

# Protocol for variables from DVDD

The overall aim of this project is to identify the contributions of family and early life determinants on the development, management and care of diabetes and the diseases that may arise following a diabetes diagnosis, under a life-course framework. The justification for requesting data on multiple disease areas directly follows the primary aim of this project. We investigate this aim focusing on diabetes as the central disease of interest. Diabetes consists of different subtypes (Type 1, Type 2, LADA, MODY, gestational diabetes, secondary diabetes, rare monogenic forms) each with a different set of risk factors, presentation and pathophysiological characteristics. The familial and social effects that are the subject of this project are likely to be different for each of these diabetes subtypes. E.g. for some types of diabetes, caused predominantly by auto-immune mechanisms, familial associations to other auto-immune diseases are more likely than for type 2 diabetes, which is driven to a strong degree by obesity, low physical activity and insulin resistance.

All forms of diabetes have an increased blood glucose level as their central hallmark, and are associated with major and minor complications. The vascular complications are generally subdivided into large-vessel disease (macrovascular like myocardial infarction, stroke, peripheral vascular disease) and small-vessel disease. The occurrence of these complications is not dependent solely on the elevated glucose levels, but also on disturbance of other metabolic risk factors, familial predisposition and pre-existing conditions. Beyond these classical complications, increasingly links between diabetes and other complications are being recognised: depression, cancer, loss of cognitive function, skin conditions.

An important feature of diabetes is that it can be undetected for several years, and that the diabetic complications can sometimes be the first presentation of the disease. In order to study the occurrence of diabetic complications in the context of family we need to assess the complication status for all traditional and novel diabetic complication.

Adequate treatment of diabetes depends on long-term engagement and motivation of the patient for self-management of different aspects of the disease. The capacity to respond adequately to this challenge depends to a large degree on socio-economic status, including the degree of social support in the direct environment surrounding the patient. These effects occur in interaction with other chronic conditions, including mental health conditions.

The justification for the requested list of variables falls into four categories:

1. Diagnosis of diabetes itself, in all its forms and subtypes.
2. Conditions that are an established cause of diabetes, and diseases which have an emerging association with diabetes, which we wish to investigate
3. Major and minor complications and other consequences / signs of diabetes
4. Conditions needed to adjust our analyses for the simultaneous occurrence of other chronic health problems (co-morbidity)
5. Metabolic biomarker variables used for additional analyses and adjustments.

Cardiovascular disease is the most common cause of death and disability among people with diabetes. The cardiovascular diseases that accompany diabetes include angina, myocardial infarction (heart attack), stroke, peripheral artery disease and congestive heart failure. High blood pressure, high cholesterol, high blood glucose and other risk factors contribute to the increased risk of cardiovascular complications.

Since we will be studying associations of various exposures (for instance, family environment while growing up) on the risk for developing diabetes, we need to identify who develops diabetes in the Danish registers. We use algorithms developed within Steno for classifying individuals with diabetes (e.g. see <http://bendixcarstensen.com/DMreg/DMreg2018.pdf>). These algorithms need specific variables from DVDD.

We also want to study what exposures (for instance, whether other family members have diabetes) increase the risk of developing complications (like cardiovascular disease) for those who already have diabetes. We rely on the work of colleagues to determine which variables they used to classify these complications or which metabolic variables to include, which we have requested. DVDD is one of a few sources of metabolic variables in the registers when studying diabetes.

## **Budget**

The cost of the application to access data from the registers as well as any associated costs is covered by Steno Diabetes Center Aarhus.