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Societal Costs of Diabetes Mellitus 2025 and 2040—Forecasts Based on Real World Cost Evidence and Observed Epidemiological Trends in Denmark

Camilla Sortsø[1*], Martha Emneus[2], Anders Green[3], Peter Bjødstrup Jensen[3], Thomas Eriksson[4]

[1]Centre of Health Economics Research (COHERE), Department of Business and Economics, University of Southern Denmark, Copenhagen, Denmark
[2]Institute of Applied Economics and Health Research (ApEHR), Copenhagen, Denmark
[3]Odense Patient Data Explorative Network (OPEN), Odense University Hospital, University of SouthernDenmark, Copenhagen, Denmark
[4]Institute of Applied Economics and Health Research (ApEHR), Copenhagen, Denmark
Email: *caso@sam.sdu.dk

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Abstract

Aim: The objective is to contribute with real world evidenced economic forecasts of diabetes attributable costs in 2025 and 2040 differentiated according to patients' morbidity status which is a novel approach within forecasting. Methods: Method of forecasting is based on an annual calendar year prediction of diabetes attributable costs by using the BOX-model, an established and tested epidemiological transition-state model. The study population includes all Danish diabetes patients presented in 2011 (*N*= 318,729) according to the Danish National Diabetes Register. Forecasting is based on individual patient data from 2000 to 2011 for incidence, mortality, patterns of morbidity and complication rates combined with demographic population projections from Statistics Denmark. The 2011 estimation of diabetes attributable costs were applied to the epidemiological framework. Forecasting was performed for three different epidemiological scenarios.Results: Our three epidemiological scenarios indicate that within the shorter time span increases in the prevalent population are difficult to change primarily due to the already achieved historic improvements in diabetes mortality and morbidity. These will approximately double societal costs of diabetes in the next 10 years,assuming current trends in morbidity and mortality are maintained.The resulting diabetes population will incur three times current costs in 2040.A 20% re-

*Corresponding author.

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duction in cost per PYRS shows how the relative distribution of patients with complications is expected to change over time with patients living better with their disease and hence incur a lower demand for health and nursing care services.

Keywords

Forecasts, Cost of Illness, Diabetes Mellitus, Health Care Costs, Register Research, Societal Costs

1. Introduction

Chronic diseases are one of this century's greatest threats towards public health with almost epidemic prevalence increases globally and expectations of significant increases in the future [1]. Diabetes Mellitus is, with around 350 million people globally suffering from this disease [2] [3], one of the most burdensome chronic diseases associated with major disability, reduced quality of life and shortened length of life [2] [4].

Various factors are expected to cause future increase in the prevalence of diabetes: demographic changes[5], sedentary life styles and obesity [6]-[8], improved survival [9] [10] epidemiology [11], screening efforts [12] and new morbidity patterns implying that diabetes is increasingly seen in younger ages [13] [14]. Management of the increasing diabetes population implies, among others, an economic challenge, which societies must face, as diabetes patients require increased health care, pharmaceuticals and nursing services for their remaining lifetime[4] [15] [16]. Long term models can identify where a society may be heading, providing policy makers with a foundation on which decisions concerning future strategic prioritization can be grounded [17].

Forecasts of the burden of diabetes exist in great numbers in the literature, see for example, King *et al*. 1998 [18],Bagust *et al*. 2002 [19], Huang *et al*. 2009 [20], Mainous *et al*. 2007 [21] or Tunceli *et al*. 2009 [22]. Our forecasting model (the BOX-model) is an established and tested epidemiological disease model, which has proven its global applicability for different diseases with largely accurate predictions showing only nonessential deviations[9] [23] [24]. The BOX-model is simple and intuitive, based on epidemiological drivers observed over more than a decade and economic cost estimates for 2011 calculated on the individual level from national registers.

Based on a comprehensive epidemiological framework, this study forecasts diabetes attributable costs in Denmark for the period 2012-2040 according to sectors and patient's morbidity status. Denmark has optimal conditions due to data availability, coverage of the diabetes population and richness of information in national registers [25]. In addition, Denmark is a typical European country in terms of treatment availability and population structure. The study was part of a large-scale register based on observational investigation, the Diabetes Impact Study 2013 [26], which investigated epidemiological, health economic and socioeconomic aspects of diabetes in Denmark [11] [16] [27].

2. Method

Estimating the size of future costs attributable to diabetes, the epidemiological dynamics underlying the prevalence of diabetes must be taken into account. Each year, new patients are diagnosed, patients develop complications and yet other patients will die. These dynamic structures are appreciated in the forecasts through the underlying epidemiological framework, presented in the BOX-model.

2.1. The BOX-Model

To model the future prevalent diabetes population, this study uses a simple multi-state transition model, the BOX-model, a flexible epidemiological framework, based on individual data from the entire Danish diabetes population. The BOX-model, (**Figure 1**) has been validated [9] and thoroughly described elsewhere [11].

In the BOX-model, an individual is either non-diabetic (population at risk) or belongs to one of the diabetic complication groups: CG0, no complications; CG1, minor complications or CG2, major complications. ICD-codes defined for each complication group is given in the supplementary material (A). Health states in the model are mutually exclusive and collectively exhaustive meaning that each patient can only be in one state in a cycle and must be in a state in each cycle. Cycles are measured in calendar years [28]. Irreversibility is assumed and,therefore,

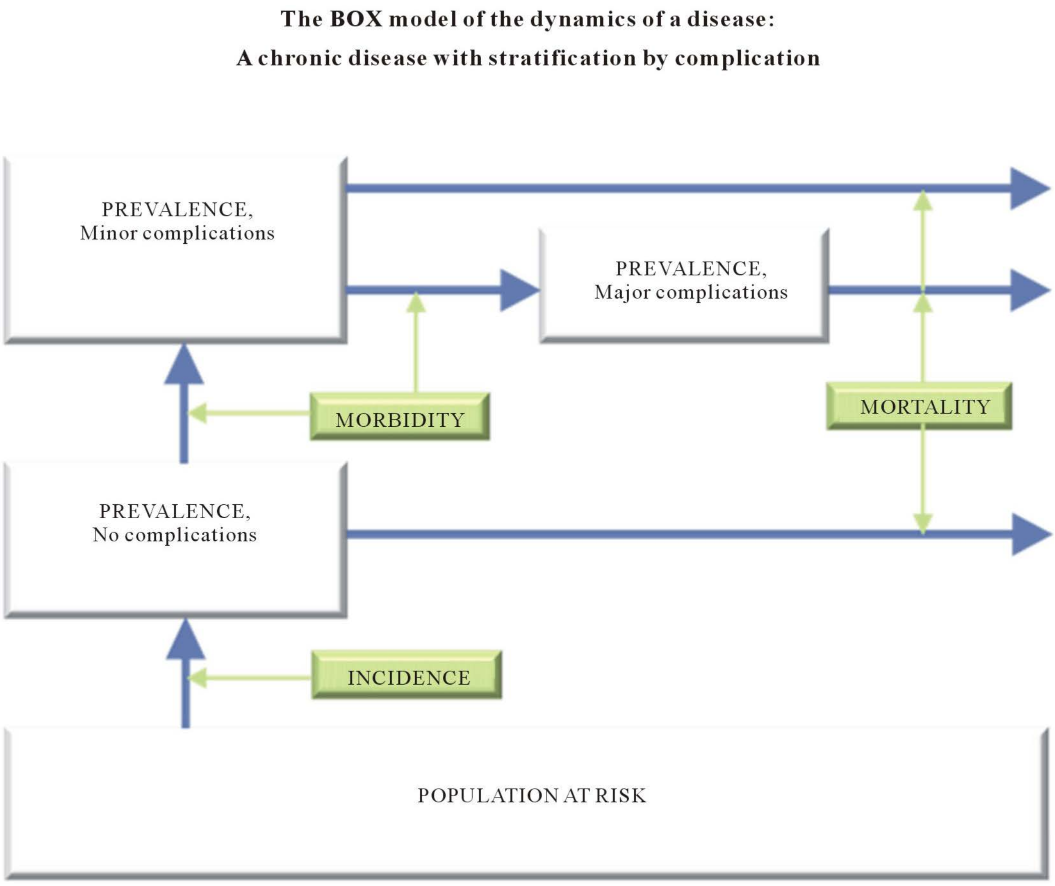

Figure 1. The BOX-model.

patients can only move forward in the model. Influx (new incident cases) and outflux (mortality) as well as influx to each of the complication groups were accounted for on an annual basis. Forecasting is based on patient groups defined by gender and age at diagnosis in 25 year age intervals.

2.2. Study Population

The study population was based on the entire diabetes population in Denmark in 2011, adjusted according to shortcomings in the Danish National Diabetes Register, specified elsewhere [29], *N* = 318,729. Person years (PYRS), defined as 365 person days, *N*=297,378 in 2011 were applied. The study population was compared to the Danish diabetes-free population (*N*= 5,261,714) and to a matched (gender, age and municipality of residence) control population from the diabetes-free population (*N*= 1,462,872).

2.3. Data Sources for Epidemiological Forecasting

The epidemiological forecasting was based on observed individual patient level data on the entire Danish diabetes population from 1997 through 2011 through Danish national registers [11]. Transition probabilities between states were extrapolated from the observed data resulting in a prevalence (PYRS) in each health state in every calendar year. This means that the exact number of projected PYRS in 2011 deviates from the observed number, however the deviation is <1%. To facilitate comparison with earlier studies [11] [16] [27], we state the observed numbers from 2011. PYRS were stratified by gender and age at diagnosis in 25 year age intervals. The diabetes-free population, and hence population time at risk of developing diabetes, for each calendar year until 2040 was calculated from demographic population projections from Statistics Denmark based on recent trends for vital demographic events: birth rate, death rate, immigration, emigration and naturalization, converging towards a long time perspective level based on annual forecasts [29]. This epidemiological forecasting make up the framework on which 2011 cost estimates are added.

2.4. Data Sources for Economic Forecasting

Age at diagnosis, gender and complication status, among other characteristics, influence on patients costs [16]. Estimates for diabetes attributable costs according to these characteristics were calculated and applied to the epidemiological model.Diabetes attributable costs for 2011 were calculated as the difference between total costs of a person with diabetes and the expected total costs given the annual resource consumption of the control population stratified according to gender and five-year age intervals. The included cost components are listed in **Table 1** along with measurement of cost components and described in more detail elsewhere [16].

Table 1. Cost components, cost units and method of calculation.

Cost component	Cost unit and method of calculation
Inpatient and outpatient services delivered in Danish hospitals registered in DNPaR	Diagnosis Related Grouping system tariffs, year 2012 [30].The DRG tariff system is developed for administrative purposeand based on rough average costs across hospitals for specific diagnostic groups. Excludes interest and depreciation of buildings and equipment while other overhead costs are included.
Primary care services delivered by general practitioners andprivately practicing specialists such as: dentists, physiotherapists, chiropractors and chiropodists who are registered in DNHSR	Reimbursement fees between the National Health Insurance scheme and private practicing physicians are used as cost units. General practitioners are compensated by regions through a combination of per capita fee (app.30% of total) and fee for service (app. 70%) [31]. To reflect this payment scheme in the unit cost, 43.8% of the fee for service in general practice was added on top. Overhead costs covered by capitation fee were, hence not distributed across numbers of visits, as would have been most appropriate, but by resource burden.
Prescribed pharmaceuticals dispensed by Danish pharmacies and registered in DNPrR (Pharmaceuticals consumed in hospitals are included in DRG-tariffs. Over-the-counter drugs are not included in the statements)	Total Sales Price (TSP) includes patient Out of Pocket Payments (OPP), since costs of prescribed pharmaceuticals are shared between the patient and the primary health care sector by a copayment scheme, where patients are reimbursed according to their need. These costs were aggregated, since total costs are measured regardless of who pays. While pharmaceutical consumption includes value added tax (VAT), Danish health care services are exempted from VAT. Given that VAT is 25% in Denmark, 20% of pharmaceutical consumption was subtracted to get comparable net costs.
Costs of living in a nursing home/sheltered accommodation Based on individually registered address in SD	Unit cost was calculated as total annual costs of running these facilities divided by the number of inhabitants, 51,486 DKK (exclusive of capital costs) per person living in nursing homes per year. Hereto was added average number of hours of nursing received by persons living at nursing homes or sheltered accommodation calculated by SD equal to 18.6 hours per week per person or 565,283 DKK applying a unit cost of 588 DKK per hour. In total 616,769 DKK per person per year. The cost unit included overhead and administration but not capital costs.
Referred monthly personal nursing and practical care in own home per year based on individual registrations in SD	Registrations on volume of services were, incomplete whereas whereas number of individuals receiving care appeared rather completely registered. Therefore, national volume estimates from SD were applied together with the number of PwD receiving care compared to the expected number given the observed frequency among the diabetes-free population, in gender and age strata, to estimate the amount of nursing services received attributable to diabetes. Average number of hours of nursing received by persons living in their own home was estimated to be 3.6 hours. The unit cost was defined as average costs for one hour of nursing delivered in the given year (calculated as the total costs for nursing divided by number of hours of care delivered in the year),based on data published by SD, equal to 588 DKK per hour.
Home nurse visits per year based on individual registrations in SD	Number of visits by home nurse appeared rather completely registered on an individual basis. Unit cost was calculated as average costs for home nurses per inhabitant times the Danish population divided by the total number of services,based on data published by SD.One service is estimated to be 456 DKK.

Continued

Productivity loss based on data from SD	Lost productivity attributable to diabetes were accounted for through an estimation of 1) Annual mean gross income difference from expected income given educational level, gender and age; 2) Premature mortality; 3) Abseentism. 1) Sum of absolute difference in annual gross income between PwD and controls aggregated for patients older than 14 years and younger than 69 in strata by gender, age in 5 year intervals and four educational levels (1: < 11 years of education; 2: < 16years; 3: < 18 years and 4: 18+ years) 2) Sum of annual foregone income due to lost years of productivity in cases of premature death for: 2a) 2011 and 2b) productivity loss in 2011 due to deaths attributable to diabetes occurred prior to 2011. Since data is not available on deaths attributable to diabetes for the past 45 years, we used attributable deaths in 2011 and the production loss that will incur in the future until the age of 69 to mirror the foregone production well knowing that this method builds on the simplified assumption that diabetes mortality and labour market patterns the past decades have not changed. For persons between the age of 15 and 69, number of relative deaths by gender and 10-year age group was compared between PwD and controls and the difference is assumed to represent deaths attributable to diabetes. Number of attributable deaths in each strata was multiplied with the average wage of a diabetes-free person in that strata. 2a) Strata were aggregated and the sum was divided by 2 assuming deaths are equally spread over the entire calendar year. 2b) Mid age in each age-interval was used as proxy and then number of years until the age of 69 was calculated and multiplied with number of attributable deaths in the given strata again multiplied with the average annual gross income among a diabetes-free person in that strata. 3) Number of days of absence due to diabetes is calculated based on literature estimates of 3 extra days a year. Daily wage is calculated as the mean annual income among PwD divided by 200 working days.
SMBG costs (meters and sticks) and insulin pumps	Cost of SMBG (for the 22% of PwD using insulin) was estimated on the basis of a study of SMBG costs in Canada to annually 860 US$ equivalent to 6175 DKK (2011 prices) [32]. According to the Danish Ministry of Health and the Danish Diabetes Association [33] pumps were used by approximately 2100 PwD and the annual cost ranged from 22,000 to 39,000 DKK in 2010. For 2011,we have applied a conservative cost estimate of 22000 DKK for80% of all T1 children (0-14 year) and for 5% of the rest of the T1 population in total amounting to 2450 PwD. Censors are not included in this cost and would approx. double the annual cost of pumps.
Appliances (blind assistance, protese crus, femur, wheel chairs, sticks)	Unit costs of blind assistance was calculated on the basis of the MTV report [34]and includesassistance outside home, sticks and guide dogs, IT solutions for blind parents, blind library appliances and amounted to 99,137 DKK per year (2011 prices). The cost cover needs for the 1.1% -1.6% (amounting to approx. 3372 persons) of the diabetes population that is considered socially blind [34]. The cost of a crus and femur prosthesis was estimated to be respectively 17,000 and 44,000 DKK per year. In 2011, 1348 (crus) and 768 (femur) persons with diabetes lived with an amputation and respectively 75% and 50% of those were assumed to have a prosthesis. The rest of the amputated persons are assumed to use wheel chairs. The cost of wheel chairs was calculated from an average of different chair types (ranging from a cost of 2,589 to 34,109 DKK) [35]to an annual average cost of 2,450 DKK. 25% of diabetes patients (above 45 years) with complications are assumed to need a wheel chair.
Prevention, education and psychological assistance	A total of 4 hours per diabetes patient under 29 years (3%) and all persons diagnosed during 2011 (10%) and 1 hour for 50% of the rest of the diabetic population was applied as an estimate of the received support in any of the following forms (prevention initiatives, educational training or psychological assistance, telemedicine etc.) An hourly cost of 588 DKK was applied.
Patients' own time to monitor their disease and informal care takers support for relatives (0-15 years and above 75 years)	According to an evaluation [36] [37] by diabetes educators, experienced diabetes patients controlled by oral agents would use 2 hours a day when asked to follow the American Diabetes Association self-care recommendation and elderly and handicapped patients would use more. Exercise and diet, required for self-care of many chronic conditions, are the most time-consuming tasks. We included a conservative estimate of patients' time (1 hour per week per patient) and informal caregivers' time (8 hours per year per patient) at a cost of 25% of the productive value.
Depreciation	Data on costs of capital depreciation in secondary care and for nursing services were included with 20% of secondary care and nursing costs.

Given that cost estimates for the year 2011 were originally calculated according to age in five year intervals,these estimates were recalculated to age at diagnosis in 25 year age groups. Due to data limitations, this recalculation was not possible for nursing services and additional cost components. Therefore, we applied the same cost structure between age and age at diagnosis for these two cost components as found for health care costs. Furthermore, we maintained total attributable cost estimates calculated on age groups and applied the estimated cost structure between age and age at diagnosis across strata based on these totals. Cost calculations of productivity loss due to premature mortality were calculated based on assumptions concerning the mortality rate. Hence, the model considers the annual assumed mortality rate and adjusts productivity loss due to premature mortality correspondingly. Calculation of depreciation of capital was based on the size of the secondary health care sector cost component. All costs were calculated in fixed 2011 values.

3. Scenarios

Comparison between three contrasting scenarios was deployed. Each scenario was related to the same base year (2011) and outlines a situation specified according to observed epidemiological trends in incidence, mortality and complication progression from 1997-2011. The three scenarios represent: 1) continuation of observed epidemiological trends under the assumption that these trends will continue as historically observed (core); 2) continuation of the observed trends regarding mortality and complication rates but a constant rate of incidence as observed in 2011, reflecting the assumption that incidence will stabilize and discontinue the increase (intermediate); 3) all epidemiological drivers are kept constant on the level observed in 2011 to reflect no further improvements in mortality and morbidity among diabetes patients and no further incidence increase (constant). Scenarios are presented in **Table 2**.

For each scenario, the BOX-model calculates a distribution of PYRS. By adding estimates of diabetes attributable costs specific for gender and age at diagnosis, total diabetes attributable sector costs for every calendar year are arrived at.

Table 2. Epidemiological scenarios.

Scenario	Drivers	Description
Core Continuation of trends	Incidence	Continuation of 2001-2011 observed increasing trend
	Mortality	Continuation of 2001-2011 observed decreasing trend until X
	Complication rate transitions	Continuation of 2001-2011 observed trends: reduction in transition from CG0 to CG1 and CG2 until X
Intermediate Stagnation in incidence + continuation of trends in morbidity and mortality	Incidence	Stabile rate as observed in 2011
	Mortality	Continuation of 2001-2011 observed decreasing trend until X
	Complication rate transitions	Continuation of 2001-2011 observed trends: reduction in transition from CG0 to CG1 and CG2 until X
Constant Continuation of 2011 level	Incidence	Stabile rate as observed in 2011
	Mortality	Stabile rate as observed in 2011
	Complication rate transitions	Stabile rate as observed in 2011

4. Economic Potentials

The cost forecasts mirror the observed cost structure and level in 2011, though it is obvious that the future will not hold the same investments and treatment/cost structures as in 2011. A prerequisite for the proposed epidemiological scenarios is, therefore, to capture some structural changes and potential relevant investment cases. On the one hand, the continuation of treatment improvements as assumed in scenarios (core and intermediate) cannotbe expected without some future investments in pharmaceuticals and health care. On the other hand, the cost levels in health care, nursing and pharmaceuticals will ultimately be decided, by what is politically possible in the years to come. Hence, the challenge is to quantify implications hereof for the cost forecasts. To accommodate this in our model, we suggested a number of hypotheses representing, on one hand, potentials for freeing of resources if certain efficiency improvements are realized or of a given political or administrative initiative and, on the other hand, budget limitation or economic potentials of a given investment. Based on the Core scenario each of the hypotheses was estimated under the assumption of everything else held constant.

Hypotheses, rationale and corresponding model adjustments are described in **Table 3** and **Table 4**.

Table 3. Description of hypotheses, rationale and model adjustment method: economic potential of investments.

Hypothesis	Rationale	Model adjustment method
Economic potential of a given investment		
H1: Increased investments in primary care	Focus on patient self-care initiatives and improved health among patients with diabetes can be expected to move patients from secondary to primary care.	5% annual increase in costs per PYRS in primary care (200% increase in 2040)
H2: Increased investments in pharmaceuticals	Investments in new and better pharmaceuticals plus a more proactive medication of PwD can be expected to increase pharmaceutical costs.	2.5% annual increase in costs per PYRS for pharmaceuticals
H3: Increased investments in secondary prevention such as telemedicine	Telemedicine for patients with chronic diseases as diabetes are in rapid development [38] [39]. Investments in telemedicine have the potential to reduce patients' need for health care services and improve their daily regulation. Increased investments in secondary prevention to increase self-management can be expected to improve the regulation of diabetes patients, who have not yet developed complications from their disease.	2.5% annual increase in cost per PYRS for —H3a SMBG —H3b patient education —H3c patients' own time for managing their disease

Table 4. Description of hypotheses, rationale and model adjustment method: potential for freeing of resources of a given initiative.

Hypothesis	Rationale	Model adjustment method
Potential for freeing of resourcesof a given political oradministrative initiative		
H4: Efficiency improvements in a) the health care sector b) nursing services	Annual productivity gains are achieved in the Danish health care sector/nursing sector. In the period 2003-2011, the annual productivity gains in the Danish health care sector has been 2.3% and in 2011 alone 5.3% [40].	Annual 1% reduction ofcostper PYRS for H4a—primary andsecondary care H4b—all nursingcomponents
H5: Reduced usage of nursing services	Patients with diabetes live longer and better with their diabetesand in comparison with 2006 estimates, the 2011 cost structureimplies relatively less costs fornursing [16]. This can also be aconsequence ofstructural changes in the Danish nursing sectorwith reduced services. If these developments are continued, theneed for/usage of nursing services per PYRS can be expectedto further decrease over time. The number of nursing homesand similar housing for elderly in 2011 have decreased with62% of the level in 2005 [41].	Annual 2.5% reductionperPYRS in all nursingcost components
H6: Reduced usage of secondary care services		Annual 2.5% reduction in costs per PYRS in secondary care
H7: Reduced productivity loss among patients in CG0	Improved regulation of diabetes patients who have not yet developed complications from their disease. If CG0 patients were able to contribute more equal to thediabetes-free population on the labour market, productivitylosses due to lower income and excess absence could bedecreased.	Annual 2.5% reduction perPYRS in productivity lossdue to difference in annualincome and excess absence for patients in CG0

5. Results

All cost estimates are presented in 2011 EUR based on a conversion rate from DKK to EUR of 7.4647 DKK.

5.1. Total Attributable Costs of Diabetes 2011-2040—The Three Scenarios

We have previously estimated total attributable costs of diabetes to the Danish society in 2011 to be at least 4.27 billion EUR, corresponding to 14,349 EUR per PYRS [16]. Forecasting estimates of total diabetes attributable costs and costs per PYRS for each cost component in the three epidemiological scenarios are presented for the years 2025 and 2040 in **Table 5**. More detailed specification of distribution of costs according to sectors and complication groups together with epidemiological indicators are given in supplementary material (B).

Table 5. Prevalence, total attributable costs and cost per PYRS 2011, 2025 and 2040 in three epidemiological scenarios.

Scenarios		CORE		INTERMEDIATE		CONSTANT	
Prevalence	2011	2025	2040	2025	2040	2025	2040
Total	300.769	644.738	1.183.630	564.781	862.623	516.239	660.102
Comp 0	166.327	372.443	708.091	320.497	504.314	270.745	320.276
Comp 1	57.415	123.738	219.485	112.333	171.215	106.545	139.486
Comp 2	77.027	148.557	256.055	131.951	187.094	138.949	200.340
Costs1.000 EUR	2011	2025	2040	2025	2040	2025	2040
Health care	725.464	1.431.167	2.455.206	1.286.964	1.842.157	1.315.790	1.850.934
Pharmaceuticals	149.954	306.039	532.748	274.265	400.288	267.676	359.782
Nursing	849.716	1.619.462	2.706.185	1.468.785	2.063.159	1.544.347	2.236.536
Production loss	1.750.026	3.064.095	4.923.290	2.746.838	3.698.946	3.127.798	4.207.509
Additional costs	761.957	1.529.690	2.638.948	1.369.600	1.974.463	1.356.548	1.849.551
Total	4.237.117	7.950.453	13.256.377	7.146.452	9.979.014	7.576.581	10.452.805
Costs1.000 EUR	2011	2025	2040	2025	2040	2025	2040
CG 0	1.000.176	2.136.663	3.976.832	1.848.713	2.829.577	1.653.206	1.942.922
CG 1	780.826	1.587.383	2.735.883	1.452.635	2.152.001	1.486.812	1.966.886
CG 2	2.456.116	4.226.406	6.543.662	3.845.104	4.997.437	4.436.563	6.542.998
Cost per PYRS	2011	2025	2040	2025	2040	2025	2040
Health care	2.412	2.220	2.074	2.279	2.136	2.549	2.804
Pharmaceuticals	499	475	450	486	464	519	545
Nursing	2.825	2.512	2.286	2.601	2.392	2.992	3.388
Production loss	5.819	4.752	4.159	4.864	4.288	6.059	6.374
Additional costs	2.533	2.373	2.230	2.425	2.289	2.628	2.802
Total	14.088	12.331	11.200	12.653	11.568	14.676	15.835
Cost per PYRS							
Comp 0	6.013	5.737	5.616	5.768	5.611	6.106	6.066
Comp 1	13.600	12.829	12.465	12.932	12.569	13.955	14.101
Comp 2	31.887	28.450	25.556	29.140	26.711	31.929	32.659

In **Figure 2**and **Figure 3** respective total cost estimates and cost per PYRS for the three contrasting scenarios until 2040 are presented.

The core scenario predicted the Danish Diabetes population to increase to 1,183,630 patients in 2040, nearly four times the level in 2011, if current trends in incidence, mortality and complication progression were continued. This resulted in total diabetes attributable costs of 13.3 billion EUR in 2040 corresponding to 11,200 EUR per PYRS. The constant scenario, where all epidemiological indicators were held constant, resulted in the lowest prevalence and lowest total costs (660,102 patients and 10.5 billion EUR in 2040), however the highest costs per PYRS (15,835 EUR). This reflects that the core scenario assumes continued improvements in treatment results and hereby a less morbid, however, larger diabetes population where the constant scenario results in a smaller and more disease burdened diabetes population due to higher mortality and morbidity. Intermediate scenario was placed in between the two in respect to prevalence with 862,623 patients, but with the lowest total costs (9.98 billion EUR and more or less the same cost per PYRS as Core 11,568 EUR). Cost per PYRS decrease with time in both the core and the intermediate scenario as a result of the larger however less morbid diabetes population whereas an increase is seen in the constant scenario. The estimated total cost in 2025 are quite similar in the three scenarios ranging from 7.1 over 7.6 to 8.0 billion EUR varying hereby with less than 12% from the lowest to highest estimate reflecting the inertia of the future development in the diabetes population due tohistoric

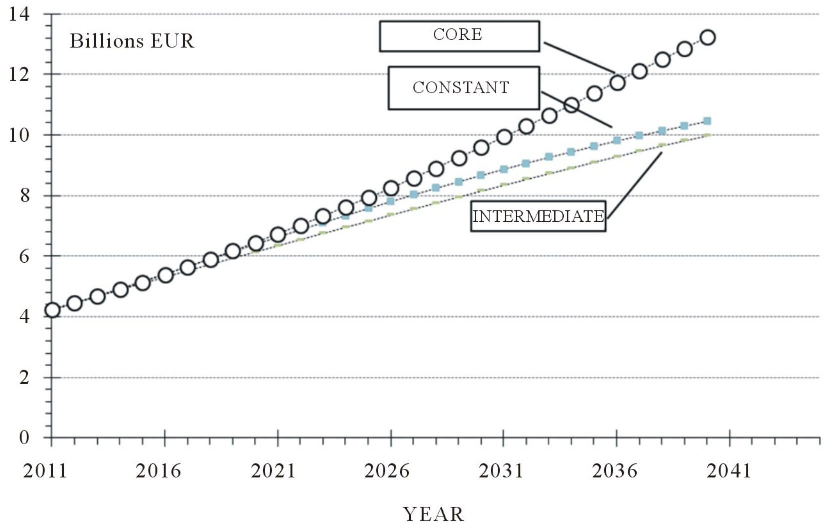

Figure 2. Total diabetes attributable costs 2011-2040 for the three epidemiological scenarios.

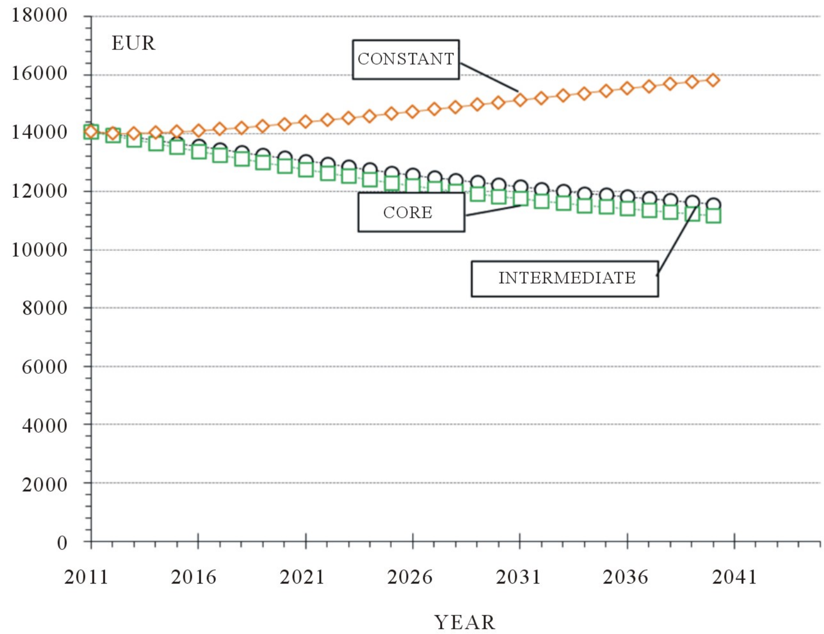

Figure 3. Cost per PYRS 2011-2040 for the three epidemiological scenarios.

developments and improvements in mortality and morbidity. Not much can be changed in the period up to 2025, while after 2025 the impact of different visions for trends setting from the year 2011 can be seen. For 2040, the range was 10.0 and 13.3 billion EUR representing a variation of maximum 33%.

5.2. Cost Distribution According to Sectors

Looking at costs in the health care sector, these are projected to be between 1.8 and 2.5 billion EUR in 2040 (1.3 and 1.4 billion EUR in 2025). This is 1.8-2 times (2025) and 2.5- 3.4 times (2040) the current level in 2011. The same patterns are projected for pharmaceutical consumption and nursing services resulting in a demand for pharmaceuticals in 2040 of between 360 and 530 million EUR and a demand for nursing services in 2040 of between 2.7 and 3.4 billion EUR.

5.3. Cost Distribution According to Complication Groups

Cost distributions within the three complication groups in 2011 and in 2040 across the three epidemiological scenarios are depicted in **Figure 4**.

The relative distribution of costs between complication groups were more or less similar in the core and the intermediate scenario, whereas a greater proportion of costs were spent among patients in CG2 in the constant scenario (63% compared to relatively 49% and 50%). This was mainly due to a greater volume of patients in CG2 in the constant scenario but also due to a steeper cost gradient from CG0 to CG2 in this scenario of 5.4 times higher cost in CG2 than CG0 compared to 4.6 and 4.8 times in the core and the intermediate scenario, respectively. In 2011 the 25% of patients with major complications consumed 58% of the total resource use consumed by diabetes patients. The part of resource use consumed by patients with major complications decreases in 2040 in both the core and the intermediate scenario to app. 50%, whereas it increases in the constant to the mentioned 63%. The share of resources consumed by patients with no complications will respectively be 30% and 18% in the core and the constant scenario where CG0 will make up 60%, compared to 49% of patients.

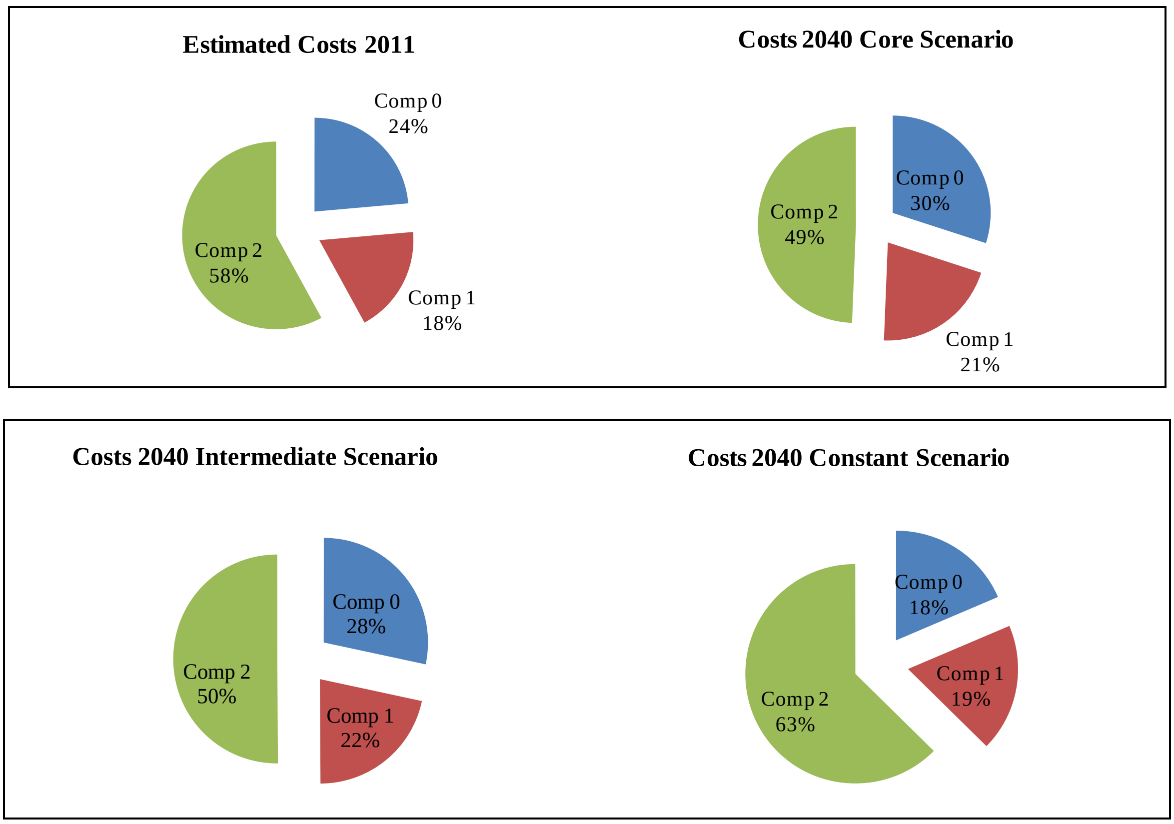

Figure 4. Distribution of diabetes attributable costs by complication group and epidemiological scenario.

5.4. Economic Potentials

To illustrate the understanding that future epidemiological development in the diabetes population would require some form of investment compared to the level of costs in 2011, we created some cases showing, on one hand, the level of economic resources that future investments require and, on the other hand, how economic space arefreed if certain efficiency improvements are realized. Important conclusions from these analyses were: If investments in primary care were set to increase with 5% annually (H1), investment in new pharmaceuticals with 2.5% annually (H2), and investment in secondary prevention with 2.5% (SMBG and Patient education) (H3a+H3b), the costs incurred by investments in 2025 will be in the range of 250 million EUR in 2025. In 2040 thecost (H1, H2, H3a+b) incurred will be 1.1 billion. If patients' own time (H3c) is included, 300 million EUR should be added for 2025 and 1.3 billion EUR for 2040.

If productivity increases by 1% per year in primary and secondary health care and nursing sectors0.4 and 1.3 billion EUR would be freed in 2025 and 2040 respectively (H4a and H4b). If usage of secondary care services are reduced by 2.5% annually this will free resources in the range of 400 million EUR in 2025 and 1.2 billion EUR in 2040 (H5). For nursing services the corresponding numbers are 500 million and 1.4 billion EUR in 2025 and 2040 (H6). Reduced productivity loss (H7) among patients in CG0 of 2.5% annually will free resources in the range of 280 million EUR in 2025, which is more than the sum of the suggested investments in primary care, pharmaceuticals and secondary prevention, when patients' own time are not taken into account. Results of each of the hypotheses are given in thesupplementary material (C+D).

6. Discussion

The point of departure for the forecasted scenarios are all centrally available data in Danish national health registers for all Danish diabetes patients in 2011 providing comprehensive estimates of real world evidenced costs attributable to diabetes forecasted according to 14 years of epidemiological data and a categorization of diabetes patients in three complication groups. This is a novel approach enabling an intuitive understanding of forecasting results as indicators of where diabetes, in a public health perspective, is heading. This study attempts to forecast trends in the future diabetes patient population and, hence, expected costs given the current resource consumption and productivity loss among diabetes patients. Model input are of highest possible quality, distinguishing the BOX-model from majority of international models based on data from population surveys, and the model has been validated showing only nonessential deviations[9] [23] [24]. Our analysis is distinct using societal attributable costs to diabetes including both resource consumption and productivity loss. Furthermore, we take into account the dynamics of diabetes and the expected natural history of disease in relation to development of late complications.

The BOX-model is general and intuitive aiming to guide decision makers as to where this disease is heading more than making accurate future projections. Trends from the forecasted scenarios may probably be generalized across countries. They indicate that increasing prevalence of diabetes and, hence, costs of diabetes are difficult to change within the shorter time span and will approximately double the next 10 years primarily due to the already achieved historic improvements in diabetes mortality and morbidity. Hereafter, the span is wider depending on the epidemiological trends occurring, however, it is realistic to assume a 2.5 or tripling of the patient population and, hence costs in 2040. Such estimates correspond well with international projections [20]. On the cost side, the predictions concerning health care, pharmaceuticals and nursing services are conditional on current rates of utilization and supply, which of course will change over time. From a societal perspective, the constant scenario can be viewed as a minimum cost under the assumption that 2011 cost structures and supplies are continued. This means that incidence rates are stable and no further progress in the health of diabetes patients in relation to morbidity or mortality occurs. This is probably unrealistic expectations, however,it sets the frame for comparison with the core scenario where the difference in costs (2.8 billion EUR in 2040) reflects the amount of extra resources necessary, if prevalence increases continues as observed until 2011. The intersmediate scenario compared to the core reflects the general public health expectation that primary prevention will result in stable or decreased incidence rates compared to historic trends. If this succeeds, a 25% reduction in costs can be expected in 2040 compared to the costs in the core scenario.

We believe that our estimations present intuitive understandable perspectives valuable for decision makers, for instance, for the health care system to be ready to meet this chronic disease challenge of a doubling in resource demand already in 2025 under current structures. With estimation of economic potentials to the core scenario, we aim to highlight how the scenarios can guide cost effectiveness discussions. For instance, interventions aiming to shift treatment of diabetes patients from secondary care to primary care can be compared to the threshold of around 500 million EUR in 2025 freed, if a goal of an annual 2.5% decrease is reached. In comparison, a 5% increased investment in primary care will cost an amount in the range of 45 million EUR in 2025. We do not argue for a given causal effect of a specific intervention, but merely point out the economic potentials if suggested goals were reached or specific investments were made.

Another important conclusion is that prevalence is a poor measure of disease control when it comes to chronic diseases. Lower cost per patient year might be more desirable than lower prevalence as this means that each patient is living better with his or her disease contributing to a larger prevalent population. Categorization of patients according to their complication status in three groups is a novel approach, which allows a more general view on the disease, which is easy to interpret and communicate. We have previously shown how health care costs and nursing costs increased markedly when patients with diabetes develop minor or major complications. Hence, there is great cost saving potential in preventing development of complications among patients with diabetes. This is reflected in the intermediate scenario, where focus is placed on efforts to sustain historic improvement in epidemiological indicators into the future, but incidence rates are assumed constant. We further project a shift in resource consumption from patients with major complications to patients without complications due to the volume of patients living with diabetes without complications in the future.

It must be stressed that the basic patient population in the scenarios has obtained its size and age composition as a consequence of access to diabetes treatment and care during decades prior to year 2001. Therefore, a comparison of PYRS experienced under competing scenarios reflects the cumulative effect of access to treatment over previous decades. In prolonging of this, it is important to bear in mind that costs are an expression of supply and demand meaning that patients' demand will only increase to the extent that the supply is available. In the model, discrete time intervals of one calendar year are used and not continuous time reflecting our wish for a simple and intuitive modeling approach. Age at diagnosis, and not running age, was used to reflect that the model follows a patient with diabetes from diagnose until death concerning age and gender specific costs and morbidity and mortality drivers. Forecasting 25 years ahead in time it is obvious that changes over time, in health care queues, waiting lists and treatment offers cannot be accommodated for in the model, as these are unknown. It is inevitable that modelers will make different choices and apply different assumptions. The included hypotheses can throw light on consequences of different assumptions, however, the model will never be a perfect representation of the real world [42].

7. Conclusion

Our projections indicate that within the shorter time span increases in the prevalent population, and therefore the associated cost, are difficult to change primarily due to the already achieved historic improvements in diabetes mortality and morbidity. These will approximately double societal costs of diabetes the next 10 years,assuming current trends in morbidity and mortality are maintained.The resulting diabetes population will incur three times the current costs in 2040, although the costs per PYRS are falling during the whole period.A 20% reduction in cost per PYRS shows how the distribution of patients with complications are expected to change over time with patients living better and, hence, on average become less resource demanding with their disease. Prevalence is, therefore, a poor measure of disease control in a public health perspective. With marked increases in diabetes prevalence, not only resource demand for health care, nursing and pharmaceuticals will increase but also societal productivity loss due to the increasing number of patients in the working age.Despite wide uncertainty around projections of the future, they enable us to appreciate better the implications for societies of currently observed epidemiological trends. Hereby, projections provide a basis for discussing future resource demand and consequently the necessary investments and structural changes.

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Conflicts of Interest

Neither the Danish Diabetes Association nor the consortium of sponsors from the pharmaceutical industry has had any influence on the conduct of the study.

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Abbreviations

CG0: Complication group 0 (no complications)
CG1: Complication group 1 (minor complications)
CG2: Complication group 2 (minor complications)
M: Men
PIN: Danish Personal Identification Number
PP: Per person
PYRS: Patient Years
PWD: Patients with Diabetes
SD: Statistics Denmark
W: Women

Supplementary Materials

Table A. Grouping of diagnoses and interventions used for classifying hospital activities by complication states of relevance for diabetes, and with respect to diagnostic specificity for diabetes.

Diagnosis or procedure	Qualifying for complication state[a]	Specificity for diabetes[b]
Diabetes in pregnancy, childbirth and the puerperium	0	1
Diabetes, without indication of chronic complication	0	1
Hypoglycaemiccoma NOS	0	0
Screening for diabetic retinopathy	0	1
Drug treatment or instruction specific for diabetes	0	1
Acute myocardial infarction	1	0
Diabetes with complication, not further specified	1	1
Diabetes with complications in peripheral vascular system	1	1
Diabetes with eye complication	1	1
Diabetes with footulcer	1	1
Diabetes with microangiopathy	1	1
Diabetes with neurological complication	1	1
Diabetes with peripheral angiopathy	1	1
Diabetes with renal complication	1	1
Diabetic cataract	1	1
Diabetic polyneuropathy	1	1
Diabetic retinopathy not otherwise specified	1	1
Diseases of the lens	1	0
Polyneuropathy	1	0
Proliferative diabetic retinopathy	1	1
Uraemia	1	0
Simplex diabetic retinopathy	1	1
Cataract, retinopathy in diabetes	1	1
Diabetic angiopathy in extremities	1	1
Diabetic nephropathy, Kimmelstiel-Wilson syndrom	1	1
Neuropathy, diabetic polyneuritis, diabetes	1	1
Amputation at or below ankle level	1	0
Coronary bypass operation	1	0
Surgery for eye complication	1	0
Teatment of ulcer of lower limb	1	0
Diabetes with gangraene	2	1
Diabetes with multiple complications	2	1
Diabetic maculopathy	2	1
Dialysis	2	0
Diseases of the retina	2	0
Heart failure	2	0
Kidney transplantation	2	0
Renalfailure	2	0
Stroke	2	0
Blindness	2	0
Diabetic gangraene	2	1
Gangrena of lower limb	2	0
Intracerebral haemorrhage	2	0
Amputation above ankle level	2	0

[a]Value indicates classification state (0, 1 or 2, respectively). [b]Values 1 and 0 indicate that item is specific for diabetes and unspecific for diabetes, respectively.

Table B. Prevalence, total attributable costs and cost per PYRS 2011, 2025 and 2040 in three epidemiological scenarios.

Scenarios		CORE	CORE	INTERMEDIATE	INTERMEDIATE	CONSTANT	CONSTANT
Main results	2011	2025	2040	2025	2040	2025	2040
Prevalence	300.769	644.738	1.183.630	564.781	862.623	516.239	660.102
Comp 0	166.327	372.443	708.091	320.497	504.314	270.745	320.276
Comp 1	57.415	123.738	219.485	112.333	171.215	106.545	139.486
Comp 2	77.027	148.557	256.055	131.951	187.094	138.949	200.340
Incidence	29.451	46.756	62.694	34.289	35.967	34.289	35.967
Mortality	11.714	16.139	23.443	14.246	17.125	21.080	29.281
Costs	2011	2025	2040	2025	2040	2025	2040
Health care	725.464.495	1.431.166.663	2.455.206.345	1.286.964.483	1.842.156.831	1.315.790.252	1.850.934.097
Pharma	149.953.681	306.038.534	532.748.176	274.264.799	400.288.479	267.676.403	359.781.970
Nursing	849.715.906	1.619.462.228	2.706.184.561	1.468.784.708	2.063.159.419	1.544.346.999	2.236.535.856
Prod	1.750.025.792	3.064.095.305	4.923.289.744	2.746.838.024	3.698.946.354	3.127.797.930	4.207.509.369
Add	761.956.851	1.529.690.283	2.638.947.964	1.369.600.181	1.974.463.293	1.356.548.093	1.849.550.722
Total	4.237.116.724	7.950.453.013	13.256.376.791	7.146.452.195	9.979.014.377	7.576.581.375	10.452.804.987
Costs	2011	2025	2040	2025	2040	2025	2040
Comp 0	1.000.175.623	2.136.663.476	3.976.831.728	1.848.713.102	2.829.576.658	1.653.206.164	1.942.921.596
Comp 1	780.825.699	1.587.383.184	2.735.883.493	1.452.635.301	2.152.000.515	1.486.812.323	1.966.885.574
Comp 2	2.456.115.402	4.226.406.354	6.543.661.570	3.845.103.792	4.997.437.204	4.436.562.888	6.542.997.816
Total	4.237.116.724	7.950.453.013	13.256.376.791	7.146.452.195	9.979.014.377	7.576.581.375	10.452.804.987
Cost per PYRS	2011	2025	2040	2025	2040	2025	2040
Health care	2.412	2.220	2.074	2.279	2.136	2.549	2.804
Pharma	499	475	450	486	464	519	545
Nursing	2.825	2.512	2.286	2.601	2.392	2.992	3.388
Prod	5.819	4.752	4.159	4.864	4.288	6.059	6.374
Add	2.533	2.373	2.230	2.425	2.289	2.628	2.802
Total	14.088	12.331	11.200	12.653	11.568	14.676	15.835
Cost per PYRS							
Comp 0	6.013	5.737	5.616	5.768	5.611	6.106	6.066
Comp 1	13.600	12.829	12.465	12.932	12.569	13.955	14.101
Comp 2	31.887	28.450	25.556	29.140	26.711	31.929	32.659
Total	14.088	12.331	11.200	12.653	11.568	14.676	15.835
CostsComp 0	2011	2025	2040	2025	2040	2025	2040
Health care	89.858.530	192.519.334	357.882.722	167.209.450	254.934.374	146.323.763	173.757.001
Pharma	49.838.798	110.062.768	207.478.714	95.344.235	147.955.413	81.928.854	96.563.562
Nursing	42.624.350	94.604.864	179.036.012	82.877.432	130.048.675	73.656.667	91.717.861
Prod	570.851.210	1.193.708.678	2.203.162.563	1.030.274.736	1.561.946.494	944.518.912	1.100.545.460
Add	247.002.735	545.767.832	1.029.271.717	473.007.250	734.691.702	406.777.968	480.337.711
Total	1.000.175.623	2.136.663.476	3.976.831.728	1.848.713.102	2.829.576.658	1.653.206.164	1.942.921.596
CostsComp 1							
Health care	140.219.673	302.987.736	535.364.206	276.895.072	420.743.614	265.840.227	352.108.316
Pharma	41.115.818	87.645.991	152.374.975	80.431.870	120.556.747	78.113.986	104.168.247
Nursing	132.137.580	279.397.935	486.999.832	256.937.075	387.705.039	251.399.983	339.344.222
Prod	342.957.246	651.973.536	1.099.551.688	594.900.265	857.994.243	655.209.285	856.531.503
Add	124.395.382	265.377.986	461.592.792	243.471.020	365.000.871	236.248.842	314.733.286
Total	780.825.699	1.587.383.184	2.735.883.493	1.452.635.301	2.152.000.515	1.486.812.323	1.966.885.574
Costs Comp 2							
Health care	495.386.292	935.659.594	1.561.959.417	842.859.962	1.166.478.842	903.626.263	1.325.068.780
Pharma	58.999.065	108.329.774	172.894.487	98.488.694	131.776.319	107.633.562	159.050.161
Nursing	674.953.976	1.245.459.429	2.040.148.717	1.128.970.201	1.545.405.705	1.219.290.350	1.805.473.773
Prod	836.217.336	1.218.413.092	1.620.575.493	1.121.663.023	1.279.005.617	1.528.069.732	2.250.432.405
Add	390.558.733	718.544.466	1.148.083.456	653.121.912	874.770.720	713.521.284	1.054.479.725
Total	2.456.115.402	4.226.406.354	6.543.661.570	3.845.103.792	4.997.437.204	4.436.562.888	6.542.997.816

Table C. Results of the economic potentials: investments.

Hypotheses	Core Scenario	
Description	Continuation of observed epidemiological trends and 2011 cost structure	
	2025	2040
Total costs	€7,934,796,435	€13,230,271,423
	Core adjusted—H1	
	Investments in primary care (annual +5%)	
	2025	2040
Total costs	€7,979,606,895	€13,459,970,529
cost difference 2011 Core	−€44,810,460	−€229,699,106
	Core adjusted—H2	
	Investments in pharmaceuticals (annual +2.5%)	
	2025	2040
Total costs	€8,060,933,449	€13,786,645,242
cost difference 2011 Core	−€126,137,015	−€556,373,819
	Core adjusted—H3a	
	Investments in secondary prevention—SMBG (annual +2.5%)	
	2025	2040
Total costs	€7,986,769,133	€13,466,526,139
cost difference 2011 Core	−€51,972,699	−€236,254,715
	Core adjusted—H3b	
	Investments in secondary prevention—Patient education (annual +2.5%)	
	2025	2040
Total costs	€7,954,901,428	€13,321,575,284
cost difference 2011 Core	−€20,104,993	−€91,303,861
	Core adjusted—H3c	
	Investments in secondary prevention—Patients' own time (annual +2.5%)	
	2025	2040
Total costs	€8,229,416,849	€14,562,020,821
cost difference 2011 Core	−€294,620,415	−€1,331,749,397

Table D. Results of the economic potentials: efficiency improvements.

Hypotheses	Core	
Description	Continuation of observed epidemiological trends and 2011 cost structure	
	2025	2040
Total costs	€7,934,796,435	€13,230,271,423
	Core adjusted—H4a	
	Effiency improvements in health care (annual −1%)	
	2025	2040
Total costs	€7,747,319,738	€12,610,749,158
cost difference 2011 Core	€187,476,697	€619,522,265
	Core adjusted—H4b	
	Efficiency improvements in nursing (annual −1%)	
	2025	2040
Total costs	€7,722,653,826	€12,547,419,820
cost difference 2011 Core	€212,142,608	€682,851,603
	Core adjusted—H5	
	Reduced usage of nursing services (annual −2.5%)	
	2025	2040
Total costs	€7,452,435,378	€11,825,506,131
cost difference 2011 Core	€482,361,057	€1,404,765,292
	Core adjusted—H6	
	Reduced usage of secondary care (annual −2.5%)	
	2025	2040
Total costs	€7,522,166,828	€11,994,126,929
cost difference 2011 Core	€412,629,607	€1,236,144,494
	Core adjusted—H7	
	Reduced productivity loss among patients in CG0 (annual −2.5%)	
	2025	2040
Total costs	€7,655,644,969	€12,332,342,573
cost difference 2011 Core	€279,151,466	€897,928,850