

# Epidemiological Aspects of Cardiovascular Morbidity and Mortality Among Individuals With Diabetes

## The Relative Importance of Cardiovascular Risk factors

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i Arvid Carlssons hörsal, Göteborgs universitet, Medicinaregatan 3, den 11:e oktober 2018 klockan 09.00

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### Avhandlingen baseras på följande delarbeten

- I. Rawshani A, Rawshani A, Franzén S, Eliasson B, Svensson A-M, Miftaraj M, McGuire D.K, Sattar N, Rosengren A, Gudbjörnsdottir S. **Mortality and cardiovascular disease in type 1 and type 2 diabetes.** *The New England Journal of Medicine. N Engl J Med* 2017; 376:1407-1418
- II. Rawshani A, Rawshani A, Franzén S, Eliasson B, Svensson A-M, Miftaraj M, McGuire DK, Sattar N, Rosengren A, Gudbjörnsdottir S. **Range of risk factor levels: control, mortality, and cardiovascular outcomes in type 1 diabetes mellitus.** *Circulation* 2017 Apr 18;135(16):1522-1531
- III. Rawshani A, Rawshani A, Franzén S, Sattar N, Eliasson B, Svensson A-M, Zethelius B, Miftaraj M, McGuire DK, Rosengren A, Gudbjörnsdottir. **Risk factors, mortality and cardiovascular outcomes in patients with type 2 diabetes.** *The New England Journal of Medicine. N Engl J Med.* 2018 Aug 16;379(7):633-644.
- IV. Rawshani A, Sattar N, Franzén S, Rawshani A, Hattersley AT, Svensson A-M, Eliasson B, Gudbjörnsdottir S. **Excess mortality and cardiovascular disease in young adults with type 1 diabetes in relation to age at onset: a nationwide, register-based cohort study.** *Lancet* 2018 Aug 11;392(10146):477-486.
- V. Rawshani A, Rawshani A, Sattar N, Franzén S, McGuire DK, Eliasson B, Svensson A-M, Zethelius B, Miftaraj M, Rosengren A, Gudbjörnsdottir S. **Relative prognostic importance and optimal levels of risk factors for mortality and cardiovascular outcomes in type 1 diabetes.** *Submitted.*

# Epidemiological Aspects of Cardiovascular Morbidity and Mortality Among Individuals With Diabetes: the Relative Importance of Cardiovascular Risk factors

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## Abstract

**Background:** Long-term trends of cardiovascular complications and death among patients with diabetes have not been studied extensively. In addition, we aimed to examine the effect of multifactorial risk factor control, as well as optimal levels- and relative importance of cardiovascular risk factors, in patients with type 1 diabetes and type 2 diabetes. The analyses for patients with diabetes were compared to the general population.

**Method:** We used data from the National Diabetes Register along with other Swedish health registries and applied different statistical methods such as survival analysis and different machine learning models to study our research questions. We have focused on the following outcomes: all-cause mortality, acute myocardial infarction, coronary heart disease, cardiovascular disease, stroke and heart failure.

**Results:** During the period 1998-2014, patients with type 1 diabetes experienced approximately 40% greater relative risk reduction for cardiovascular complications, compared to matched controls, while patients with type 2 diabetes experienced roughly 20% greater risk reduction than their matched controls. A paradoxical finding was the lower relative risk reduction of fatal outcomes in patients with diabetes. Nevertheless, death and complications have decreased substantially during the last two decades.

Multifactorial risk factor control is associated with significant risk reduction for patients with diabetes. Still, patients with type 1 diabetes display 82% and 97% elevated risk for myocardial infarction and heart failure, respectively. For type 2 diabetes, we observed marginally increased risk of death and cardiovascular complications in patients with all risk factor at target level. Moreover, there is a monotone relationship between number of risk factor at target level and excess risk of outcomes in patients with diabetes. Patients with type 2 diabetes and all risk factors at target level had 16% lower relative risk for myocardial infarction, compared to the general population. The most important risk factors for cardiovascular complications were glycated hemoglobin, physical activity level, systolic blood pressure, low-density lipoprotein cholesterol, albuminuria, as well as risk factors that in some form denote exposure time to the disease (e.g. age, duration of diabetes and age at onset of disease). Lower levels for glycated hemoglobin, systolic blood pressure and low-density lipoprotein cholesterol is associated with reduced risk for cardiovascular complications, compared to matched controls. The relative importance analyses suggest that risk factors contribute differently between outcomes and type of diabetes.

**Conclusion:** Morbidity and mortality have decreased significantly among individuals with diabetes. Multifactorial risk factor control is associated with significant risk reduction and could perhaps even eliminate the excess risk for cardiovascular disease. Lower levels for selected risk factors than recommended target levels is associated with lower risk for complications. Heart failure is an emerging diabetes-related complication and young individuals with diabetes are at the highest risk of complications.

**Keywords:** type 1 diabetes mellitus, type 2 diabetes mellitus, cardiovascular epidemiology, cardiovascular medicine, cardiology, epidemiology, all-cause mortality, cardiovascular disease, coronary heart disease, stroke, heart failure, machine learning.

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