

Overall research theme:

Diabetes, metabolic syndrome and cardiovascular disease – epidemiology, prevention and genetic studies

Latest update:

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Characteristics of the research group:

The research group combines a background in clinical medicine with epidemiology and preventive medicine. The focus of the group is to plan and conduct epidemiological studies focusing on diabetes, the metabolic syndrome and cardiovascular disease, to identify biological and genetic markers associated with these conditions and to develop and evaluate early screening and intervention strategies to prevent development of CVD in high risk individuals with diabetes, IGT or the metabolic syndrome.

The work is conducted in close collaboration with several centres outside the Steno Diabetes Centre and with the molecular biology group at Steno Diabetes Centre.

Running projects: Titles and abstracts:

DiaRisk – the diabetes arm of the INTER-99 study

Cardiovascular disease is the single leading cause of death in westernized societies. The incidence of CVD is decreasing, but epidemiological studies and prediction models suggests that the prevalence and incidence of type 2 diabetes is increasing at alarmingly high rates. This may well alter the otherwise positive trends with respect to CVD in Denmark and many other countries. The Inter-99 study, established at Centre for Preventive Medicine, Glostrup, was established to test whether targeted, tailored, non-pharmacological intervention in high risk individuals can reduce the incidence of and mortality from CVD. The study includes more than 60.000 individuals aged 30-60 years at entry. The diabetes/metabolic syndrome arm of the study estimates the prevalence and 5-year incidence of diabetes and IGT in the general population, and evaluate the possibility of reducing the incidence of diabetes in high risk individuals and of reducing the cardiovascular risk score in individuals with Diabetes, IGT and the metabolic syndrome through lifestyle intervention. The study started in 1999, baseline examination terminated by end of 2000 and 5-year follow-up examination will take place in 2004/2005.

ADDITION; The Anglo-Danish-Dutch study of Intensive Treatment and Complication Prevention in type 2 diabetic patients identified by Screening

Type 2 diabetes is a disease associated with a 2-4 times increased risk of dying from CVD. The prevalence of diagnosed diabetes is 3-4% above the age of 40 years, but an equal number of individuals have diabetes without knowing it. This has raised the question whether screening and early, intensive treatment should be recommended. No randomised controlled trials can answer this question. Thus the ADDITION-study was established:

- **To develop strategies for early detection of type 2 diabetes**
- **To study whether a multifactorial treatment strategy can reduce mortality and reduce the incidence of late diabetic complications**
- **Treatment strategy: motivational interviewing, behavioural changes (dietary advises, physical activity, smoking cessation)**

- **Intensive pharmacological treatment of blood pressure, blood glucose, and serum lipids**
- **To identify genetic markers predicting diabetic complications**
- **To evaluate health economical consequences**

The study includes a stepwise screening for type 2 diabetes in general practice. General practitioners are randomised to target driven intensive pharmacological and non-pharmacological intervention or standard care. The study will include 3.500 screen-detected type 2 diabetic patients, and the pre-screening involves 200-250.000 individuals. The primary end-points of the study includes all cause mortality and cardiovascular morbidity and mortality.

The study started in 2001. Case-recruitment will continue through out 2003, and follow-up will continue for five years after recruitment of the last participant of the study.

DIACARD – DIAbetes and prevention of CARDiovascular disease

Diabetes is associated with a highly increased risk of developing cardiovascular disease, but still patients with diabetes are receiving insufficient attention when it comes to treatment and prevention of CVD. To optimize treatment for patients with diabetes we assume that better tools for individual risk assessment would be helpful. Based on a large, cross-European data-base including all major population based studies of diabetes and CVD a computerised programme for risk prediction and assessment of treatment effects have been developed. The programme is currently being tested and evaluated in general practice as well as in Steno Diabetes Centre.

Diabetes and CVD in the Inuit population

According to most textbooks the prevalence of diabetes and CVD is low in the Inuit population. During the last decades dramatic changes in life style and living conditions have occurred. In other original populations world wide these changes in live conditions are known to have induced rapid increases in the prevalence of diabetes and the metabolic syndrome. To evaluate the consequences of the westernization of life style among the Inuit population of Greenland a population-based study was set up including Inuit living in Greenland and Denmark. The study includes more than 2000 inhabitants in Greenland including the capital, a smaller town and 4 villages and 400 Inuit living in Denmark Data collection in Greenland has ended, and the Danish part of the survey will end by October 2002.

Microalbuminuria and CVD

Microalbuminuria was first recognised as a marker of development of CVD among diabetic patients in the late 1980's. In the early 1980's we initiated two stuies in the non-diabetic population, both confirming that very mildly increased urinary albumin excretion rates are associated with increased risk of CVD, and that this association is equally strong as the association between smoking and CVD. The group I still involved in epidemiological studies in this area, but is currently testing the effect of intervention with ACE-inhibitors specifically in this group of patients with and without diabetes.

Recent publications (1996-2002) related to the projects described above:

- Jensen JS, **Borch-Johnsen K**, Jensen G, Feldt-Rasmussen B. Insulin sensitivity in clinically healthy individuals with microalbuminuria. *Atherosclerosis* 1996; 119: 69-76.
- Yokoyama H, Uchigata Y, Otani T, Saeiki A, Aoki K, Kasahara T, Omori Y, **Borch-Johnsen K**. Metabolic regulation and microangiopathy in a cohort of Japanese IDDM-patients. *Diabetes Research and Clinical Practice*, 1995, 29: 203-9.
- Deckert T, Yokoyama H, Mathiesen ER, Rønn B, Jensen T, Feldt-Rasmussen B, **Borch-Johnsen K**, Jensen JS. Cohort study of predictive value of urinary albumin excretion for atherosclerotic vascular disease in insulin-dependent diabetes. *Br Med J*, 1996; 312: 871-4.
- Jensen JS, Clausen P, **Borch-Johnsen K**, Jensen G, Feldt-Rasmussen B. Detecting microalbuminuria by urinary albumin/creatinine concentration ratio. *Nephrol Dial Transplant*, 1997; 12 (suppl 2): 6-9.
- Clausen J, **Borch-Johnsen K**, Ibsen H, Bergman R, Hougaard P, Winther K, Pe-dersen O. Insulin sensitivity index, Acute Insulin Response and Glucose Effect-iveness in a population-based sample of 380 young healthy Caucasians: Analysis of the impact of gender, body fat, physical fitness and life style factors. *J Clin Invest*, 1996; 98: 1195-1209.
- Clausen J, Ibsen H, Ibsen KK, **Borch-Johnsen K**. Association of body mass index, blood pressure and serum levels of triglycerides and high-density lipoprotein cho-lesterol in childhood with the insulin sensitivity index in young adulthood: A 13-year follow-up. *J Cardiovascular Risk*, 1996; 3: 427-33.
- Jensen JS, **Borch-Johnsen K**, Feldt-Rasmussen B, Appleyard M, Jensen G. Urinary albumin excretion and history of acute myocardial infarction in a cross-sectional study of 2,613 individuals. *J Cardiovasc Risk*, 1997; 4: 121-5

Jensen JS, Feldt-Rasmussen B, **Borch-Johnsen K**, Clausen P, Appleyard M, Jensen G. Microalbuminuria and its relation to cardiovascular disease and risk factors. A population based study of 1254 hypertensive individuals. *Hypertension*, 1997; 11: 727-32.

Tuomilehto J, **Borch-Johnsen K**, Molarius A, Forsen T, Rastenyte D, Sartill C, Reu-nanen A. Incidence of cardiovascular disease in IDDM subjects with and without diabetic nephropathy. *Diabetologia*, 1998; 41: 784-90.

The DECODE-study group on behalf of the EDESG (**Knut Borch-Johnsen** corresponding author). New diagnostic criteria for diabetes mellitus - will they change the phenotype of the diabetic subjects? *BMJ*, 1998; 317: 371-5.

Borch-Johnsen K, Feldt-Rasmussen B, Strandgaard S, Schroll M, Jensen JS. Urinary Albumin Excretion. An Independent Predictor of Ischemic Heart Disease. *Arterioscler Thromb Vasc Biol*. 1999; 19 (8) 1992-1997.

DECODE-Study (Writing Committee: Tuomilehto J, **Borch-Johnsen K**, Balkau B, Qiao Q). Glucose tolerance and mortality. Comparison of the WHO and ADA diagnostic criteria. *The Lancet* 1999; 354 (9179) 617-621.

Jensen JS, Feldt-Rasmussen B, Strandgaard S, Schroll M, **Borch-Johnsen K**. Arterial hypertension, microalbuminuria, and risk of ischemic heart disease. *Hypertension* 2000; 35 (4) 898-903.

The Decode Study Group on behalf of the European Diabetes Epidemiology Group. Glucose Tolerance and Cardiovascular Mortality. Comparison of Fasting and 2-Hour Diagnostic Criteria. *Archives of Internal Medicine* 2001; 161, 397-404.

Lauritzen T, Griffin S, **Borch-Johnsen K**, Wareham NJ, Wolffenbuttel BHR, Rutten G for the ADDITION Study Group. The ADDITION study: proposed trial of the cost-effectiveness of an intensive multifactorial intervention on morbidity and mortality among people with Type 2 diabetes detected by screening. *International Journal of Obesity*, 2000; 24, S6-S11.

Drivsholm T, Ibsen H, Schroll M, Davidsen M, **Borch-Johnsen K**. Increasing prevalence of diabetes mellitus and impaired glucose tolerance among 60-year old Danes. *Diabetic Medicine* 2001; 18, 126-132.

The Decoda Study Group on behalf of the International Diabetes Epidemiology Group. Comparison of the fasting and the 2-hour glucose criteria for diabetes in different Asian cohorts. *Diabetologia*, 2000; 43(12).

The Decode Study Group on behalf of the European Diabetes Epidemiology Group. Glucose Tolerance and Cardiovascular Mortality. Comparison of fasting and 2-hour diagnostic criteria. *Archives of Internal Medicine*, 2001; 161 (3) 397-405.

Clausen P, Jensen JS, Jensen G, **Borch-Johnsen K**, Feldt-Rasmussen B. Elevated urinary albumin excretion is associated with impaired arterial dilatory capacity in clinically healthy subjects. *Circulation* 2001; 103 (14) 1869-1874.

Gyllenberg J, Rasmussen SL, **Borch-Johnsen K**, Heitmann BL, Skakkebaek NE, Juul A. Cardiovascular risk factors in men: The role of gonadal steroids and sex hormone-binding globulin. *Metabolism* 2001; 50 (8) 882-888.

Thomsen T, Davidsen M, Ibsen H, Jørgensen T, Jensen G, **Borch-Johnsen K**. A new method for CHD prediction and prevention based on regional risk scores and randomised clinical trials: *the PRECARD^o-programme*. *Journal of Cardiovascular Risk* 2001; 8 (6) 291-297.

Bjerregaard P, Jørgensen ME, Lumholt P, Mosgaard L, **Borch-Johnsen K**, and the Greenland Population Study. Blood pressure is higher among Inuit migrants in Denmark than among the Inuit in Greenland. *Journal of Epidemiology and Community Health* 2002; 56, in press.

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Bjerregaard P, Jørgensen ME, Lumholt P, Mosgaard L, **Borch-Johnsen K** and the Greenland Population Study. Higher blood pressure among Inuit migrants in Denmark than among the Inuit in Greenland. *Journal of Epidemiology & Community Health*. 2002; 56 (4): 279-284.