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# The rise in intermediate hyperglycaemia between 1989 and 2006 in the Caucasian population of the Netherlands. Results from the Hoorn Study and the New Hoorn Study

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# ABSTRACT

Information on changes in the prevalence of glucose metabolism disorders in westernized Caucasian populations is scarce. We investigated trends in the prevalence of glucose metabolism disorders and related (risk)factors in the Netherlands between 1989 and 2006. Data were obtained from two random samples of the general population of the Netherlands 50-65 years of age: 1,576 subjects from the Hoorn Study (1989) and 1,734 subjects from the New Hoorn Study (2006). A standard 75-g OGTT was performed to identify normal glucose metabolism (NGM), intermediate hyperglycaemia (IH), newly-diagnosed diabetes (NDM) and known diabetes (KDM). In addition, blood pressure, cholesterol level, body mass index, waist circumference, smoking behaviour and physical activity were determined. Between 1989 and 2006, the prevalence of IH increased from 14.4% to 17.6%. There was no significant change in the prevalence of diabetes. The mean levels of cholesterol and triglycerides had significantly improved in 2006, and the prevalence of smoking had decreased significantly. Moreover, the self-reported amount of physical activity had increased. However, the prevalences of hypertension, adiposity (high body mass index) and abdominal adiposity (large waist circumference) had increased significantly, especially in men. Therefore, a future increase in diabetes in this high risk population is to be expected.

# INTRODUCTION

International literature has shown that diabetes is becoming a major health problem. The International Diabetes Federation estimated that in 2000 approximately 151 million people worldwide had diabetes, and they expect this number to have increased to 438 million in 2025, representing 6.6% of adult population in the entire world (1).

An increase in the prevalence of diabetes is expected to be a result of several worldwide trends. First of all, populations are aging, and older age is one of the most important risk factor for diabetes (2;3). Secondly, the life-expectancy of patients with diabetes might be improving as a result of better treatment strategies for diabetes (4). Thirdly, in the ratio of diagnosed versus undiagnosed diabetes patients there is a trend towards more diagnosed diabetes patients, due, for example to earlier detection (5). However, The Hoorn Study showed that half of the patients with diabetes were undiagnosed in 1989 (6) and no improvement in this proportion was observed in the DECODE and Inter99 studies in 2003 (3;7). Finally, emerging westernized lifestyles result in an increase in the main risk factors for diabetes, i.e. adiposity and lack of physical activity (2).

To determine whether the above-mentioned trends have, indeed, resulted in a change in the prevalences of diabetes (fasting glucose ≥ 7.0 mmol/l and/or postload glucose ≥ 11.1 mmol/l according to the WHO'06 criteria (8)) and intermediate hyperglycemia (IH: fasting glucose 6.1-7.0 mmol/l and/or postload glucose 7.8-11.1 mol/l according to the WHO'06 criteria (8)), a comparison of population-based studies using random samples of the population is needed. Moreover, a standard 75g oral glucose tolerance test (OGTT) should be used to diagnose glucose metabolism disorders, since this is the worldwide guideline for the diagnosis of diabetes and IH (8). Despite this, many estimates of changes in the burden of diabetes are based on 1) the registration of known diabetes patients (9-11), which provides an incomplete overview because undiagnosed diabetes patients are missing, 2) studies in which only fasting glucose measures or non-standardized OGTTs (75g) are used (12-14), which ignore the large proportion of diabetes patients with isolated postload hyperglycemia (15) and are not in accordance with the current gold standard for the diagnosis of diabetes, 3) the modeling of demographic variables (1;16), with which no real change in the prevalence is measured, 4) studies in high-risk populations (17;18), which do not provide a representative overview of the total population.

As a result, information on changes in the prevalence of diabetes and IH in a representative population is scarce, especially in westernized Caucasian populations. The results of two studies, one in Mauritius and one in Bangladesh, using random samples of the population and OGTTs, suggest an increase in diabetes in these populations (19;20). Our aim was to investigate whether there is a change in the prevalence of diabetes (diagnosed and undiagnosed) and IH in the Caucasian population of the Netherlands, based on a comparison of the results of two large population-based studies with random samples of the population, performed in 1989 and 2006. Moreover, we aimed to investigate whether changes in glucose metabolism coincided with changes in markers for cardiovascular disease, lifestyle and adiposity.

# MATERIALS AND METHODS

For this study we used data from the Hoorn Study (1989) and the New Hoorn Study (2006), both of which are cohort studies of diabetes and diabetes complications in the general population of the Netherlands. The cohorts and the baseline measurements have been described in detail elsewhere (6;21). Briefly, in 1989 a random selection of 3,553 men and women, 50 to 75 years of age, was made from the population register of the middle-sized Dutch town of Hoorn. A total of 2,540 (71.5%) subjects agreed to participate, and after the exclusion of 56 non-Caucasian participants the population consisted of 2,484 men and women. In 2006, 6,180 men and women, 40-65 years of age were randomly selected from the population register of Hoorn. A total of 2,804 subjects (45.3%) agreed to participate. After the exclusion of 312 non-Caucasian participants, the study population consisted of 2,492 men and women. For this analysis, a comparison was made between the overlapping age-group of 50-65 years in the cohorts, which included 1,592 subjects in 1989 and 1,718 subjects in 2006.

## Baseline examinations of the Hoorn Study and the New Hoorn Study

*Anthropometry.* During the baseline medical examination, a fasting blood sample was taken from all participants after overnight fasting, and an oral 75g glucose load was given. Weight and height were measured, and body mass index (BMI) was calculated as the ratio of weight and height squared. In addition, waist circumference was determined. Blood pressure was measured twice on the right arm after a 10 minute rest with a random-zero sphygmomanometer (Hawksley-Gelman Ltd, Lancing, UK) in 1989, and three times on the right arm after a 10 minute rest with a Colin Press BP 8800p Non-Invasive Blood Pressure Monitor (Colin Medical Technology Coorporation, USA) in 2006.

*Biochemical indicators.* Fasting and 2-hour postload venous plasma glucose concentrations were determined with a glucose dehydrogenase method (Merck, Darmstadt Germany) in 1989, and by a glucose-oxidase method (Glucoquant/hexokinase/G6P-DH; Boehringer-Mannheim, Mannheim, Germany) in 2006. HbA1c levels were determined by ion-exchange high performance liquid chromatography (HPLC) on a modular type 2 diabetes monitoring system (Bio-rad, Veenendaal, the Netherlands) in 1989 and by a DCCT standardized reversed-phase cation exchange chromatography (HA 8160 analyzer, Menarini, Florence, Italy) in 2006. With the help of an internal validation study in our laboratory, in which a linear regression model describing the association between the two methods was provided, the HbA1c values in 1989 were converted to DCCT-standardized values.

Triglycerides and total and HDL-cholesterol were determined from fasting blood samples with enzymatic techniques (Boehringer-Mannheim, Mannheim, Germany) in both study samples.

*Questionnaires.* Self-report questionnaires were used to assess physical activity, smoking behaviour and level of education. Physical activity was graded according to the reported hours per week spent on cycling, walking, gardening and sports. Reported current smoking was used to indicate smoking status. Finally, participants were asked to report their highest educational qualification, which was used to determine the level of educational.

In both study samples, written informed consent was obtained from all participants, and the study protocols were approved by the Medical Ethics Committee of the VU University Medical Center in Amsterdam.

## Statistical analysis

The analyses were stratified according to gender and differences between the two cohorts with regard to mean values of continuous variables were then analysed with the independent-samples T-test. Moreover, categorical variables were created as follows: 1) Glucose tolerance was sub-divided into 4 categories, according to the WHO'06 criteria (8). Normal glucose tolerance (NGT) was defined as fasting plasma glucose <6.1 mmol/L (<110 mg/dL) and 2-hr blood glucose <7.8 mmol/L (≤140 mg/dL). Intermediate hyperglycaemia (IH) was defined as fasting plasma glucose 6.1-6.9 mmol/L (110-125 mg/dL) and/or 2-hr blood glucose 7.8-11.0 mmol/L (141-199 mg/dL). Newly-diagnosed type 2 diabetes (NDM) was defined as fasting plasma glucose ≥7.0 mmol/L (≥126 mg/dL) and/or 2-hr blood glucose ≥11.1 mmol/L (≥200 mg/dL). Known diabetes (KDM) was defined by the use of insulin and/or oral hypoglycaemic agents and self-reported diabetes. 2) Body composition: normal weight (BMI < 25 kg/$m^2$), overweight (BMI 25-30 kg/$m^2$) and obesity (BMI > 30 kg/m2). 3) Abdominal overweight: waist circumference ≥ 102 cm in males and ≥ 88 cm in females (dichotomous, yes/no). 4) Physical activity: ≥

30 minutes cycling, walking, gardening and sports a day (dichotomous, yes/no). 5) Hypertension: systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, and/or when using anti-hypertensive medication (dichotomous, yes/no). 6) Hypercholesterolaemia: total cholesterol level ≥ 6.5 mmol/l and/or use of cholesterol-lowering medication (dichotomous, yes/no). 7) Low HDL cholesterol: HDL cholesterol level < 1.0 mmol/l in males and < 1.3 mmol/l in females (dichotomous, yes/no). 8) High triglyceride levels: triglyceride levels ≥ 1.7 mmol/l (dichotomous, yes/no). 9) Smoking: self-reported current smoker (dichotomous, yes/no) 10) Level of education (3 categories): primary school, education unknown or lower secondary education (primary level), upper secondary education or lower tertiary education (secondary level) and higher tertiary education or university degree (high level).

Significant differences between categorical variables were tested with Chi-square tests.

All analyses were performed with SPSS, version 15.0, and a p-value of ≤ 0.05 was considered to be statistically significant.

**Table 1.** Comparison of glucose metabolism categories between 1989 and 2006, stratified according to gender

| | TOTAL POPULATION | | MALES | | FEMALES | |
|---|---|---|---|---|---|---|
| | **1989** | **2006** | **1989** | **2006** | **1989** | **2006** |
| N (% of total population) | 1592 (100) | 1718 (100) | 755 (30.4) | 821 (32.9) | 837 (33.7) | 897 (36.0) |
| Age (mean, SD) | 57.2 (4.2) | 57.0 (4.3) | 57.0 (4.2) | 57.3 (4.3) | 57.3 (4.3) | 56.8 (4.3)* |
| NGT (%) | 77.9 | 74.4* | 74.4 | 70.4* | 81.0 | 78.2 |
| IH (%) | 14.4 | 17.6* | 16.8 | 20.4 | 12.1 | 15.0 |
| Diabetes (%) | 7.8 | 8.0 | 8.8 | 9.2 | 6.9 | 6.8 |
| Known diabetes (%) | 2.4 | 3.7* | 2.7 | 5.0* | 2.2 | 2.5 |
| New diabetes (%) | 5.4 | 4.2 | 6.1 | 4.2 | 4.7 | 4.3 |
| Use of glucose lowering medication or insulin (%) | 2.0 | 2.7 | 2.3 | 4.3* | 1.8 | 1.3 |
| FPG (mean, SD) | 5.7 (1.6) | 5.7 (1.0) | 5.8 (1.2) | 5.8 (1.1) | 5.6 (1.6) | 5.5 (0.9) |
| 2hr PG (mean, SD) | 5.7 (2.7) | 6.0 (2.5)* | 5.7 (2.6) | 6.1 (2.8)* | 5.8 (2.7) | 5.9 (2.3) |
| HbA1c (mean, SD) | 5.4 (0.8) | 5.5 (0.5)* | 5.4 (0.7) | 5.5 (0.6)* | 5.4 (0.8) | 5.5 (0.5)* |

*SD = standard deviation, NGT = normal glucose tolerance, IH = intermediate hyperglycaemia, FPG = fasting plasma glucose, 2hrPG = postload plasma glucose.*

* $p \leq 0.05$

# RESULTS

## Differences in glucose metabolism

Table 1 shows the results of the comparison of glucose metabolism categories between 1989 and 2006. In men and women, there were no significant differences in the mean values of fasting plasma glucose between 1989 and 2006. The postload plasma glucose level in men was significantly higher in 2006 [5.7 (2.6) mmol/l in 1989 and 6.1 (2.8) mmol/l in 2006]. HbA1c levels remained stable at 5.4% in both years. The prevalence of IH in men increased from 16.8% to 20.4%, accompanied by a significant decrease in NGT from 74.4% to 70.4%. There was no significant difference in the total number of diabetes patients (8.8% and 9.2%), although the prevalence of KDM increased significantly from 2.7% in 1989 to 5.0% in 2006. In women there was a non-significant increase in the prevalence of IH in 2006 (15.0%), compared to 1989 (12.1%), accompanied by a decrease from 81% to 78.2% in the prevalence of NGT. No significant differences in the prevalence of total diabetes (6.9% and 6.8%), KDM (2.2% and 2.5%) or NDM (4.7% and 4.3%) were observed among women.

**Table 2.** Comparison of body composition, physical activity, blood pressure, lipid profile and socioeconomic factors between 1989 and 2006

| | TOTAL POPULATION | | MALES | | FEMALES | |
|---|---|---|---|---|---|---|
| | **1989** | **2006** | **1989** | **2006** | **1989** | **2006** |
| **ADIPOSITY** | | | | | | |
| Body Mass Index (BMI; kg/m²) Mean (SD) | 26.4 (3.5) | 26. 4 (3.9) | 26.2 (3.0) | 26.7 (3.5)* | 26.5 (3.9) | 26.2 (4.2) |
| Normal weight: BMI < 25 kg/m² (%) | 36.0 | 40.7* | 33.6 | 35.0 | 38.2 | 45.9* |
| Overweight: BMI 25-30 kg/m² (%) | 49.4 | 43.3* | 54.8 | 49.6* | 44.4 | 37.6* |
| Obesity: BMI >30 kg/m² (%) | 14.6 | 16.0* | 11.6 | 15.4* | 17.4 | 16.6* |
| Waist circumference (cm) Mean (SD) | 90.1 (10.8) | 90.9 (11.4)* | 94.7 (9.0) | 95.7 (9.9)* | 86.0 (10.7) | 86.5 (10.9) |
| Abdominal overweight: waist circumference ≥ 102 cm (♂) or ≥ 88 cm (♀) (%) | 30.0 | 33.5* | 18.4 | 25.5* | 40.5 | 40.9 |
| **PHYSICAL ACITIVITY** | | | | | | |
| Physical activity | | | | | | |
| - cycling (% ≥ 30 min/day) | 37.7 | 26.9* | 37.0 | 32.5 | 38.4 | 21.7* |
| - sport activities (% ≥ 30 min/day) | 8.3 | 21.5* | 9.8 | 24.6* | 6.9 | 18.6* |
| - total of cycling, walking, gardening and sports (% ≥ 30 min/day) | 69.7 | 78.2* | 71.0 | 81.2* | 68.6 | 75.5* |
| **BLOOD PRESSURE** | | | | | | |
| Systolic blood pressure (mmHg) Mean (SD) # | 128.8 (17.3) | 133.6 (17.1)* | 129.7 (15.4) | 135.8 (16.1)* | 128.0 (18.8) | 131.7 (17.8)* |
| Diastolic blood pressure (mmHG) Mean (SD) # | 81.2 (9.8) | 77.0 (10.3)* | 82.9 (9.0) | 79.8 (9.5)* | 79.6 (10.1) | 74.6 (10.3)* |
| Hypertension: ≥ 140/90 mmHg (%) # | 31.9 | 33.1 | 34.0 | 38.8 | 29.9 | 28.0 |
| Use of anti-hypertensive medication (%) | 15.4 | 20.1* | 14.6 | 21.4* | 16.1 | 19.0 |
| Hypertension: ≥ 140/90 mmHg or use of anti-hypertensive medication (%) | 42.4 | 46.5* | 43.6 | 51.9* | 41.2 | 41.6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **LIPID PROFILE** | | | | | | |
| Total cholesterol (mmol/l) Mean (SD) [$] | 6.6 (1.2) | 5.6 (1.0)* | 6.4 (1.1) | 5.4 (1.0)* | 6.8 (1.2) | 5.8 (1.0)* |
| HDL cholesterol (mmol/l) Mean (SD) [$] | 1.3 (0.37) | 1.5 (0.42)* | 1.2 (0.31) | 1.4 (0.34)* | 1.4 (0.37) | 1.7 (0.42)* |
| High total cholesterol: ≥ 6.5 mmol/l (%) [$] | 53.0 | 18.8* | 45.1 | 14.1* | 60.3 | 23.0* |
| Low HDL cholesterol: ♂ <1.0 mml/l or ♀ <1.3 mmol/l (%) [$] | 36.6 | 22.8* | 68.9 | 46.1* | 6.8 | 1.9* |
| Use of cholesterol-lowering medication (%) | 1.4 | 14.1* | 1.3 | 18.3* | 1.6 | 10.4* |
| Hypercholesterolemia: total cholesterol ≥ 6.5 mmol/l or use of cholesterol-lowering medication (%) | 55.2 | 31.8* | 48.1 | 30.9* | 61.6 | 32.7* |
| Triglycerides (mmol/l) Mean (SD) | 1.6 (1.1) | 1.5 (1.0)* | 1.7 (1.1) | 1.6 (1.2)* | 1.5 (1.0) | 1.4 (0.7)* |
| High triglycerides: ≥ 1.7 mmol/l (%) | 34.0 | 30.2* | 39.1 | 34.3* | 29.4 | 26.3 |
| **SOCIOECONOMIC FACTORS** | | | | | | |
| Smoking (% yes) | 36.0 | 20.1* | 39.0 | 20.9* | 33.3 | 19.3* |
| Primary education (%) | 60.8 | 29.3* | 54.0 | 23.0* | 66.8 | 35.1* |
| Secondary education (%) | 26.3 | 37.4* | 28.1 | 36.6* | 24.6 | 38.1* |
| Higher education (%) | 13.0 | 33.3* | 17.9 | 40.4* | 8.6 | 26.7* |

*SD = standard deviation, HDL = high-density lipoprotein*
* *$p \leq 0.05$*
[#] *participants taking anti-hypertensive medication were excluded*
[$] *participants taking cholesterol-lowering medication were excluded*

## Differences in risk factors for glucose metabolism disorders

In Table 2, trends in body composition, physical activity, blood pressure, lipid profile and socioeconomic factors are shown. A significant increase was observed in mean BMI and the prevalence of obesity in men, but not in women. A comparison of physical activity between 1989 and 2006 revealed that overall, a significant increase in the prevalence of self-reported moderate to vigorous activity for an average of 30 minutes or more a day was seen in both men and women. This was mainly the result of a significant increase in the proportion of people reporting to engage in sport activities on average 30 min/day. The proportion of women reporting to cycle on average 30 min/day decreased significantly. In 1989, 39.0% of men and 33.3% of women reported that they were current smokers. This percentage decreased to 20.9% and 19.3%, respectively, in 2006. Mean systolic blood pressure increased and mean diastolic blood pressure decreased in both men and women, accompanied by an increase in the prevalence of hypertension, especially in men (from 43.6% in 1989 to 51.9% in 2006). The lipid profile of the population became more favourable between 1989 and 2006, with significantly lower mean total cholesterol and triglycerides levels and higher mean HDL cholesterol values. The use of lipid-lowering medication increased from 1.4% to 14.1%. In addition, the prevalence of hypercholesterolaemia decreased significantly in both men and women. Large differences were found in the three levels of education in both men and women between 1989 and 2006. In 1989, about two-thirds (60.8%) of the population had a primary education, whereas in 2006 almost equal percentages in the groups had a primary, secondary and higher education (29.3%, 37.4% and 33.3%, respectively).

# DISCUSSION

To summarize, comparing Caucasian men and women, 50-65 years of age, between 1989 and 2006, we found an increase in the prevalence of IH, while the prevalence of diabetes remained the same. In men, but not in women, the proportion of KDM patients increased. The change in the prevalence of glucose metabolism disorders coincided with an increase in the prevalence of (abdominal) adiposity and hypertension in men, a decrease in the prevalence of smoking in both sexes, and improvements in the lipid profile and amount of physical activity in both men and women.

There are very few studies in which two random samples of the population have been compared in order to study the prevalence of OGTT-diagnosed diabetes and IH. NDM, diabetes based on postload hyperglycemia, and the prevalence of IH are usually not included in the estimations that have been made (10;13;14). Soderberg et al. investigated the prevalence of OGTT-diagnosed diabetes and IH in 1987,1992 and 1998 among over 5,000 inhibitants of Mauritius, who were between 25 and 75 years of age. They observed a change in the prevalence of diabetes from 12.8% in 1987 to 15.2% in 1992, and 17.9% in 1998. The prevalence of KDM also increased, but there was no change in the prevalence of IH. The differences between their results and the results of our study could be due to the timing and duration of the different studies. Moreover, ethnic differences between the populations, or other differences in the characteristics of the population, for example in age-distribution, might play a role.

Glucose metabolism disorders are known to be influenced by several risk factors, such as lack of physical activity, adverse lipid levels, adiposity and hypertension (22-24). The Westernized lifestyle, characterized by insufficient physical activity and unhealthy nutrition, is thought to have an negative impact on the prevalence of adiposity and, as a result, on the prevalence of diabetes. On the other hand, there has been an increase in education on healthy behaviour and interventions based on changes in lifestyle in the past decade. The MONICA Study investigated world-wide trends in cholesterol, blood pressure and BMI between 1979 and 1996 in people between 35 and 64 years of age (25). Some differences with our results should be noted. The prevalence of smoking decreased in the Netherlands between 1989 and 2006 in both sexes, while the MONICA Study reported decreases in men and increases in women. Systolic blood pressure increased in our study, which is in contrast with the decrease observed throughout the world. The differences in time frame and age-group studied might underlie the differences presented, accompanied by other cohort- or period-effects. The strong improvement in lipid profile and the increase in the prevalence of adiposity in men, are in accordance with the world-wide trends presented by the MONICA project.

We observed an increase in physical activity, especially sport activities, between 1989 and 2006. On the other hand, daily routine physical activity, for example the amount of time spent on cycling, did not show improvements and even decreased in women. These trends are in accordance with the results of earlier studies carried out in the Netherlands, in which increases in sport activities since 1979 are reported, accompanied by a decrease in daily physical activities like housekeeping (26). Despite the increase in especially sport activities, the prevalence of adiposity increased in men. This might be the result of factors related to the occurrence of adiposity which were not measured in this study, for example nutritional factors.

The increase in the prevalence of KDM can be caused by several factors. First of all, due to increased awareness about diabetes and diabetes-related risk factors, primary health care providers are more likely to test patients for diabetes. Secondly, the change in diagnostic criteria for diabetes over time might also play a role. In 1989, a fasting glucose level of 7.8 mmol/l was the threshold for a diagnosis of diabetes, and this was reduced to 7.0 mmol/l in 1999. In our 1989 population, 45 people had fasting glucose levels between 7.0 and 7.8 mmol/l, and could therefore not have been diagnosed with diabetes by their primary care practitioner. If the threshold had already been lowered to 7.0 mmol/l in 1989, it is to be expected that not all 45 people would have had such a diagnosis. Therefore, we can not estimate the extent to which this influenced the reported prevalence data. Thirdly, an increase in KDM might also be the result of an increase in the life-expectancy of diabetes patients (4). An increase in incidence, accompanied by a decrease in mortality, can have an influence on the observed increase in the prevalence of diabetes (27;28). In 2006, there were more men than women diagnosed with diabetes. The fact that fasting glucose is mainly used for the diagnosis of diabetes in general practice in the Netherlands (29) could also be of influence. Large population studies have shown that more women than men have isolated postload hyperglycemia (3). Indeed, in 2006, 34.2% of the women with NDM and 17.6 % of the men with NDM in our study had isolated elevated postload glucose (data not shown), which decreases the chance of a diagnosis in women.

Between 1989 and 2006 the use of anti-hypertensive medication and cholesterol-lowering medication increased significantly, indicating a positive trend towards prevention in primary care. However, the increase in anti-hypertensive medication did not lead to a decrease in hypertension. In fact, mean systolic blood pressure increased and diastolic blood pressure decreased, indicating an increase in brachial pulse pressure, which is a marker for arterial stiffness. In contrast to anti-hypertensive medication, the increase in cholesterol-lowering medication coincided with a decrease in the prevalence of an adverse lipid profile, indicating an effective treatment strategy for hypercholesterolemia. Earlier research has shown that the decrease in hypercholesterolemia in Europe is not only attributable to the introduction of cholesterol lowering-medication in the Netherlands (30). The changes in the prevalence of smoking and physical activity found in our study might also have had a positive influence on the lipid profile of the population of the Netherlands.

A strength of the present study is that both the Hoorn Study and the New Hoorn Study used random samples of the Caucasian population in the same region to examine the prevalence of glucose intolerance. In addition, both cohorts used OGTTs to screen for diabetes, and were able to estimate the prevalence of both diagnosed and undiagnosed diabetes and IH. In 1989, the participation rate was 71.5%, indicating that the sample was representative of the Caucasian population in the Netherlands. In 2006 the participation rate was 45.3%. To check whether this influenced our prevalence data, we identified the reasons given by people who were unwilling to participate in 2006. Of the 1,286 people who were unwilling to participate, 3.3% gave 'I already have diabetes' as a reason for non-participation. The percentage of KDM in our 2006 sample was 3.5%. We furthermore hypothesized that, based on the trend towards a higher level of education in the Netherlands (26), confirmed by the results presented in Table 2, in 2006 there we less people with a primary education, who might have a higher prevalence of glucose metabolism disorders due to a more unhealthy lifestyle. Therefore, we conducted a sensitivity analysis with a 'worst case scenario': what prevalences of IH and diabetes would we have found if the participation rate in both cohorts was 100% and all current non-participants had a primary education? This revealed that we might have under-estimated the prevalence of IH in 2006 (17.5% in current analysis, 18.7% in sensitivity analysis), but that there would have been no differences between the prevalence of diabetes in 1989 and 2006 (data not shown).

Our study has some limitations. To minimize errors resulting from the use of different procedures, the operational procedures of the 1989 study were also applied in the 2006 study. However, we cannot exclude potential differences in the results, due to changes in equipment and laboratory procedures. For example, blood pressure was measured with a random-zero sphygmomanometer in the Hoorn Study, and with a Blood Pressure Monitor in the New Hoorn Study. Since research has shown that monitors tend to overestimate systolic blood pressure and underestimate diastolic blood pressure as compared to sphygmomanometers, this differences in device between 1989 and 2006 might have influenced the results on blood pressure reported. Secondly, more research is needed to establish changes in the prevalence of diabetes and IH in other ethnic populations and other age-groups. Finally, other lifestyle factors that contribute substantially to the burden of diabetes and IH might not have been included in our analysis. For example, we were not able to present trends in nutritional behaviour.

In conclusion, between 1989 and 2006 the prevalence of IH in the population of the Netherlands, between 50 and 65 years of age, increased. While the prevalence of diabetes remained the same, the amount of reported physical activity increased, and the lipid profile became more favourable. On the other hand, an increase in the prevalence of adiposity and hypertension that was observed. Since epidemiological studies have shown that people with IH have a high risk of developing diabetes (31) and cardiovascular disease (32), and that adiposity and hypertension are closely related to multiple health-related issues, this may lead to an increase in the prevalences of cardiovascular disease and diabetes in the Netherlands in the near future.

## Conflict of interest

There are no potential conflicts of interest relevant to this article.

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