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Burden of disease of type 2 diabetes mellitus: cost of illness and quality of life estimated using the Maastricht Study

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Abstract

Aims To estimate the societal costs and quality of life of people with type 2 diabetes and to compare these results with those of people with normal glucose tolerance or prediabetes.

Methods Data from 2915 individuals from the population-based Maastricht Study were included. Costs were assessed through a resource-use questionnaire completed by the participants; cost prices were based on Dutch costing guidelines. Quality of life was expressed in utilities using the Dutch EuroQol 5D-3L questionnaire and the SF-36 health survey. Based on normal fasting glucose and 2-h plasma glucose values, participants were classified into three groups: normal glucose tolerance (n = 1701); prediabetes (n = 446); or type 2 diabetes (n = 768).

Results Participants with type 2 diabetes had on average 2.2 times higher societal costs than those with normal glucose tolerance (€3,006 and €1,377 per 6 months, respectively) and had lower utilities (0.77 and 0.81, respectively). No significant differences were found between participants with normal glucose tolerance and those with prediabetes. Subgroup analyses showed that higher age, being female and having two or more diabetes-related complications resulted in higher costs (P < 0.05) and lower utilities.

Conclusions This study showed that people with type 2 diabetes have substantially higher societal costs and lower quality of life than people with normal glucose tolerance. The results provide important input for future model-based economic evaluations and for policy decision-making.

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Introduction

Type 2 diabetes has a direct negative effect on an individual's quality of life and imposes an economic burden on society as a whole [1,2]. Burden-of-disease studies aim to estimate the impact of a given disease in terms of quality of life and economic costs. The results of these studies are used widely in policy decision-making. Accordingly, the results of a burden-of-disease study can provide crucial information to guide setting of priorities in healthcare [3].

There are two approaches to estimating the burden of disease: top-down, which uses national statistics, and bottom-up, which uses more precise primary data [4]. Current published burden-of-disease studies for type 2 diabetes rarely estimate the cost from a bottom-up (person-based) approach in a large population [5–7], nor do they use a societal perspective, i.e. the studies reflect costs regardless of who incurs them [8]. This involves the inclusion of costs outside the healthcare sector, such as productivity losses and informal care. Furthermore, published studies have seldom included a comparator group to assess the incremental cost of type 2

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What's new?

- The high costs of type 2 diabetes, together with its impact on quality of life, place a great burden on both the individual affected and society as a whole.
- People with type 2 diabetes have, on average, 2.2 times higher societal costs and experience a lower quality of life than people without type 2 diabetes.
- The total societal costs for people with ≥2 diabetes complications are 4.4 times higher than total societal costs for people without complications.

diabetes. This information could be beneficial in determining the main target group for preventive interventions. The aim of the present study, therefore, was to gain insight into the societal costs and quality of life (in terms of utilities) of type 2 diabetes, and to compare the results with those of people with normal glucose tolerance and people with prediabetes. Furthermore, we aimed to investigate the associations of diabetes-related complications and other social determinants with the costs related to type 2 diabetes and with the quality of life of people with the disease.

Participants and methods

Study design

This prevalence-based, bottom-up study used data from the Maastricht Study and focused on the economic impact (in monetary terms and utilities) of people with type 2 diabetes as compared to people with normal glucose tolerance and people with prediabetes.

Study population

Data from the Maastricht Study, an observational, prospective, population-based cohort study focusing on the aetiology, pathophysiology, complications and comorbidities of type 2 diabetes, were used. The Maastricht Study is characterized by an extensive phenotyping approach. All individuals aged between 40 and 75 years and living in the southern part of the Netherlands were eligible for participation. Individuals were recruited through mass media campaigns and from the municipal registries and the regional Diabetes Patient Registry via mailings. For reasons of efficiency, recruitment was stratified according to known type 2 diabetes status, with an oversampling of individuals with type 2 diabetes. Further details about the design and methodology of the Maastricht Study can be found elsewhere [9].

The present study included cross-sectional data from people who completed the baseline survey between November 2010 and September 2013. All examinations were performed within a time window of 3 months. Individuals were excluded from this analysis if they had type 1 diabetes or did not complete the resource-use questionnaire. Participants were divided into groups by diabetes status based on a 75-g 2-h oral glucose tolerance test, according to WHO (2006) criteria [10]: participants with a normal fasting glucose value of <6.1 mmol/l and a 2-h plasma glucose value of <7.8 mmol/l and who took no diabetes medication were classified as having normal glucose tolerance; those with impaired fasting glucose (fasting glucose 6.1 to <7.0 mmol/l and 2-h plasma glucose <7.8 mmol/l with no medication) and/or impaired glucose tolerance (fasting glucose <7.0 mmol/l and 2-h plasma glucose ≥7.8 to <11.1 mmol/l and no diabetes medication) were classified as having prediabetes; and those with fasting glucose ≥7.0 mmol/l and/or 2-h plasma glucose ≥11.1 mmol/l, and/or receiving (prescribed) diabetes medication were classified as having type 2 diabetes.

Identification and measurement

This burden-of-disease study used a prevalence-based approach, which estimates the economic burden of a condition over a specific period by estimating the costs attributable to a certain disease in a given timespan [11].

Dependent variables

Costs were measured from a societal perspective, including all costs related to type 2 diabetes and not merely healthcare costs. Cost information was retrieved through a cost questionnaire (Appendix S1) on the frequency of healthcare use and non-healthcare costs over the past 6 months, which was developed based on the state-of-the-art technique used in the UK for resource-use measurement based on patient recall [12]. Total costs were estimated using a bottom-up approach, whereby information on each element of service use is multiplied by an appropriate unit cost and summed to provide an overall total cost [8]. Unit costs per service are shown in Table S1. Total societal costs were calculated as the sum of three cost categories: healthcare costs, patient and family costs, and costs in other sectors.

Total healthcare costs included the total cost of medical visits and the total cost of medicine intake over the preceding 6 months. Drug use was measured via an interview during which trained staff registered the generic names of all drugs being taken. Medication costs were retrieved from the GIPdatabank, which is controlled by the National Healthcare Institute (*Zorginstituut Nederland*).

Total patient and family costs included the informal care received. Participants reported how many hours of help they received, on average per week, over the preceding 6 months, from family or friends (informal care).

Costs in other sectors included the costs of loss of both paid and unpaid work. Participants reported the number of days, over the preceding 6 months, on which they were unable to perform daily activities as a consequence of their health status.

Quality of life was assessed using the Dutch EuroQol 5D-3L questionnaire (EQ-5D) and the SF-36 health survey. Both questionnaires are validated, self-reported utility instrument questionnaires and are meant for generic use [13,14].

Independent variables

Subgroup analyses were conducted for costs and quality of life based on age categories (40–65 and 65–75 years), gender (men/women), socio-economic status measured in terms of educational level [low (no education to lower vocational education), medium (intermediate vocational education or higher secondary education) and high (higher professional or academic education)], and number of diabetes complications for people with type 2 diabetes (0, 1 and ≥2). Diabetes complications included history of cardiovascular disease (yes/no), retinopathy (yes/no based on fundus photographs), neuropathic pain (DN4 scale outcome score of ≥3) [15], and nephropathy (chronic kidney disease, defined as an estimated GFR <60 ml/min per 1.73m^2 and/or a urinary albumin excretion rate ≥30 mg/24 h) [16–18].

Valuation

Healthcare costs and costs of informal care were based on 2014 reference values [19]. Discounting was not necessary. Although the 'friction cost method' is recommended in the Netherlands, loss of paid work was calculated using the human capital method, as this was the only possible option for the available data. The human capital method takes an individual perspective and counts any hour not worked as an hour lost [20]. Participants were asked about their employment status [employed (including type of job), unemployed or retired]. For employed participants, the number of registered days on which they were unable to perform daily activities was considered as loss of paid work. For unemployed or retired people, this was considered loss of unpaid work.

Utilities were calculated from the EQ-5D and the SF-36 health survey scores using algorithms [21,22]. Utilities indicate preference-based health states and range from 0 to 1, where 0 indicates death and 1 indicates full health [23].

Statistical methods

Despite the usual skewness in the distribution of costs, mean values are considered the most appropriate measure for interpreting cost data [24]. The Kolmogorov–Smirnov test was used to investigate the normality of the cost distribution. Both the Kolmogorov–Smirnov test ($P < 0.001$) and the Shapiro–Wilk test ($P < 0.001$) indicated a significant difference from a normal distribution; therefore, bootstrapping (1000 simulations) was performed to calculate 95% CIs, based on the 2.5 and 97.5 percentiles. Non-parametric bootstrapping is a method for testing for statistical differences in costs; it is based on random sampling with a replacement based on people's individual data [25]. Statistical analyses were performed using SPSS v.23 or v.25.

First, average utilities and costs in all three groups were analysed. Second, a multiple linear regression model was performed to calculate the association between several determinants and the square root of the total societal costs. Square root transformation was used to reduce skewness [26]. Determinants included were age, gender and educational level. Diabetes status was added as a determinant to investigate the association of having diabetes on total societal costs while adjusting for other variables. Third, a second multiple linear regression model was performed to further investigate the association of (the number of) complications in addition to having type 2 diabetes, while adjusting for the same remaining independent variables. Last, a generalized linear regression model using a gamma distribution was used to compare the regression models.

Ethics

The study was approved by the institutional medical ethical committee (NL31329.068.10) and the Minister of Health, Welfare and Sports of the Netherlands (Permit 131088-105234-PG). All participants gave written informed consent.

Results

Demographics

Of the first 3451 participants in the Maastricht Study, 2915 were included in the present burden-of-disease study. Individuals were excluded if they had type 1 diabetes (n = 41) or did not complete the resource-use questionnaire (n = 495). Table S2 shows the background characteristics for the different groups. The type 2 diabetes group included more men (69%), was older on average (and more were therefore retired), and included fewer highly educated participants, compared to the other groups.

Costs

Average individual societal costs per group

As shown in Table 1, the average individual total societal costs for the participants with type 2 diabetes were €3,006 per 6 months; this is 2.2 times higher than for participants with normal glucose tolerance (€1,377) and 2.7 times higher than for participants with prediabetes (€1,127).

Bootstrapping results showed a significant difference in total societal costs for participants with type 2 diabetes in comparison to both participants with prediabetes and those with normal glucose tolerance. No significant difference in total societal costs was found between participants without type 2 diabetes and those with prediabetes.

The number of users, mean resource use and mean costs per person are shown in Tables S3–S5 . An increase in mean resource use per person and a relative increase in the proportion of users resulted in higher total societal costs

Table 1 Mean costs per person per group based on diabetes status over a 6-month period

	Normal glucose tolerance (*n* =1701)	Bootstrap	Prediabetes (*n* = 446)	Bootstrap	Type 2 diabetes (*n* = 768)	Bootstrap
General practitioner	€47		€60		€95	
Medical specialist	€85		€89		€188	
Paramedic	€82		€77		€110	
Mental health	€38		€17		€36	
Medicines	€96		€196		€470	
Hospitalization	€29		€22		€89	
Paid home care	€210		€216		€1119	
Total healthcare costs	€587	586 (431–810)	€676	676 (471–967)	€2108	2,107 (1451–2910)
Informal care	€383		€237		€514	
Total patient and family costs	€383	382 (233–543)	€237	237 (96–429)	€514	514 (295–801)
Paid work	€392		€202		€342	
Unpaid work	€15		€11		€42	
Total costs in other sectors	€407	406 (306–511)	€213	213 (94–385)	€384	384 (234–551)
Total societal costs	€1377	1,376 (1,087–1,685)	€1127	1,127 (810–1,499)	€3006	3,006 (2,185–3,994)

for participants with type 2 diabetes in comparison to participants with normal glucose tolerance or those with prediabetes. Paid home care is the main cost driver for societal costs. The largest difference in resource use was seen for general practitioner visits, hospitalized days and days of unpaid work loss.

Costs: subgroup analyses

For each group, the total societal costs were higher for participants in the 40–65-year age category than for those in the 65–75-year age category, as shown in Fig. S1. For each group, women had higher total societal costs (Fig. S2). In all sectors, participants with a low level of education had higher costs than participants with a medium or high level of education (Fig. S3). The total societal costs for participants with type 2 diabetes but without complications were higher than the average costs for participants with normal glucose tolerance. For participants with type 2 diabetes and one complication, the total societal costs were 1.6 times higher and for participants with two or more complications, the total societal costs were 4.8 times higher (Fig. S4).

Costs: multiple linear regression

Multiple linear regression analyses were performed to examine the association of different variables on the square root of the total societal costs. A significant regression equation was found [$F(6,2914) = 26.980$; $P < 0.001$] with an R^2 of 0.053. A high level of education ($\beta = -4.40$, $P = 0.003$), age ($\beta = -0.19$, $P = 0.013$), being female ($\beta = 4.00$, $P < 0.001$) and having type 2 diabetes ($\beta = 16.89$, $P < 0.001$) were found to be significant determinants of the square root of the total societal costs (Table 2). In Table 3, the association of costs with the number of complications was investigated for participants with type 2 diabetes. This model [$F(6,767) = 6.572$; $P < 0.001$] with an R^2 of 0.049, showed that having two or more complications was a significant determinant of higher total societal costs ($\beta = 22.61$, $P < 0.001$). Having one complication was not found to be a significant determinant of higher costs. Examining the association using generalized linear model regression with a gamma distribution yielded similar results regarding significant predictors of total societal costs. Medium education level also had a significant effect (Tables S6 and S7).

Utilities

Mean utility per group

The utilities derived from the EQ-5D are shown in Table 4; results show an average utility of 0.92 for people with normal glucose tolerance, an average utility of 0.91 for

Table 2 Multiple linear regression results: the association of included determinants on the square root of the total costs

	Parameter estimates, β	95% CI Lower bound	95% CI Upper bound	Significance
(Constant)	29.18	18.602	39.757	$P < 0.05$
Medium education	–2.00	–5.084	1.078	n.s.
High education	–4.40	–7.254	–1.543	$P < 0.05$
Gender (women)	4.00	1.585	6.421	$P < 0.05$
Age in years	–0.19	–0.341	–0.040	$P < 0.05$
Prediabetes	2.29	–1.108	5.681	n.s.
Type 2 diabetes	16.89	13.973	19.794	$P < 0.05$

n.s., nonsignificant. $P < 0.05$ indicates statistical significance.

Table 3 Multiple linear regression results: the association of the number of diabetes complications on the square root of the total cost for people with type 2 diabetes

Type 2 diabetes complications*	Parameter estimates, β	95% CI Lower bound	Upper bound	Significance
1	3.366	–3.07	9.80	n.s
≥2	22.607	14.48	30.74	$P < 0.05$

n.s., nonsignificant. $P < 0.05$ indicates statistical significance. *Corrected for determinants: high education, gender, age.

Table 4 Uncorrected bootstrapping results for the EQ-5D and the SF-36 health survey: mean utility and 95% CI per group

	Normal glucose tolerance (n = 1701)	Prediabetes (n = 446)	Type 2 diabetes (n = 768)
SF-36 health survey	0.81 (0.81–0.82)	0.81 (0.80–0.82)	0.77 (0.77–0.78)
EQ-5D	0.92 (0.91–0.92)	0.91 (0.90–0.92)	0.86 (0.84–0.87)

EQ-5D, Dutch EuroQol 5D-3L questionnaire.

people with prediabetes and an average utility of 0.86 for people with type 2 diabetes. The utilities derived from the SF-36 health survey were consistently lower than the utilities derived from the EQ-5D; however, both indicated the same differences between groups. The mean utilities derived from bootstrapping were equal to the mean utilities derived from the data. Confidence intervals indicated a significant difference in utility between participants with type 2 diabetes and those with normal glucose tolerance, and between participants with type 2 diabetes and those with prediabetes.

Utilities: subgroup analysis

Both the EQ-5D and the SF-36 health survey (Tables S8 and S9) showed consistently lower utilities for people with type 2 diabetes (0.86 and 0.77) than for the participants with normal glucose tolerance (0.92 and 0.81) or prediabetes (0.91 and 0.81). For the subgroup analyses, lower utilities (for both EQ-5D and SF-36) were found for the lower age category and for women. Although not significant, people with a medium level of education had higher utilities than those with a low level of education, but lower utilities than people with a high level of education. In addition, a higher number of diabetes complications was associated with a lower utility score.

Discussion

This study is the first study to report the societal costs and quality of life (in terms of utilities) of type 2 diabetes and compares these results with those of people with normal glucose tolerance and people with prediabetes. The societal burden of individuals with type 2 diabetes was on average €3,006 (€2,185–€3,994) per 6 months, of which €2,108 was attributable to the healthcare sector. Per year, the societal costs amounted to €6,012 per person for participants with type 2 diabetes. These costs were 2.2 times higher than for participants with normal glucose tolerance. Paid home care was identified as the main cost driver, although only a small percentage of the participants received paid home care. This might be explained by its high standard deviation.

With regard to utilities, both the EQ-5D and the SF-36 health survey showed that those with type 2 diabetes had a lower average utility, by 5–7%. For both costs and utilities, no difference was found between participants with normal glucose tolerance vs those with prediabetes.

Subgroup analyses highlight the impact of diabetes complications. Participants with ≥2 complications of type 2 diabetes had 4.4 times higher societal costs than participants with type 2 diabetes without complications. Moreover, quality of life was lower for participants with one or multiple complications. However, the R^2 values of the regression analyses suggest that 5% of the variability within the data is explained through the derived models. Subgroup analyses also showed that women had higher resource use than men, which is in line with previous studies [27,28]. There is not one single explanation for these differences between genders [27], however, as characteristics among the three study groups differed, comparisons should be interpreted with caution.

Other cost-of-illness studies showed similar results in terms of costs of type 2 diabetes, even when using a different methodology [5–7]. The comparison with normal glucose tolerance and prediabetes, the number of participants, the adoption of a societal perspective, and the use of a bottom-up approach for costing are strengths of the present study. We believe that the recruited sample is representative of the Dutch type 2 diabetes population. The study also has several limitations. First, use of a self-reported questionnaire to estimate healthcare consumption may have led to recall bias. Second, to calculate productivity losses it was assumed that inability to perform daily activities resulted in temporary sick leave; however, as it is possible that not all participants took days off, this may have led to an overestimation. Third, as only people within the age range of 40–75 years are included in the Maastricht Study, the representativeness of the study cohort for the elderly population with type 2 diabetes is limited. Fourth, the complication rate for people with type 2 diabetes enrolled in this study was relatively low in comparison with other studies [29]. As complications increase total societal costs, this could have led to an underestimation of the impact of type 2 diabetes.

The methodology used in the present study could serve as a standard for future burden-of-disease studies. Future research could first investigate the difference between individuals with normal glucose tolerance and prediabetes on a larger scale, as there were no significant differences observed in this study. Future research could also investigate which factors have a predictive role regarding the use of healthcare for the different diabetes statuses. Last, as some studies calculating costs of diabetes in relation to glycaemic control have shown different results [30,31], future research could investigate the costs of diabetes with diabetes as an interval scale (e.g. glucose tolerance levels) instead of the present ordinal scale (yes/no).

This study showed the burden of type 2 diabetes and gave better insight into the costs attached to type 2 diabetes and the association with an individual's quality of life. These findings address the need to have better insight into diabetes care costs [32] and can be used in model-based economic evaluations to investigate the cost-effectiveness of diabetes-related interventions. Policymakers could use the results of this study for prioritizing between diseases to guide efficient resource allocation.

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Competing interests

None declared.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Fig S1. Subgroup analyses based on age categories (40-65 years and 65-75 years), resulting in average costs per sector per group.
Fig S2. Subgroup analyses based on gender (men/women), resulting in average costs per sector per group.
Fig S3. Subgroup analyses based on educational level (low, medium, high), resulting in average costs per sector per group.
Fig S4. Subgroup analyses for participants with TYPE 2 DM based number of diabetes complications (0, 1, ≥2), resulting in average costs per sector per group.
Appendix S1. Cost questionnaire.
Table S1. Unit costs based on Dutch costing guidelines.
Table S2. Background characteristics of all participants per group based on diabetes status.
Table S3. Number of users, mean resource and mean costs per person for participants with normal glucose tolerance over a 6-month period.
Table S4. Number of users, mean resource-use and mean costs per person for participants with prediabetes over a 6-month period.
Table S5. Number of users, mean resource-use and mean costs per person for participants with type 2 diabetes over a 6-month period.
Table S6. Generalized linear regression model using gamma distribution - the association of included determinants on total societal costs.
Table S7. Generalized linear regression model using gamma distribution - the association of the number of diabetes complications on the total societal cost for people with type 2 diabetes.
Table S8. Utilities derived from the EQ-5D per group, including SD, for different subgroup analyses.
Table S9. Utilities derived from the SF-36 per group, including SD, for different subgroup analyses.