

European Science Foundation
Standing Committee for the European Medical Research Councils (EMRC)

ESF/EMRC EXPLORATORY WORKSHOP

**DEVELOPMENT OF A EUROPEAN NETWORK OF
PREVENTION OF TYPE 2 DIABETES MELLITUS**

Scientific Report

Krems, Austria

1-2 February 2003

**Convened by: Jaakko Tuomilehto¹,
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1. Executive Summary

Changes in human lifestyle over the last century have resulted in a dramatic increase in the incidence of diabetes worldwide. The epidemic is chiefly of type 2 diabetes and the associated conditions known as 'metabolic syndrome'. Type 2 Diabetes (T2D) mellitus and its precursing states affects already more than 20% of the European population and requires up to 15-20% of the national health care budgets. In conjunction with environmental and behavioural factors, type 2 diabetes is brought on by genetic susceptibility. Recent studies have however proved that reinforced lifestyle modification and early pharmacological intervention can significantly reduce the risk of Type 2 Diabetes by up to 58% in risk individuals. There is evidence that the prevention of type 2 diabetes in persons on risk for the diseases is possible and also highly successful affordable.

To prevent the personal and socio-economic burden of type 2 diabetes interventions should be directed to people at an increased risk of the disease. The major task for public health now is to identify those individuals who would benefit from intensive lifestyle counselling. To identify such individuals Finnish researchers have developed a Diabetes Risk Score as a simple, practical and informative scoring system to screen and characterise individuals according to their future risk of type 2 diabetes.

For an affordable success in diabetes prevention the effort to prevent the disease needs to start address all susceptibility factors of diabetes mellitus long term and continuously. Therefore the interaction of genetic and environmental factors responsible for developing diabetes and the mechanisms of diabetes prevention needs to be addressed. According to the recent study results large effort is going on in different European countries to establish diabetes prevention intervention programs and formulate national diabetes prevention campaigns. Beside the evidence that diabetes prevention is successful in a study setting there are several open questions:

1. How the design of a diabetes prevention programme can be implemented in a population-based setting and how successful it will be in the general population?
2. What are the mechanisms of diabetes prevention and what are genetic and environmental parameters that best predict successful intervention outcome for diabetes prevention?
3. In the future it will be also important to find out to what extent complications associated with type 2 diabetes can be prevented by lifestyle intervention among people at high risk of diabetes.

Therefore members of 25 European groups interested in parameters of genetics of diabetes and diabetes risk, lifestyle intervention, epidemiology, psychology, practical expertise in medicine met at the ESF Exploratory Workshop in Krems, Austria. In a combination of plenary lectures and workshops during the evidence of prediction of diabetes, screening, prevention of diabetes with lifestyle and pharmacological intervention and evidence for implementation of the recent study results under practical socio-economic requirements into the national health care systems in European countries was discussed and a new collaborative research plan will be outlined.

The core point of the project will be to identify the underlying genetic and environmental mechanisms for the success of an intervention strategy for diabetes prevention. In addition to these usual observational genetic studies, we will also examine the gene-environment interaction in the unique setting where environmental factors are actually modified. Thus, we will for the first time implement a large study of the gene-environmental interaction that includes both the level of the exposure in the past and the changes in the exposure. During the workshop the project strategies were discussed with the objectives

- a) identification of risk for T2D,
- b) intervention strategies and
- c) data issues and statistical considerations.

a) identification of risk for T2D

The basis of identification of high-risk subjects will be the Diabetes Risk Score questionnaire. Its application can be directed to individuals who are likely candidates for high risk, i.e. previous gestational diabetic women, siblings and offspring of type 2 diabetic patients, hypertensive subjects, obese subjects, etc. Score value of 12 will be considered to indicate high risk, and such individuals shall be the target of lifestyle intervention. Before the intervention they should be characterised regarding genetic and metabolic factors, including an oral glucose tolerance test. Standardised methods will be developed for these assessments to be done in several laboratories.

b) intervention strategies

In the workshop it was stated that there is large evidence that diabetes prevention worked in a study designs but little is known about intervention population based. For the PLAN_GRASS project members agreed to define a standardised intervention mandatory for each group. The challenge will be to standardise intervention for different centres in different countries. The presented TUMAINI-prevention concept from Germany could be a working reference but needs to be adopted. Establishing such a standardised protocol between different centres and partners with different expertise is a valuable tool for knowledge transfer and training between the partners.

The plan of the intervention protocol should depend on the national health system and existing intervention tools. Existing infrastructure can be used according strict acceptance of the standard protocol. No control population is recommended at this stage since it would be ethically difficult. However, among the participants in intervention programmes, it is assumed that a wide variation in lifestyle changes will occur. The reasons for varying success will be evaluated.

c) data issues and statistical considerations

Data management and evaluation responsibility and protocol add-ons will be realised based on the expertise of each partner. This difference will allow a European network of knowledge transfer and teaching. The sample size will be sufficiently large so that there is sufficient power to evaluate the efficacy of the interventions, and to carry out gene-environment interaction analyses.

A major point should be the evaluation of the “economic” mechanisms of diabetes prevention. Therefore health insurance and food industries should be involved in the project discussion.

Discussing the value of pharmacological intervention it was seen as valuable for so called “non responder” in lifestyle intervention. After a 3 years period in the PLAN-GRASS project a pharmacological intervention or adding a dietary supplement could be considered for “non responder” by a scientific committee.

After screening the intervention will divide into an actual intervention (schooling, group session, eye to eye intervention) and post intervention period to maintain the lifestyle effect and identify “Non responders”. The intensity and management of this “post intervention” needs to be defined. The attached concept could be a working reference.

2. Scientific content of the event

During the meeting scientific lectures were given by the participating experts on various topics related to type 2 diabetes covering:

- epidemiology
- genetics
- pathophysiology
- obesity and physical inactivity as risk factors
- prevention trials

Small group work was arranged in order to have deeper discussions related to specific issues relevant to the future development of a European-wide project.

3. Assessment of the results, contribution to the future direction in the field

The ultimate aim of this **European-Diabetes-Prevention-Network** is to detect the mechanisms of diabetes prevention and to develop a standardised risk detection strategy and standardised core programme for diabetes prevention, which can be implemented into the European national health care systems under practical socio-economic conditions. This work will fit into the European Policy as defined in the priority area 1.1.1.ii.a (diabetes prevention). The proposed project will bundle and **integrate multidisciplinary international and national expertise** to reduce the human and financial burden of the disease and to increase the quality of life for people at risk of type 2 diabetes.

Therefore a detailed plan to prepare a research funding applications for submission to the EU 6th Framework Programme and/or to the European Science Foundation, as well as other national funding organisations should be prepared. The project will follow the Expression of interest for an Integrated Project of the FP6 submitted on the 6th June 2002 – project title PLAN_GRASS, but clearly modified and having even stronger emphasis on genetics and gene-environmental interaction in the prevention of type 2 diabetes and its major complications.

The participants of the workshop agreed to develop a project/research protocol with the working title “**What are the mechanisms of diabetes prevention**”.

4. Final programme

Saturday 1st February 2003

14.00	Presentation of the ESF and the EMRC Marianne Minkowski, <i>ESF Senior Scientific Secretary</i>
14.15	Review of the scientific need and bases of prevention of Diabetes mellitus <ol style="list-style-type: none">1. Emerging Epidemics of Diabetes mellitus in European populations Jaakko Tuomilehto2. Genetic risk factors for Diabetes mellitus Graham Hitman3. Pathophysiology of Diabetes risk and Diabetes mellitus John Nolan
16.00	Coffee break
16.30	Experiences from trials on the prevention of diabetes mellitus <ol style="list-style-type: none">1. Finnish diabetes prevention study Jaana Lindström2. Dutch prevention program Ellen Blaak3. German intervention project Peter Schwarz4. Physical activity and central obesity Michael Lean
18.30	Heuriger

Sunday 2nd February 2003

09.00

Translation of essence of regional trials on diabetes prevention into the development of a European Network

1. **Requirement of European Network Collaboration**
Jaakko Tuomilehto
2. **Introduction into the working groups**
3. **Working Groups**

13.00

Lunch break

11.00-15.00

- a) Identification of carrier of increased diabetes risk
- b) Intervention strategies in diabetes prevention lifestyle versus pharmacological intervention
- c) Data requirements – parameters, assessment, methodology, statistics

16.00

Final Session

Chair: Michael Brainin

1. **Reports from each Working Group**
2. **General discussion for the plan of a European Network in diabetes prevention and a European 6th Framework proposal**

5. Final list of participants

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