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Direct costs in diabetic and non diabetic people: The population-based Turin study, Italy

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KEYWORDS

Costs; Cost of illness; Drugs; Economics; Health expenditures; Survey **Abstract** Background and aims: We compared direct costs of diabetic and non diabetic people covered by the Italian National Health System, focusing on the influence of age, sex, type of diabetes and treatment.

Methods and results: Diabetic people living in Turin were identified through the Regional Diabetes Registry and the files of hospital discharges and prescriptions. Data sources were linked to the administrative databases to assess health care services used by diabetic (n=33,792) and non diabetic people(n=863,123). Data were analyzed with the two-part model; the estimated direct costs per person/year were €3660.8 in diabetic people and €895.6 in non diabetic people, giving a cost ratio of 4.1. Diabetes accounted for 11.4% of total health care expenditure. The costs were attributed to hospitalizations (57.2%), drugs (25.6%), to outpatient care (11.9%), consumable goods (4.4%) and emergency care (0.9%). Estimated costs increased from € 2670.8 in diabetic people aged <45 years to € 3724.1 in those aged >74 years, the latter representing two third of the diabetic cohort; corresponding figures in non diabetic people were € 371.6 and € 2155.9. In all expenditure categories cost ratios of diabetic vs non diabetic people were higher in people aged <45 years, in type 1 diabetes and in insulin-treated type 2 diabetes.

Conclusion: Direct costs are 4-fold higher in diabetic than in non diabetic people, mainly due to care of the elderly and inpatient care. In developed countries, demographic changes will have a profound impact on costs for diabetes in next years.

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Prevalence of diabetes is increasing worldwide [1]. In developed countries, the disease is more frequent in the frailer subgroups of the population, ethnic minorities, women, people with low socioeconomic level and the elderly [2,3]. Public health interventions are needed at individual and population levels to improve lifestyle habits and to identify asymptomatic people. From a public health perspective, however, there is also the need to recognize that increasing ageing of the general population and improved survival of diabetic people will necessarily cause an increasing trend in the prevalence of the disease and, finally, a profound impact on overall health care costs [4]. Focusing on national strategies of diabetes prevention is necessary, but a parallel realistic planning of health care costs due to burden of the disease is needed [5,6].

To perform optimization of resources allocation, policy makers need updated epidemiological data on the impact of the disease. Comparing diabetic and non diabetic population-based cohorts living in the same area allows to estimate the excess of costs attributable to the disease, taking into account the effect of confounding factors, such as age and sex. This approach allows a more accurate extrapolation of the amount of expenditure due to the disease at a country level. Few studies, however, have provided detailed figures of direct costs of diabetic people [7-15]. They mainly examined clinic-based cohorts or national representative samples of diabetic people and then extrapolated the total costs of the disease through the bottom-up approach, rather than identifying a large population-based cohort of diabetic and non diabetic people and then measuring the incremental cost of the disease.

In previous reports of the Turin Study, a large population-based cohort of Italian people with diabetes, we have assessed prevalence of the disease [3], its impact on prescription costs [16] and quality of health care provided as part of the National Health System [17]. In this report, we have expanded our database to estimate the overall impact of diabetes on direct costs and to assess heterogeneity in costs by sex, age groups, type of diabetes and hypoglycemic treatment.

Methods

The study base includes all residents in the city of Turin (896,915 inhabitants) with a diagnosis of diabetes on 31 July 2003. As described in detail elsewhere [3,16], three data sources were employed to identify diabetic people: the file of subjects registered in the Regional Diabetes Registry (an administrative database including all people who obtained exemption from payment of drugs, syringes, and glucose monitoring strips due to a diagnosis of diabetes mellitus), the file of prescriptions of hypoglycemic drugs, and the file of persons discharged from regional and national hospitals with a primary or secondary diagnosis of diabetes. All data sources were matched by a deterministic linkage procedure using the fiscal code as unique identifier, and were linked to the Turin Population Register to include only people alive on July 31, 2003 and to determine each individual's educational level [3]. Type of diabetes was classified according to information provided by the Regional Diabetes Registry and the Registry of type 1 diabetes of the Province of Turin [18]. People with unclassified diabetes were considered as type 1 diabetes if they were <30 years, type 2 diabetes elsewhere (n=5766). Treatment was classified into three groups: diet only, oral hypoglycemic drugs and insulin. Information about therapy was retrieved from the Regional Diabetes Registry and, for patients not registered in this data source, from the files of prescriptions of hypoglycemic drugs. Subjects who were prescribed both insulin and oral hypoglycemic drugs were assigned to the insulin treatment category; all diabetic individuals not registered in the Regional Diabetes Registry and in the file of hypoglycemic drug prescriptions were identified through the third data source (hospital discharges) and were considered within the diet treatment category (1986 individuals).

All Italian citizens, irrespective of social class or income, are cared for by a general practitioner and obtain all health care services as part of the National Health System, which are recorded in a regional database. All drug prescriptions, laboratory tests, specialist medical examinations, prescriptions related to diabetes care (test strips, syringes, glucometers), hospital discharges and emergency room admission from August 1, 2003 to July 31, 2004 were linked to the overall Turin population. Health care services used by diabetic and non-diabetic people and their costs. as defined by regional and governmental contracts, were then analyzed. Private health care services were not considered, as data were not available; their impact on overall health care costs, however, is generally quite low. The cumulative cost for a drug was calculated by multiplying the units prescribed by the cost for each fill. The cumulative cost for hospitalizations was calculated by multiplying each episode of hospitalization by the unit cost for each Diagnosis Related Group (DRG). The cumulative costs for specialist visits, laboratory tests and other consumable goods were calculated by multiplying each of them by their unit cost. The proportion of individuals with specific outpatient visits or tests and their mean costs per cared patient were calculated using the main specialist branch involved in each episode of care. The cost for emergency care was based on laboratory tests and specialist consultations performed.

The statistical distribution of costs was strongly asymmetric due to the high number of subjects not using health services, particularly among non-diabetic people. Estimated costs per person/year for people with and without diabetes were then calculated by means of the two-part model according to the following conditional probability:

$$\textit{E}\left(\textit{Y}/\textit{X}\right)\!=\!\textit{P}(\left(\textit{Y}>0/\textit{X}\right)\textit{E}\left(\textit{Y}/\textit{X},\,\textit{Y}>0\right))$$

where *Y* represents the cost and *X* represents the vector of covariates [18].

The first part was fitted by logistic models; odds ratios for probabilities of using health services were then estimated. The second part was estimated by using a generalized linear model assuming a gamma distribution of costs and a logarithmic link function; cost ratios of diabetic vs non diabetic people were estimated. Both logistic and gamma models were adjusted for age and sex; educational level was not included in the final model as its contribution was not statistically significant. Estimated costs for diabetic and non diabetic people were then calculated multiplying the

Table 1	Characteristics of	diabetic and r	non diabetic p	eople of the Turin Study.

	Diabetic people			Non diabetic people			
	N.	People with zero cost		N.	People with zero cost		
		N.	%		N.	%	
All cohort	33,792	433	1.3	863,123	185,711	21.5	
Sex							
Men	17,152	253	1.5	411,967	111,495	27.1	
Women	16,640	180	1.1	451,156	74,216	16.5	
Age group (year)							
<45	1671	43	2.6	449,958	131,520	29.2	
45-54	3008	62	2.1	116,556	25,945	22.3	
55-64	7725	90	1.2	115,747	16,592	14.3	
65-74	11,508	98	0.9	101,366	7145	7.1	
>74	9880	140	1.4	79,496	4509	5.7	
Type of diabetes							
Type 1	1703	21	1.2				
Type 2	32,089	412	1.3				
Treatment							
Diet	7087	433	6.1				
Oral drugs	17,828	0	0				
Insulin	8877	0	0				

expected probability of spending for health care by the estimated costs for people using health care. Confidence intervals (95% CI) for estimated costs were calculated by a bootstrap process with 100 samples. Separate models were performed by sex, age groups (<45, 45–54, 55–64, 65–74>74 years), type of diabetes and antidiabetic treatment. Costs were estimated by health care services (hospitalization, emergency care, outpatient care, drugs, consumable goods); we also analyzed hospitalization data by main diagnosis and outpatient care data by clinical unit, according to the same methodological approach. Statistical analyses were conducted using SAS System, version 9.1.

Results

The study base included 33,792 diabetic and 863,123 non-diabetic people living in the city of Turin on July 31, 2003.

Mean age of diabetic and non-diabetic people was 67.7 years and 44.3 years, respectively. Of the diabetic cohort, 21.0% were treated with diet, 52.8% with oral drugs and 26.2% with insulin; 1703 people (0.05%) where considered as type 1 diabetes, while 32,089 people (99.5%) as type 2 diabetes.

Costs data were typically skewed because a relatively small proportion of people incurred extremely high costs, whereas a subgroup (21.5% among non diabetic people and 1.3% among diabetic people) had zero costs (Table 1). As shown in Table 2, estimated direct costs/year were \in 3660.8 in diabetic people and \in 895.6 in non-diabetic people (cost ratio = 4.1). The excess of direct cost in diabetic than in non diabetic people was similar between sexes, whereas it was strongly affected by age, being 7-fold higher in people aged <45 years and 1.7-fold higher in those aged >74 years.

Table 2	Estimated direct costs of	f diabetic and non dial	abetic people in the	Turin Study.
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	Diabetic people (Diabetic people ($N = 33,792$)		Non diabetic people ($N = 863,123$)		
	Cost (€) per person/year ^a	CI 95% ^b	Cost (€) per person/year ^a	CI 95% ^b		
Total	3660.8	3651.3-3671.5	895.6	894.2-897.1	4.1	
Sex						
Men	3898.0	3877.8-3921.2	896.5	893.4-899.0	4.3	
Women	3430.2	3415.4-3447.0	902.8	901.2-904.4	3.8	
Age group (yea	ar)					
<45	2670.8	2642.2-2698.8	371.6	371.2-372.0	7.2	
45-54	2600.5	2590.6-2609.3	688.9	688.3-689.5	3.8	
55-64	2983.4	2974.2-2990.6	1075.8	1075.0-1076.6	2.8	
65-74	3661.7	3650.6-3673.9	1742.6	1740.6-1744.3	2.1	
>74	3724.1	3715.9-3734.9	2155.9	2154.2-2157.9	1.7	

^a derived by two parts models, adjusted for age and sex.

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^b derived by bootstrapping method.

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Table 3 Estimated costs of diabetic and non diabetic people in the Turin Study, by health care service.

	Diabetic people ($N = 33,792$)			Non diabetic people ($N = 863,123$)			Cost ratio
	People with 0 cost N (%)	Cost (€) per person/year ^a	CI 95% ^b	People with 0 cost N (%)	Cost (€) per person/year ^a	CI 95% ^b	
Health care servi	ce						
Hospitalizations	24,482 (72.5)	2065.4	2051.1-2079.8	768,788 (89.1)	664.4	661.7-667.6	3.1
Emergency care	24,886 (73.6)	31.5	31.4–31.7	680,740 (78.9)	16.55	16.54–16.56	1.9
Outpatient care	2466 (7.3)	427.7	426.9-428.7	356,363 (41.3)	151.4	151.2-151.6	1.8
Drugs	1233 (3.7)	923.6	920.9-926.5	327,915 (38.0)	222.9	222.6-223.4	2.8
Consumable goods	17,071 (50.5)	154.5	154.0–154.9	861,062 (99.8)	0.628	0.622-0.633	246.0

^a derived by two parts models, adjusted for age and sex.

Table 3 shows estimated costs in diabetic and diabetic people by health care services; apart from consumable goods, the highest difference between diabetic and non diabetic people was found for drug costs (costs ratio = 2.8) and the lowest for outpatient care (cost ratio = 1.7). The distribution of direct costs among health care services was almost unaffected by the disease: in diabetic people, 57.2% of direct costs were due to hospitalizations (vs 62.9% among non diabetic people), 25.6% to drugs (vs. 21.1%), 11.9% to outpatient care (vs. 14.3%), 0.9% to emergency care (vs. 1.6%) and 4.4% to consumable goods related to diabetes care (nearly absent in non diabetic people).

As shown in Table 4, people with type 1 diabetes had the highest overall estimated costs, mainly due to the highest employment of consumable goods (5-fold higher in type 1 than type 2 diabetes). Diabetic people treated with diet only had higher estimated costs for hospitalizations and outpatient care than people treated with oral drugs, whereas insulin-treated people had the highest estimated costs in each expenditure category.

Table 5 shows costs for hospitalizations and outpatients services in diabetic and non diabetic people; cardiovascular and kidney diseases were the most common complications of the disease requiring hospitalization and outpatient care.

Discussion

This report provides a comprehensive picture of direct costs for diabetes in a large city of Northern Italy, under the coverage of the universalistic National Health System. In 2003–2004 the per capita direct costs for diabetes were € 3661/year (~4575 USD). Considering a prevalence of diabetes of 4.8% [3,19,20], we can estimate that in the whole Piedmont Region (4,330,000 inhabitants in 2004; Turin the main city) at least 208,000 persons had diabetes, accounting for € 761 millions of direct costs, that is 11.4% of total health care expenditures [21]. The health care cost of a person with diabetes was 4 fold higher than a person without diabetes of similar age and sex. The impact of the disease was highest in insulin-treated people and in the youngest age group. The distribution of costs among categories of health care services was rather similar between diabetic and non-diabetic people, the largest proportion of costs being due to inpatient care. Apart from consumable goods, the largest differences in direct costs between persons with and without diabetes were due to hospitalizations (3.1 folds) and drugs (2.8 folds). These findings have implications for health care planners. As increasing prevalence of the disease in developed countries is mainly due to the increasing ageing of the general population and the improved survival of diabetic people [22], diabetes-related health care costs are likely to increase progressively in next years, having a profound impact on National Health System expenditure. This expected trend needs to be recognized by health care planners in order to adequately allocate resources to manage the burden of the disease.

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Few studies have provided detailed data on direct costs of diabetic and non-diabetic persons. Main limitations of studies conducted in the United Stated [7-9], Canada [10], Australia [11], Sweden [13], Spain [14], Germany [15] are: 1) the recruitment of either clinic-based or health-insured cohorts, thus limiting the generalizability of results; 2) the limited number of recruited people, thus lowering the power of estimates; 3) the absence of comparative data of non diabetic people living in the same area, thus not allowing to control estimates of costs for strong confounding factors, such as age and sex. With regard to Italy, the ARNO study provided similar results on direct costs; data in diabetic people, however, were compared to pharmacologicallytreated non-diabetic people, thus providing biased downward estimates of excess of costs in diabetic people [23]. Our study, based on a large population-based cohort of both diabetic and non-diabetic people, provides actual rather than estimated data, and strong evidence of heterogeneities in health care costs depending on age, type of diabetes and treatment. Although the highest costs were due to care of the elderly with diabetes, the same increasing trend by age is evident also in non-diabetic people. The final result is that the highest costs ratio is that of the youngest people (7-fold excess) whereas in the elderly this excess was 70% only. In absolute terms, however, the elderly were responsible for the highest proportion of consumption of health care resources. In the last decade, prevalence of diabetes has more than doubled in people aged 75 years and over [3], thus the impact of the disease on National Health System will probably be much stronger in next years [22,24]. In Europe, Italy is the third country for expected years of life in people

^b derived by bootstrapping method.

Table 4	Estimated direct costs of diabetic	people in the Turin Stud	y, Italy, by type of diabetes and treatment.

	Cost (€) per	CI 95% ^b	Diabetic/non diabetic
	person/year ^a		cost ratio
All services			
Type 1 diabetes	4406.8	4304.1-4521.9	4.9
Type 2 diabetes	3532.8	3522.7-3544.9	3.9
Treatment			
Diet	3389.2	3354.1-3415.7	3.8
Oral drugs	2511.1	2502.2-2522.3	2.8
Insulin	6038.8	5988.2-6082.7	6.7
Hospitalizations			
Type 1 diabetes	1703.3	1602.7-1811.7	2.6
Type 2 diabetes	2071.0	2058.4-2086.0	3.1
Treatment			
Diet	2231.9	2200.9-2263.3	3.4
Oral drugs	1449.3	1435.8-1461.4	2.2
Insulin	3130.6	3091.2-3164.9	4.7
Emergency care			
Type 1 diabetes	31.8	31.2-32.3	1.9
Type 2 diabetes	31.5	31.3-31.6	1.9
Treatment			
Diet	29.5	29.1-29.8	1.8
Oral drugs	27.5	27.3-27.7	1.7
Insulin	41.1	40.7-41.4	2.5
Outpatient care			
Type 1 diabetes	418.5	410.4-425.2	2.8
Type 2 diabetes	422.9	422.0-423.9	2.8
Treatment			
Diet	451.0	448.0-454.3	3.0
Oral drugs	312.0	310.8-312.8	2.1
Insulin	618.3	614.9-621.2	4.1
Drugs			
Type 1 diabetes	1165.3	1133.2-1207.0	5.2
Type 2 diabetes	884.7	882.3-887.2	4.0
Treatment			
Diet	678.7	673.4-684.9	3.0
Oral drugs	772.6	770.4-775.6	3.5
Insulin	1376.9	1367.6-1387.1	6.2
Consumable goods			
Type 1 diabetes	596.6	589.3-602.3	950.0
Type 2 diabetes	135.3	135.0—136.6	215.4
Treatment			
Diet	11.7	11.5-11.9	18.6
Drugs	36.5	36.4-36.6	58.1
Insulin	515.9	514.0-518.0	821.5

^a derived by two parts models, adjusted for age and sex.

aged 50 years, after Denmark and Malta [25]. On the other hand, involving mainly retired people, direct costs of diabetes should increase more than indirect costs, that is productivity losses associated with the illness. Data on indirect costs of diabetic people living in European countries, however, are very limited [14].

The highest direct costs of diabetic people were due to inpatient care. Large regional variations in hospitalization rates have been found within Italy; as the availability of outpatients services are inversely related to hospitalizations [26], diabetologists, general practitioners and health care planners should take into proper consideration these data to reduce health care costs. Moreover, our data shows that people treated with diet only had higher costs for hospitalizations and outpatient care that people treated with oral drugs, suggesting the hypothesis that in this subgroup of diabetic people the quality of control of the disease might be inadequate due to therapeutic inertia. Unfortunately, no clinical data are available at present to test this hypothesis. In this cohort, one third of costs for hospitalizations was due to cardiovascular diseases; as diabetes has generally an extended asymptomatic period,

^b derived by bootstrapping method.

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Table 5 Estimated costs for inpatient and outpatient care of diabetic and non diabetic people in the Turin Study.

	Diabetic people		Non diabetic ped	Cost ratio		
	Cost (€) per person/year ^a	CI 95% ^b	Cost (€) per person/year ^a	CI 95% ^b		
Hospitalizations						
Cardiovascular diseases	795.6	782.2-808.5	245.5	242.6-247.9	3.2	
Neoplastic diseases	223.2	220.0-227.0	119.0	117.8-120.1	1.9	
Respiratory diseases	196.2	187.2-204.5	55.8	54.7-57.2	3.5	
Kidney diseases	68.2	67.1-69.2	29.0	28.8-29.3	2.3	
Diabetes	90.8	86.2-94.6	0.2	0.14-0.19	_	
Day hospital	276.2	273.8-279.1	138.2	137.5-138.7	2.0	
Outpatient care						
Cardiology	22.1	22.0-22.2	10.2	10.16-10.24	2.2	
Vascular surgery	1.6	1.54-1.63	0.5	0.53-0.55	3.2	
Diabetology/endocrinology	33.6	33.5-33.7	1.8	1.77-1.79	18.7	
Internal medicine	8.8	8.7-8.9	2.3	2.26-2.29	3.8	
Nephrology	113.7	112.0-115.8	26.8	26.4-27.3	4.2	
Oculist	15.3	15.2-15.4	4.1	4.12-4.15	3.7	
Radiology	63.3	63.1-53.5	39.9	39.77-39.94	1.6	
Laboratory	82.1	81.9-82.2	33.1	33.0-33.1	2.5	

^a derived by two parts models, adjusted for age and sex.

early diagnosis should be implemented, particularly in middle-aged people, to reduce cardiovascular complications and related costs.

Main strengths of our study are:1) the recruitment of a population-based (i.e. unselected) cohort of diabetic and non diabetic people covered by the National Health System; 2) the inclusion of all available data of the National Health System, thus allowing to provide actual direct costs sustained for diabetes care rather than their estimates; 3) the availability of comparative data of non diabetic people living in the same area, thus allowing to control estimates for strong confounding factors, such as age and sex. Several limitations must be recognized. At first, the absence of individual data on diabetes duration, severity of the disease and indicators of diabetes control, such as HbA1c, blood pressure and lipids did not allow to explore the relationship between costs sustained by the National Health System and the quality of care provided to diabetic people. Second, it has been shown that the real cost for hospitalization for each DRG, which is an average cost, is higher for diabetic than for non-diabetic people [15], therefore our data may be underestimated. Finally, we did not consider indirect costs or informal care costs.

In conclusion, the population-based Turin study shows that direct costs of diabetic people are 4-fold higher than non-diabetic people, independently of age and sex. The large amount of direct costs is due to the care of the elderly diabetic people and inpatient care. From a public health perspective there is the need to recognize that in developed countries demographic changes will necessarily have a profound impact on direct costs for diabetes in next years.

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References

- [1] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047—53.
- [2] Espelt A, Borrell C, Roskam AJ, Rodríguez-Sanz M, Stirbu I, Dalmau-Bueno A, et al. Socioeconomic inequalities in diabetes mellitus across Europe at the beginning of the 21st century. Diabetologia 2008;51:1971—9.
- [3] Gnavi R, Karaghiosoff L, Costa G, Merletti F, Bruno G. Socioeconomic differences in the prevalence of diabetes: a population study based on administrative data sources. Nutr Metab Cardiovasc Dis 2008;18:678—82.
- [4] Gregg EW, Albright AL. The public health response to diabetes. Two steps forward, one step back. JAMA 2009;301:1596–8.
- [5] Kahn R, Anderson JE. Improving diabetes care: the model for health care reform. Diabetes Care 2009;32:1115–8.
- [6] Wilson JF. Can disease prevention Save health reform? Ann Int Med 2009;151:145–8.
- [7] American Diabetes Association. Economic costs of diabetes in the U.S. in. Diabetes Care 2007;2008(31):596–615.
- [8] Oglesby AK, Secnik K, Barron J, Al-Zakwani I, Lage MJ. The association between diabetes related medical costs and glycemic control: a retrospective analysis. Cost Effectiveness and Resource Allocation 2006;16:4–11.
- [9] Brandle M, Zhou H, Smith BR, Marriott D, Burke R, Tabaei BP, et al. The direct medical cost of type 2 diabetes. Diabetes Care 2003;26:2300-4.
- [10] Dawson KG, Gomes D, Gerstein H, Blanchard JF, Kahler KH. The economic cost of diabetes in Canada. Diabetes Care 1998; 2002(25):1303-7.
- [11] Knuiman MW, Davis WA, Hendrie D, Davis TME. Determinants of diabetes-attributable non—blood glucose—lowering medication costs in type 2 diabetes. The Fremantle Diabetes Study. Diabetes Care 2005;28:329—36.
- [12] Jönsson B. CODE-2 Advisory Board. Revealing the cost of type II diabetes in Europe. Diabetologia 2002;45:S5—12.
- [13] Henriksson F, Agardh CD, Berne C, Bolinder J, Lönnqvist F, Stenström P, et al. Direct medical costs for patients with type 2 diabetes in Sweden. J Intern Med 2000;248:387–96.

^b derived by bootstrapping method.

- [14] Oliva J, Lobo F, Molina B, Monereo S. Direct health care costs of diabetic patients in Spain. Diabetes Care 2004;27: 2616–21.
- [15] Koster I, von Ferber L, Ihle P, Schubert I, Hauner H. The cost burden of diabetes mellitus: the evidence from Germany. The CoDiM study. Diabetologia 2006;49:1498–504.
- [16] Bruno G, Karaghiosoff L, Merletti F, Costa G, De Maria M, Panero F, et al. The impact of diabetes on prescription drug costs: the population-based Turin Study. Diabetologia 2008;51: 795—801.
- [17] Gnavi R, Picariello R, Karaghiosoff L, Costa G, Giorda C. Determinants of quality in diabetes care process: the population based Torino study. Diabetes Care 2009;32:1986—92.
- [18] Mihaylova B, Briggs A, O'Hagan A, Thompson SG. Review of statistical methods for analysing healthcare resources and costs. Health Econ; 2010. doi:10.1002/hec.
- [19] Bruno G, Novelli G, Panero F, Perotto M, Monasterolo F, Bona G, et al. Group for Diabetes Epidemiology. Incidence of type 1 diabetes is increasing both in children and young adults in Northern Italy: 1984-2004 temporal trend. Diabetologia 2009;52:2531-5.
- [20] Bruno G, Merletti F, Bargero G, Melis D, Masi I, Ianni A, et al. Changes over time in the prevalence and quality of care of

- type 2 diabetes in Italy: the Casale Monferrato Surveys, 1988 and 2000. Nutr Metab Cardiovasc Dis 2008;18:39—45.
- [21] http://www.agenas.it/agenas_pdf/evoluzione_spesa_01-05. pdf. (accessed 26.03.11).
- [22] Colagiuri S, Borch-Johnsen K, Glümer C, Vistisen D. There really is an epidemic of type 2 diabetes? Diabetologia 2005;48: 1459–63
- [23] Marchesini G, Forlani G, Rossi E, Berti A, De Rosa M. The ARNO Working Group. The direct economic cost of pharmacologicallytreated diabetes in Italy, 2006. ARNO Observatory Nutr Metab Cardiovasc Dis; 2009. doi:10.1016/j.numecd.2009.10.009.
- [24] Evans JM, Barnett KN, Ogston SA, Morris AD. Increasing prevalence of type 2 diabetes in a Scottish population: effect of increasing incidence or decreasing mortality? Diabetologia 2007;50:729–32.
- [25] Jagger C, Gillies C, Moscone F, Cambois E, Van Oyen H, Nusselder W, et al. EHLEIS team. Inequalities in healthy life years in the 25 countries of the European Union in 2005: a crossnational meta-regression analysis. Lancet 2008;20:2124–31.
- [26] Giorda C, Petrelli A, Gnavi R. Regional Board for Diabetes Care of Piemonte. The impact of second-level specialized care on hospitalization in persons with diabetes: a multilevel population-based study. Diabet Med 2006;23:377–83.