Large Impact of Antidiabetic Drug Treatment and Hospitalizations on Economic Burden of Diabetes Mellitus in The Netherlands during 2000 to 2004

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Objective: To estimate the burden of diabetes mellitus (DM) and its complications in The Netherlands.

Methods: The PHARMO Record Linkage System comprised among others linked drug dispensing, hospital and clinical laboratory data from approximately 2.5 million individuals in The Netherlands. Patients with DM (type 1 and type 2) were included in the study cohort from 2000 to 2004 if they used antidiabetic drugs or had HbA1c ≥ 6.5 mmol/L or had a hospitalization for DM or a diabetic complication in the measurement year or in the preceding year. Controls, defined as subjects without a diagnosis of DM and/or subjects not prescribed glucose-lowering medication, were 1:1 matched to patients with diabetes, on birth year, zip code, and gender. Complications (hospitalizations and dispensings for cardiovascular disease/eye problems/amputations) were classified into stages. Complications attributed to DM were estimated as complication stages 1 and 2 among patients minus those among controls. Drug costs were extrapolated to The Netherlands by direct standardization.

Results: Among the total population in The Netherlands, the prevalence of DM increased from 2.8% in 2000 to 4.0% in 2004. Severe cardiovascular complications attributed to DM increased from 18,000 to 39,000 patients. Per DM patient the cost of direct treatment attributed to DM increased from €974 in 2000 to €1283 in 2004. Per 100 members of the total population, this increase was from €2764 in 2000 to €5140 in 2004. Most of these costs (65% in 2004) were because of hospitalizations.

Conclusion: Drug treatment, hospitalizations, and cost attributed to diabetes mellitus have almost doubled between 2000 and 2004, but so did the “background” costs in the general population, perhaps because of preventive efforts.

Keywords: diabetes mellitus, diabetes-related complications, direct costs, pharmacy, prevention and control.

Introduction

The prevalence of diabetes mellitus (DM) worldwide, especially of type 2 diabetes, is rising rapidly [1]. As for The Netherlands, data from the Dutch National Institute for Public Health and the Environment suggest that the annual number of patients with DM rose from 460,000 in 2000 to approximately 650,000 in 2004 and continues to rise [2]. The impact of DM complications, drug treatment, and hospitalizations on the total burden of this disease in the European and Dutch context has not fully been described. These factors are essential to a complete understanding of the economic burden of this disease.

Diabetic complications, particularly macrovascular complications including cardiovascular disease and common coexisting conditions such as hypertension and dyslipidemia are major causes of disease and mortality among patients with DM [3–6]. The ultimate goal of drug treatment of DM is driven by prevention of these complications in such a way that ultimately there would be no differences in cardiovascular complications between diabetic patients and nondiabetic subjects.

Few epidemiological studies are able to measure the impact of pharmacological intervention on outcomes of DM over longer periods of time. This is why, among others, prevalence of DM and its complications have typically been estimated using pharmaeco-economic simulation models, for example, the well-defined and validated CORE diabetes model [7–9]. Nevertheless, such estimations do not always take into account what background risk of cardiovascular disease may exist in the general population with or without overt DM. When this is done, the burden complications in a population attributed to DM can be elucidated [10].

The objective of this study was therefore to estimate the annual prevalence, the frequency of complications, treatment, and hospitalizations, and direct medical costs attributed to DM, for the period 2000 to 2004 in The Netherlands.

Methods

Study Design

A historical follow-up study was conducted among patients with DM (type 1 and type 2) compared to matched control subjects without a diagnosis of DM and/or subjects not prescribed glucose-lowering medication.

Setting

Data for this study were obtained from the PHARMO Record Linkage System (PHARMO RLS, Utrecht, The Netherlands), which includes, among other databases, the drug-dispensing records from community pharmacies linked on a patient level to hospital discharge and clinical laboratory records of approximately 2.5 million individuals in defined areas of The Netherlands. These regions are representative of all of The Netherlands [11]. The computerized drug-dispensing histories contain data concerning the dispensing date, the prescriber, the prescribed dosage regimen, the dispensed quantity, and the estimated duration of use. All drugs are coded according to the Anatomical
Patient and Control Selection
All patients with DM (type 1 and type 2) from January 1, 2000
to December 31, 2004 were included as patients. Patients were
defined as diabetic if they used “drugs used in diabetes” (ATC
code A10) or had HbA1c ≥ 6.5 mmol/L or had a hospitalization
for DM (ICD-9-CM codes 250, 251.0–251.4) in the measure-
ment year or in the preceding year. Cardiovascular complications
were defined as having a diagnosis of ischaemic heart disease
(ICD-9-CM codes 410–414), cerebrovascular accident (ICD-
9-CM codes 430–438), peripheral artery disease (ICD-9-CM
code 443.9) or hypertension (ICD-9-CM codes 401–405) or
based on antihypertensive use (ATC code C02, C03, C07, C08,
C09).

The control group comprised subjects without a diagnosis of
DM and/or subjects not prescribed glucose-lowering medication
who were 1:1 matched on year of birth, zip code, eligibility
status, and gender to patients with DM. Subjects were eligible for
selection as controls if they were present and alive in the database
at the cohort entry date of the corresponding case (= index date).
Cases and controls were followed from the index date to the end
of 2004, death, or moving out of the PHARMO area, whichever
came first.

Classification of Diabetic Complications
Diabetic complications, including macrovascular and microvas-
cular complications, were classified into stages 0, 1, or 2 accord-
ing to a modification and extension of the classification proposed
by Brown et al. [12]. Briefly, the classification involved no evi-
dence of complications (stage 0), preevent treatment (stage 1),
and postevent cardiovascular diseases (stage 2). Stage 1 was
assigned if cardiovascular medications (lipid-lowering drugs,
antihypertensives, and cardiac medication) had been supplied for
at least 180 days, and/or at least two specialty visits to a cardi-
ologist had taken place. The use of ≥3 dispensings for eye drugs
(ATC code S01) or hospitalization for cataract surgery (ICD-
9-CM codes: 362, 366, 2505) was also assigned complication
stage 1. Stage 2 was assigned if hospitalization for major
ischemic heart disease, cerebrovascular accident, or peripheral
artery disease was recorded. Hospitalizations for foot, toe and
ankle amputations (procedure codes: 58480, 58470, 58469,
58450, 8462) were also assigned complication stage 2. The
frequency of diabetic complications attributed to DM was
estimated as the difference between the frequency of complica-
tion stages 1 and 2 among patients and that frequency among
controls.

Treatment
To estimate the number of pharmacologically treated DM
patients on a yearly base, the number of DM patients with at
least one dispensing of insulin (ATC code A10A), oral glucose-
lowering drugs (OGLDs; ATC code A10B), or cardiovascular
drugs (ATC chapter C) was determined. Among controls, the
number of subjects with at least one dispensing of cardiovascular
drugs was determined. These dispensings were considered not
attributable to DM. Cardiovascular treatment attributed to DM
in a given year was estimated as the number of patients with DM
with at least one dispensing for cardiovascular drugs, minus the
number of control subjects with at least one dispensing for car-
diovascular drugs in that year.

Diabetes-Related Cost
Direct diabetes-related cost was estimated based on annual cost
of treatment with insulin, OGLD, and cardiovascular drugs, and
on annual DM-related hospitalization costs. Cost related to
treatment with insulin and OGLD were considered among
patients with DM only; these costs among control subjects
were assumed to be negligible. Cost related to treatment with car-
diovascular drugs attributed to DM was calculated as cost of car-
diovascular drugs dispensed to patients with DM minus cost of
hemocardiologic drugs dispensed to control subjects. Annual hospitalization cost estimates were
derived from admission costs. To calculate admission costs, the
costs of hospital charges were calculated per hospital and sum-
marized. These charges included admission day cost, the costs
of diagnostic and therapeutic procedures, and the specialist’s fee
for procedures, tests, operations, and visits. Admission day costs
were the costs of a single hospital and year-specific admission day
and included all costs not related to visits to medical specialists or
procedures [13–15]. All costs were based on charges made to
third-party payers, i.e. insurers or HMOs.

Statistical Analysis
Annual prevalence and cost estimates were extrapolated to
Dutch national estimates using direct standardization. The esti-
mates were stratified by gender and 5-year age groups. These
numbers were extrapolated to the 2004 national age and gender
distribution in The Netherlands by multiplying them with the
ratio of the number of inhabitants in The Netherlands divided by
the inhabitants covered by the PHARMO RLS per gender and
5-year age group [16]. Statistical significance for differences in
proportions of patients over time was tested by the chi-square
test. A P-value of 0.05 or less was considered statistically signifi-
cant. All data were analyzed using SAS programs organized
within SAS Enterprise Guide version 3.0 (SAS Institute Inc., Cary,
NC, USA) and conducted under UNIX using SAS version 9.1.

Results
Characteristics of Patients and Controls
Table 1 shows the characteristics of the 641,200 patients with
DM and their matched controls in 2004. In that year, 90.6% of
patients (and matched controls) were 40 years or older and
46.3% were male. Among patients with DM, 4568 (71.2%) were
classified as having complication stages 1 and 2. Among the
matched controls, this was 2869 (44.7%). Subtracting these fre-
quencies among the controls from the frequencies among the
patients yielded a frequency of patients with complications
attributed to DM of 1699 (26.5%). Among patients with DM,
1622 (25.3%) used insulin and 3869 (60.3%) OGLD. Cardio-
vascular (CV) drugs were used by 4489 (45.0%) patients and
617 (40.8%) controls; subtracting yielded 1871 (29.2%) patients
treated with CV drugs attributed to DM.

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Table 1 Characteristics of patients with diabetes mellitus in the PHARMO database, and extrapolated after standardization to The Netherlands in 2004

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients with diabetes mellitus</th>
<th>Age- and gender-matched controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (×100)</td>
<td>%</td>
</tr>
<tr>
<td>n</td>
<td>6412</td>
<td>100.0</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
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<tr>
<td>0–14</td>
<td>73</td>
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<tr>
<td>15–39</td>
<td>525</td>
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<td>40–64</td>
<td>3292</td>
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</tr>
<tr>
<td>≥65</td>
<td>2522</td>
<td>39.3</td>
</tr>
<tr>
<td>Gender male</td>
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<td>46.3</td>
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<td>Cardiovascular complication stage†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All stages</td>
<td>6412</td>
<td>100.0</td>
</tr>
<tr>
<td>Stage 0</td>
<td>1843</td>
<td>28.7</td>
</tr>
<tr>
<td>Stage 1</td>
<td>3849</td>
<td>60.0</td>
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<td>Stage 2</td>
<td>719</td>
<td>11.2</td>
</tr>
<tr>
<td>Cardiovascular complication stage, attributed to diabetes mellitus‡</td>
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<td></td>
</tr>
<tr>
<td>All stages</td>
<td>6412</td>
<td>100.0</td>
</tr>
<tr>
<td>Stage 0</td>
<td>4712</td>
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<tr>
<td>Stage 1</td>
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<td>20.5</td>
</tr>
<tr>
<td>Stage 2</td>
<td>386</td>
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<td>Treatment‡</td>
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<td>1622</td>
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</tr>
<tr>
<td>OGLD</td>
<td>3869</td>
<td>60.3</td>
</tr>
<tr>
<td>CV</td>
<td>4489</td>
<td>70.0</td>
</tr>
<tr>
<td>Treatment, attributed to diabetes mellitus‡</td>
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<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>1622</td>
<td>25.3</td>
</tr>
<tr>
<td>OGLD</td>
<td>3869</td>
<td>60.3</td>
</tr>
<tr>
<td>CV</td>
<td>1871</td>
<td>29.2</td>
</tr>
</tbody>
</table>

*As defined in reference 12.
†As defined in the Methods.
‡Percentages add up to more than 100% because patients used more than one treatment.
Frequency of cardiovascular disease among matched controls subtracted from number of patients with diabetes in complication stages 1 and 2 as explained in the Methods.
CV, cardiovascular drugs; n, number of subjects; OGLD, oral glucose-lowering drugs.

Prevalence of DM and Macrovascular Complications

Among the total population in The Netherlands (16,000,000), the prevalence of DM increased from 2.8% in 2000 to 4.0% in 2004. More specifically, the prevalence of DM in The Netherlands increased gradually from 454,000 in 2000 to 641,000 in 2004. Figure 1 shows this increase from year to year, by diabetic complication stage (as attributed to DM). Although the absolute number of patients with DM in diabetic complication stage 0 increased, the proportion of patients in stage 0 decreased from 76.4% in 2000 to 73.5% in 2004. Overall, the proportion of patients with complications (stage 1 and 2) among all diabetics increased from 23.6% in 2000 to 26.5% in 2004. The proportion in diabetic complication stage 2 remained approximately stable and the proportion in diabetic complication stage 2 increased from 4% in 2000 to 6% in 2004. Comparing 2004 with 2000, the changes over time were statistically significant \(P < 0.001\).

Treatment

Table 2 shows the number of pharmacologically treated DM patients on a yearly base from 2000 to 2004. Comparing 2004 with 2000, the changes over time were again statistically significant \(P < 0.001\). Whereas the proportion of patients treated with insulin decreased from 27.3% in 2000 to 25.3% in 2004, the proportion of patients treated with OGLD increased from 55.7% in 2000 to 60.4% in 2004. The absolute number of patients treated with OGLD increased with 134,000 from 253,000 in 2000 to 387,000 in 2004; this is equivalent to an increase of 53%.

The number of patients with DM treated with CV drugs increased from 262,000 patients in 2000 to 449,000 patients in 2004, or an increase of 71%. During this period, however, the number of control subjects treated with CV drugs (i.e., considered not attributable to DM) also increased with 73% from 151,000 to 262,000. Combining these numbers results in 111,000 patients treated with CV drugs attributable to DM in 2000 and 187,000 in 2004, or an increase of 68%.

DM-Related Cost

Annual direct cost estimates of treatment with insulin, OGLD, cardiovascular drugs, and annual hospitalization cost estimates are shown in Table 3. Cost estimates are given for patients with DM, control subjects as well as estimates of direct treatment cost attributed to DM. Total direct treatment costs of patients with DM increased from €717,430,000 in 2000 to €4,372,600,000 in 2004. Most of these costs were related to hospitalizations for DM (€508,813,000 in 2000 and €1,016,858,000 in 2004). Nevertheless, the total direct treatment costs of control subjects increased from €275,123,000 to €608,392,000 during this period. Combining these costs resulted in direct treatment cost attributed to DM (i.e., €442,308,000 for 2000 and €822,333,000 in 2004). The largest contribution to this estimate was direct treatment cost related to hospitalizations (i.e., €272,581,000 [62%] in 2000 and €535,672,000 [65%] in 2004).

Overall, per DM patient, the cost of direct treatment attributed to DM increased from €974 in 2000 to €1,283 in 2004, or an increase of 32%. Per 100 members of the total population, this increase was from €2764 in 2000 to €5140 in 2004, or an increase of 86%.

Discussion

In The Netherlands, among the total population, the prevalence of DM increased from 2.8% in 2000 to 4.0% in 2004. Severe cardiovascular complications attributed to diabetes increased from 18,000 to 39,000 patients. Nevertheless, the number of patients treated with antidiabetic drugs has increased less. Cost attributed to DM almost doubled, mainly because of costs related to hospitalizations for DM. In absolute terms, the cost associated with drug treatment and hospitalizations of patients with DM was €1.4 billion in 2004, but at the same time, cost of cardiovascular drugs increased with 71% from €508,813,000 in 2000 to €608,392,000 during this period. Combining these costs resulted in direct treatment cost attributed to DM (i.e., €442,308,000 for 2000 and €822,333,000 in 2004). The largest contribution to this estimate was direct treatment cost related to hospitalizations (i.e., €272,581,000 [62%] in 2000 and €535,672,000 [65%] in 2004).

This is one of the few studies that estimated the year-by-year prevalence estimates of DM and its associated costs in “real-life” population-based setting. Our observations are in line with both international and national observations that demonstrate a strong increase in the prevalence of DM [1,2,17]. Nevertheless, in our study, the advent of new patients with type 2 DM appears to remain in balance with patients progressing from stage 0 to stage 1 and 2. Preventive efforts to diagnose and treat early DM have apparently succeeded in catching up with the increased influx of new, uncomplicated cases with aging, although a decrease was not achieved. This implies a strong achievement with potentially large societal cost-saving impact. Nonetheless, these efforts have not been able to avoid a substantial number of patients progressing to complication stages 1 and 2. This is in line with findings from other studies [18,19].

Our results suggest that an increase in the proportion of complicated cases alone should not be held responsible for the increase in the clinical burden of diabetes currently observed. The
assumption that we made in calculating these figures, however, was that OGLD treatment among control subjects without DM should be set at zero. This may not correspond to the everyday life experience, that subjects who are at risk of developing DM are often treated with these drugs to prevent progression to clinically manifest DM. Nevertheless, one may argue that these OGLD treatments and the costs associated with them should be attributed to the disease burden and economic burden of DM, regardless of whether the diagnosis includes prediabetes.

Our results showed an increase of costs attributed to DM over the period 2000 to 2004. This trend is also observed in many studies investigating the economic burden of diabetes in both Europe and the United States [18–20] and remains a very important issue [17].

Figure 1 Prevalence of diabetes mellitus (DM) in the PHARMO database and the distribution of complication stages (attributed to DM) among prevalent diabetes patients during 2000–2004.

Table 2 For the period 2000–2004, annual numbers of subjects treated with insulin, OGLD and cardiovascular medication are shown for patients with diabetes mellitus and control subjects. Furthermore the numbers of patients treated, attributed to diabetes mellitus, are shown

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n*</td>
<td>%</td>
<td>n*</td>
<td>%</td>
<td>n*</td>
</tr>
<tr>
<td>Patients with diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>454</td>
<td>100.0</td>
<td>510</td>
<td>100.0</td>
<td>546</td>
</tr>
<tr>
<td>Insulin</td>
<td>124</td>
<td>27.3</td>
<td>139</td>
<td>27.3</td>
<td>145</td>
</tr>
<tr>
<td>OGLD</td>
<td>253</td>
<td>55.7</td>
<td>285</td>
<td>55.9</td>
<td>314</td>
</tr>
<tr>
<td>CV‡</td>
<td>262</td>
<td>55.7</td>
<td>306</td>
<td>60.0</td>
<td>341</td>
</tr>
<tr>
<td>Control subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>151</td>
<td>100.0</td>
<td>175</td>
<td>100.0</td>
<td>194</td>
</tr>
<tr>
<td>Insulin</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>OGLD</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>CV‡</td>
<td>151</td>
<td>100.0</td>
<td>175</td>
<td>100.0</td>
<td>194</td>
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<tr>
<td>Treatment attributed to diabetes mellitus</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>124</td>
<td>27.3</td>
<td>139</td>
<td>27.3</td>
<td>145</td>
</tr>
<tr>
<td>OGLD</td>
<td>253</td>
<td>55.7</td>
<td>285</td>
<td>55.9</td>
<td>314</td>
</tr>
<tr>
<td>CV‡</td>
<td>111</td>
<td>24.4</td>
<td>131</td>
<td>25.7</td>
<td>147</td>
</tr>
</tbody>
</table>

n*: number of subjects extrapolated to The Netherlands; OGLD, oral glucose-lowering drugs; CV, cardiovascular drugs.

†Numbers within treatment groups add up to more than total because of multiple treatments per patient.

‡Number of patients with diabetes mellitus treated with cardiovascular drugs minus number of control subjects treated with cardiovascular drugs.
market during this period. We did not correct for these factors because therapies on the market in 2004 were different as compared with those in 2000. We did not include data on the costs of GP visits. Nevertheless, in The Netherlands, these visits are rather inexpensive as compared to the very expensive hospitalizations. The largest part of the costs for DM was determined by hospitalizations for complications (65%), followed by glucose-lowering therapies. This is confirmed by other studies [17–19]. Comparison of the costs attributed to DM as assessed in PHARMO for 2004 (€822 million) with the costs reported by the Dutch National Institute for Public Health and the Environment (€832 million) shows that these costs are approximately the same, whereas the latter included GP visits [2].

A limitation of this study is the fact that macrovascular and microvascular complications of DM had to be summarized in a composite complications score. Although the vast majority of complications in this population (>90% of patients were aged >40 years and likely to have type 2 DM) probably comprised macrovascular complications, the degree of underreport of microvascular complications remains uncertain. This is in part explained by the low degree of registration of microvascular complications in clinical practice [21]. This study therefore calls for further investment into systematic monitoring of eye and foot problems with DM. What also should be mentioned is the fact that the database included noninstitutionalized study subjects (approximately 1% of the patients under study were nursing home residents). It was therefore not possible to generalize conclusions toward this population. Another limitation was that for the matching procedure, no data were available regarding social economic status. Furthermore, we did not test for differences in the outcome variables for the diabetes and nondiabetes groups. In our opinion, this was not relevant as it was not the intention of our study to compare differences between patients and controls. We defined a control group to estimate the “background” costs to determine the costs attributed to DM. Nevertheless, if this had been our intention then we had to analyze our data by pooling the matched samples. Another limitation might be that identification of diabetics (not on medication) from the hospitalization events is problematic because it biases the risk of hospitalization upward relative to the comparison group. Nevertheless, we checked our data and found that on average 0.4% of the diabetics was included solely on hospitalization. As this percentage is rather small, we think the influence of this potential bias is negligible. Finally, we only investigated pharmacological treatment of DM and we realize that this is nowadays only one aspect of diabetes treatment. Nevertheless, data on, for instance, diet and physical activity were not available in our database. However, we know from literature that the group of patients that manages their diabetes on the long-term with only diet and physical activity is rather small [22].

The increased prevalence of uncomplicated DM, which stands out as an evident result, has several implications. Whereas patients in the past have received a diagnosis of “cardiovascular disease,” they may have received a diagnosis of “diabetes with cardiovascular complications” in more recent years because of increased awareness and diagnostic suspicion of diabetes. Dutch national guidelines for preventive treatment in the primary-care setting recommend blood glucose screening on an “ad hoc” basis among individuals at high risk for cardiovascular disease [5]. This practice may lead to large variations in prevalence between countries and regions according to individual physicians’ screening policy. As an example of this, regional specialized screening programs, for example the Hoorn study, have led to substantially higher prevalence estimates than estimates based on Dutch national registration programmes [23]. The potential economic savings that such programmes could achieve are substantial. Nevertheless, these economic implications should be considered in the light of the “background” costs in the general population that will be made anyway because of an increasing burden of cardiovascular disease in an aging population.

In conclusion, the findings of this study show that preventive diagnostic and treatment efforts have succeeded in catching up with the increased influx of new diabetes patients. Nevertheless, these efforts did not prevent direct costs associated with the use of

### Table 3 Annual direct treatment cost of treatment with insulin, oral glucose-lowering drug (OGLD), cardiovascular drugs and hospitalization costs in The Netherlands attributed to diabetes mellitus, 2000–2004

<table>
<thead>
<tr>
<th>Cost type</th>
<th>2000 euros x 1000</th>
<th>2001 euros x 1000</th>
<th>2002 euros x 1000</th>
<th>2003 euros x 1000</th>
<th>2004 euros x 1000</th>
</tr>
</thead>
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<tr>
<td>Direct treatment cost of patients with diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All†‡</td>
<td>717,430</td>
<td>878,515</td>
<td>1,039,217</td>
<td>1,182,210</td>
<td>1,430,726</td>
</tr>
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<td>Insulin treatment</td>
<td>66,358</td>
<td>80,176</td>
<td>88,919</td>
<td>88,370</td>
<td>99,062</td>
</tr>
<tr>
<td>OGLD treatment</td>
<td>33,538</td>
<td>41,752</td>
<td>47,811</td>
<td>54,055</td>
<td>65,047</td>
</tr>
<tr>
<td>CV treatment</td>
<td>113,722</td>
<td>143,820</td>
<td>166,358</td>
<td>193,080</td>
<td>204,759</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>503,813</td>
<td>612,767</td>
<td>738,130</td>
<td>846,705</td>
<td>1,061,858</td>
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<td>Direct treatment cost of control subjects</td>
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<td></td>
</tr>
<tr>
<td>All‡</td>
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<td>428,673</td>
<td>493,737</td>
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<td>65,292</td>
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<td>315,173</td>
<td>363,381</td>
<td>419,064</td>
<td>526,186</td>
</tr>
<tr>
<td>Direct treatment cost attributed to diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>All‡</td>
<td>442,308</td>
<td>507,321</td>
<td>610,544</td>
<td>688,473</td>
<td>822,333</td>
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<tr>
<td>Insulin treatment</td>
<td>66,358</td>
<td>80,176</td>
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<td>99,062</td>
</tr>
<tr>
<td>OGLD treatment</td>
<td>33,538</td>
<td>41,752</td>
<td>47,811</td>
<td>54,055</td>
<td>65,047</td>
</tr>
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<td>CV treatment</td>
<td>69,832</td>
<td>87,799</td>
<td>103,065</td>
<td>118,472</td>
<td>122,552</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>33,538</td>
<td>41,752</td>
<td>47,811</td>
<td>54,055</td>
<td>65,047</td>
</tr>
</tbody>
</table>

†Does not always add up to the total because of rounding.
‡Hospitalizations as defined in the Methods.
‡Cost of diabetes mellitus-related hospitalizations of patients with diabetes mellitus minus cost of hospitalizations of control subjects.
CV, cardiovascular drugs.
antidiabetic drugs and with hospitalizations from doubling. These costs should however be offset to “background” costs in the general population that will be made anyway because of an increasing burden of cardiovascular disease in an aging population.

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References