profiles. Methods to detect and quantitate small molecular weight compounds (<1000 Da) in biological fluids by NMR spectroscopy and subsequent multivariate data analysis is fundamental in these metabolomic studies. Application of the techniques has been used in studies of metabolite profiles in urine from women with gestational diabetes and compared with controls. Future studies will elucidate the metabolomic effects of physical exercise in individuals with the metabolic syndrome.

Recently initiated projects at the Hormone Laboratory study the mechanisms leading to β - cell dysfunction and aim to identify adequate biomarkers to assess changes in β -cell health and function. Specific biomarkers enabling earlier detection of subtle changes in β -cell health and function are critically needed for disease staging as well as for non-invasive monitoring of treatments aimed at preserving or restoring functional β -cell mass, including islet transplantation. Large scale omics methods such as genomics, proteomics and metabolomics are used for this purpose. In addition we have developed a highly specific proteomic method based on LC MS/MS for elucidation of glycated serum proteins involved in late complications of diabetes.

In addition we focus on the use, quality control, and interpretation of measures of glycemic control such as HbA1c and glycated albumin. A medical student project reviewing pitfalls in HbA1c analysis and interpretation has been completed. An increased awareness of the shortcomings of HbA1c as indicator of longer term glycemic status in certain condtions has initiated new projects to reevaluate the use of fructosamine or glycated albumin.

Projects:

- 1. Prediction of early metabolite biomarkers in serum of autoimmune diabetes
- 2. Biomarkers of pancreatic β-cell mass
- Studies of metabolic profiles in gestational diabetes; in collaboration with Prof. Anne Karen Jenum
- 4. Working group for the evaluation of diagnostic use of HbA1c in Norway

Group members:

- Jens Petter Berg, MD, PhD, Professor
- Daniel Sachse, PhD student
- Per Thorsby, MD, PhD
- Milaim Pepaj, PhD
- Mette E Bornstedt, MD
- Benedicte Jørgenrud, PhD student
- May K. Bredahl, PhD
- Nina Gjerlaugsen, B.Sc
- Kari Julien, B.Sc



Registry Leader: Torild Skrivarhaug

Name: The Norwegian Childhood Diabetes Registry (NCDR)

Research focus:

The main research focus in this population-based, nation-wide childhood-onset diabetes registry:

- Epidemiology in childhood-onset diabetes, focusing on incidence, prevalence, classification of childhood-onset diabetes in Norway, ethnicity and long-term complications and mortality.
- Quality in childhood diabetes care A nationwide prospective population-based study for research and quality improvement by means of benchmarking.
- Clinical childhood diabetes, especially focusing on quality of life, diabetes treatment, comorbidity, eating disorders and the transition from paediatric to adult diabetes care.

Projects:

Epidemiology

- Incidence and prevalence of childhoodonset type 1 diabetes in Norway, assessed by linking The Norwegian Prescription Database at the National Institute of Public Health and NCDR.
- 2. Classification of childhood-onset diabetes in Norway.

To assess the epidemiology of different forms of diabetes and to classify incident cases on the basis of family history, clinical data, C-peptide, autoantibodies and HLA-genotypes.

3. The signification of analyzing Zn-antibodies at the diagnosis of T1D in children.

4. Mortality in childhood-onset type 1 diabetes.

A nationwide population based cohort study. To evaluate absolute and relative mortality rates, the effects of sex and age at diagnosis, the cause of death. To assess socioeconomic status as a risk factor for mortality in T1D.

Clinical diabetes

5. Co-morbidity in children and adolescents with type 1 diabetes.

Assessing competencies and coping; factors affecting functional and dysfunctional behaviour in children and adolescents with type 1 diabetes.

- 6. A national, population based study of the double diagnosis of celiac disease and type 1 diabetes.
- 7. Ethnicity and diabetes in the Nordic countries.

Is ethnicity an independent factor influencing metabolic control in children and adolescents with T1D residing in Nordic countries.

8. A global comparative study.

Implementations of guidelines in clinical practice – Benefits and challenges exemplified by international guidelines in Diabetes Mellitus in children.

Group members:

- Torild Skrivarhaug, Senior consultant dr.med., Director of the Norwegian Childhood Diabetes Registry
- Geir Joner, dr.med., Professor
- Knut Dahl-Jørgensen, Senior consultant dr.med., Professor
- Siv Janne Kummernes, RN, Diabetes nurse, Masterstudent
- Ann Kristin Drivvoll, MSc
- Lars Christian Stene, Senior researcher, Norwegian Institute for Public Health
- Hans-Jacob Bangstad, Senior consultant, dr.med., Professor
- Per Thorsby MD, Senior consultant
- Dag Helge Frøisland, MD, PhD student
- Line Wisting, PhD student
- Vibeke Gagnum MD, PhD student

National collaboration

- Hormone Laboratory, Oslo
 University Hospital, Aker Hospital
- Center for Diabetes Genetics, Haukeland
 University Hospital
- Department of Medical Genetics, Oslo University Hospital and University of Oslo
- RASP (Regional Centre for Eating Disorders), Oslo University Hospital
- National Public Health institute, Oslo

International collaboration:

- EURODIAB
- The Nordic Childhood Diabetes Registry Study Group

Publikasjonsliste 2013:

Thesis:

Camilla Margrethe Friis. *Maternal Body Mass index and fetal growth*. Dissertation June 2013.

Dag Helge Frøisland. Children and adolescents with diabetes, present state and future possibilities – A study of factors affecting competences and treatment results in children and adolescents with Type 1 diabetes. Dissertation June 2013.

Sara Salehi Hammerstad. *Virus and Autoimmunity in Thyroiditis*. Dissertation April 2013.

Unni Mette Stamnes Köpp. *Pathways contributing to childhood weight development and overweight in Norway*. Dissertation April 2013.

Kjersti Mørkrid. Gestational diabetes A study of prevalence and risk factors in a multi-ethnic population. Dissertation November 2013.

Per Thorsby. *Studies of candidate genes in overweight and diabetes mellitus*. Dissertation January 2013.

Anh Thi Tran. Cardiovascular disease, diabetes and ethnicity. Quality of diabetes care in a multiethnic general practice population in Oslo. Dissertation November 2013.

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Some national presentations:

Berg JP. Diabetes mellitus. Prinsippene for moderne diagnostikk. NOKLUS-møte Sandefjord 2013.

Berg JP. Hvordan skille mellom type 1 og type 2 diabetes. NOKLUSmøte Sandefjord 2013.

Berg JP. HbA1c til diagnostikk av diabetes. Noklus-seminar Oslo 2013.

Berg JP. HbA1c i diagnostikk av diabetes. OUS-symposium 2013. Bornsted ME, Gjerlaugsen N, Bredal MK, Pepaj MP, Thorsby PM. Vitamin D treatment of INS1 B-cells; influence on insulin secretion. OUS forskningsseminar 2013.

Dahl-Jørgensen K. Hvordan går det med diabetes type 1 i Norge? 30 års oppfølgning av Oslo-Studien. 22. OUS-symposium, Oslo, 2013.

Haug J. Hvordan kan vi som psykologer forstå problemkomplekset "diabetisk slitenhet"? Nasjonalt Diabetesforum, Oslo, 21. august 2013.

Haug J. Dissosiasjonsmetoder ved behandling av utmattelse og smertetilstander – kan disse anvendes ved "diabetisk slitenhet"? Nasjonalt Diabetesforum, Oslo, 21. august 2013.

Haug J. "Diabetisk slitenhet" fra en psykologs synsvinkel. Nasjonalt Diabetesforum, Oslo, 22. august 2013.

Haug J. De neglisjerte komplikasjonene. Diabeteskonferansen 2013. Diabetesforbundet, Oslo, 26. oktober 2013.

Haug J. Diabetes i kropp og sinn - de daglige psykologiske utfordringene. Nettverkskonferanse Nordlandssykehuset, Tromsø, 12. november 2013.

Haug J. "Når negative tanker står i veien. Hvordan kan vi hjelpe ungdom til bedre aksept av Realitetene?" Nasjonalt Barnediabetes Symposium, Sundvolden, 6. november 2013.

Henriksen T. How and why should we follow women who have had preeclampsia in their subsequent pregnancies? ISSHP, Tromsø, 14th June 2013.

Henriksen T. Forceps delivery. Nordisk kurs i Obstetrikk, Bergen, September 2013.

Krogvold L. Er type 1-diabetes en virussykdom? Resultater fra DiViDprosjektet. Sundvolden-symposiet 2013.

Krogvold L. Hva skyldes diabetes type 1? 22. OUS-symposium, Oslo, 2013.

Krogvold L. Diabetes virus detection study. Nasjonalt diabetesforum, Oslo, 2013.

Köpp UM. Barnets første 1000 dager – epigenetikk, betydningen av mors vekt og vektoppgang i svangerskapet. Hvilke råd skal vi gi? Foredrag på fagdag for kliniske ernæringsfysiologer i Helse Sør-Øst, Oslo, 9. november 2013.

Skrivarhaug T. How can a quality register improve quality? Health Economics, Policy, and Management (International Bachelor program), Institute of Health Management and Health Economics, Faculty of Medicine, University of Oslo, 14.02.2013.

Skrivarhaug T. Definition, ethiology, epidemiology and classification of diabetes in children and adolescents. 11.03.2013. Postgraduate medical education, course: O-25432, The Norwegian Medical Association.

Skrivarhaug T. The Norwegian Childhood Diabetes Registry. 12.03.2013. Postgraduate medical education, course: O-25432, The Norwegian Medical Association. Skrivarhaug T. Late complications in type 1 diabetes. Diabetesforum, 22. August 2013.

Skrivarhaug T. Late complications in type 1 diabetes in Norway. 22. Oslo University Hospital Symposium 8, November 2013.

Skrivarhaug T. Research in the Norwegian Childhood Diabetes Registry. Norsk studiegruppe for barnediabetes, Sundvollen, 6.11.2013.

Skrivarhaug T. The Norwegian Childhood Diabetes Registry. The Norwegian Directorate of Health, 11.11.2013.

Skrivarhaug T. How can a quality register improve quality? Health Economics, Policy, and Management (International Bachelor program), Institute of Health Management and Health Economics, Faculty of Medicine, University of Oslo, 14.02.2013.

Thorsby PM, Bornstedt M, Gjerlaugsen ME, Bredal MK, Pepaj M. Studies of non-glucose stimulated biomarkers of b-cell function, addressing the patophysiologi of diabetes. Endokrinologisk vintermøte og OUS forskningsseminar 2013.

Thorsby PM. Metabolsk syndrom og senkomplikasjoner ved diabetes. BMS møte Oslo 2013.

Thorsby PM. Senkomplikasjoner ved diabetes. Diabetesforbundet 2013.

Thorsby PM. Forebygge type 1 og 2 diabetes. Diabetesforbundet 2013.

Thorsby PM. Senkomplikasjoner ved diabetes. Novo Nordisk møte Tønsberg og Bergen 2013.

Thorsby PM. Genetikk og CVD ved diabetes. NCD kurs 2013.

Wisting L, Frøisland, DH, Skrivarhaug T, Dahl-Jørgensen K, Rø Ø: Forekomst av spiseproblemer hos norsk ungdom med type 1 diabetes – en delstudie av Barnediabetesregisteret. Nasjonalt Diabetesforum, Oslo, August 2013.

Wisting L, Frøisland, DH, Skrivarhaug T, Dahl-Jørgensen K, Rø Ø. Spiseforstyrrelser ved diabetes. Sundvolden Symposiet: Diabetes hos barn og ungdom, arrangert av Sanofi Diabetes, November 2013.



Noen av forskningssenterets medarbeidere på seminar i Son!