Abstract

Background There has been a widely documented and recognized increase in diabetes prevalence not only in high-income countries (HICs) but also in low- and middle-income countries (LMICs), over recent decades. It is less clear what is the economic burden associated with diabetes, especially in LMICs. Objective We provide a systematic review of the global evidence on the costs of type II diabetes. Our review seeks to update and considerably expand the previous major review of the costs of diabetes by capturing the evidence on overall, direct and indirect costs of type II diabetes worldwide that was published since 2001. In addition we include a body of economic evidence that has hitherto been distinct from the cost-of-illness (COI) work, i.e. studies on the labour market impact of diabetes. Methods PubMed, EMBASE, EconLit and IBSS were searched (without language restrictions) for studies assessing the economic burden of type 2 diabetes published from January 2001 to October 2014. Costs reported in the included studies were converted to international dollars ($) adjusted for 2011 values. Alongside the narrative synthesis and methodological review of the studies we conduct an exploratory linear regression analysis, examining the factors behind the considerable heterogeneity in existing cost estimates between and within countries. Results We identified 86 COI and 23 labour market studies. COI studies varied considerably in both methods and cost estimates, with most studies not using a control group, though the use of either regression analysis or matching has increased. Direct costs were generally found to be higher than indirect costs. Direct costs ranged from $242 for a study on out-of-pocket (OOP) expenditures in Mexico to $11917 for a study on the cost of diabetes in the USA, while indirect costs ranged from $45 for Pakistan to $16914 for the Bahamas. In LMICs —in much contrast to HICs— a substantial part of the cost burden arose to patients from OOP treatment costs. Our regression analysis revealed that direct diabetes costs are closely and positive associated with a country's gross domestic product (GDP) per capita, and that the USA stood out as having particularly high costs, even after controlling for GDP per capita. Studies on the labour market impact of diabetes were almost exclusively confined to HICs and found strong adverse effects, particularly for male employment chances. Many of these studies also took into account the possible endogeneity of diabetes, which was not the case for COI studies. Conclusions The reviewed studies indicate a large economic burden of diabetes, most directly affecting patients in LMICs. The magnitude of the cost estimates differs considerably between and within countries, calling for the contextualization of the study results. There remains large scope for adding to the evidence base on labour market effects of diabetes in LMICs. Further, there is a need for future COI studies to incorporate more advanced statistical methods in their analysis to account for possible biases in the estimated costs.

1 Introduction

Diabetes is a chronic disease that has spread widely, not only in high-income but also in many LMICs over the last decades. The most recent data from the International Diabetes Federation indicate that diabetes affected 382 million people worldwide in 2013, a number that is expected to grow to 592 million by 2035. The estimated global prevalence in 2013

amounts to 8.3 % among people aged 20–79 years, with the world's most populous countries India and China reaching prevalence rates between 9 and 10 %, corresponding to 65 and 100 million in absolute numbers, respectively. Particularly high prevalence rates are found in Mexico (12.6%) and Egypt (16.8%), surpassing the rates of most HICs, including the USA (9.2%) and Germany (8.2%).(International Diabetes Federation, 2014) Taken together, in 2013 about two-thirds of all individuals with diabetes lived in LMICs (International Diabetes Federation, 2014). The rising prevalence of diabetes in LMICs appears to be fuelled by rapid urbanization, nutrition transition and increasingly sedentary lifestyles (Hu, 2011). The most prevalent form of diabetes by far is type 2 diabetes, affecting about 90 % of people with diabetes while the remaining 10 % mainly have type 1 diabetes or gestational diabetes (International Diabetes Federation, 2014).

Due to its adverse effect on people's health diabetes also imposes an economic burden on individuals and households affected as well as on healthcare systems. The economic burden of diabetes was confirmed by in a review of COI studies on diabetes mellitus, published in 2004, covering the literature up to the year 2000. The authors concluded that the direct and indirect economic burden of diabetes was "large", and that costs had increased over time. However, the review also noted that significant variation in costing methodologies made it near impossible to directly compare the cost estimates. However, the studies reviewed by Ettaro et al. (2004) were almost exclusively focused on the USA, with a small part coming from European HICs and none from LMICs. The aim of this study is therefore to systematically review the literature on the economic costs of diabetes published since 2001 (i.e. the first year not covered by the Ettaro et al. (2004) review), as we expect a considerable number of new studies, also from LMICs. In addition to the COI studies we review the literature on labour market outcomes, with a specific interest in the methodological challenges involved. In doing so we substantively update and expand the scope of the Ettaro et al. (2004) review, allowing us to revisit its findings regarding the evidence base about the economic burden of type 2 diabetes globally.

COI studies generally assess the direct and indirect costs of a particular illness, where the former represent the opportunity cost of resources used for treatment. The indirect costs measure the value of resources lost due the illness, most commonly those caused by losses in productivity due to mortality and morbidity as measured in lost earnings (Segel, 2006). In addition, another approach also focuses on estimating the impact of diabetes on labour market outcomes. However, rather than trying to estimate the monetary losses that arise from a decrease in productivity, these studies typically compare labour market outcomes (e.g. employment probabilities, earnings or lost work days) between people with and without diabetes, while accounting for differences in age, education and other demographic and socioeconomic variables, that might arise between both groups and that could affect labour market outcomes as well as the chances of developing diabetes. The aim of studies in this field is to obtain a clearer picture of how diabetes causally affects these labour market outcomes, without necessarily monetizing the results. Because of the different methodologies and data requirements, these studies tend to differ considerably from traditional COI studies, which is why we reviewed them separately. To the best of our knowledge this is the first review that systematically assesses the studies in this particular field.

2 Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used as a basis for the overall study approach.(Moher et al., 2009)

2.1 Search Strategy

The electronic search was based on the following search terms: "Diabetes Mellitus"[Mesh] AND ("Costs and Cost Analysis"[Mesh] OR "Cost of Illness"[Mesh] OR "Employment"[Mesh] OR "Labor Market"[All fields] OR "Labour Market"[All fields] OR "Productivity"OR "Willingness to pay"[All fields]). The above search was run in PubMed and was then adapted for searches in EMBASE, EconLit and the International Bibliography of the Social Sciences (IBSS). The search was carried out from October 2012 to October 2014 and restricted to studies published between January 2001 and October 2014, as the earlier review had covered COI studies until 2000 (Ettaro et al., 2004). No language restrictions were applied. The references were downloaded in RIS format where possible and then transferred to Mendeley. Authors were contacted for further information if clarification was needed after the full text analysis.

2.2 Inclusion and Exclusion Criteria

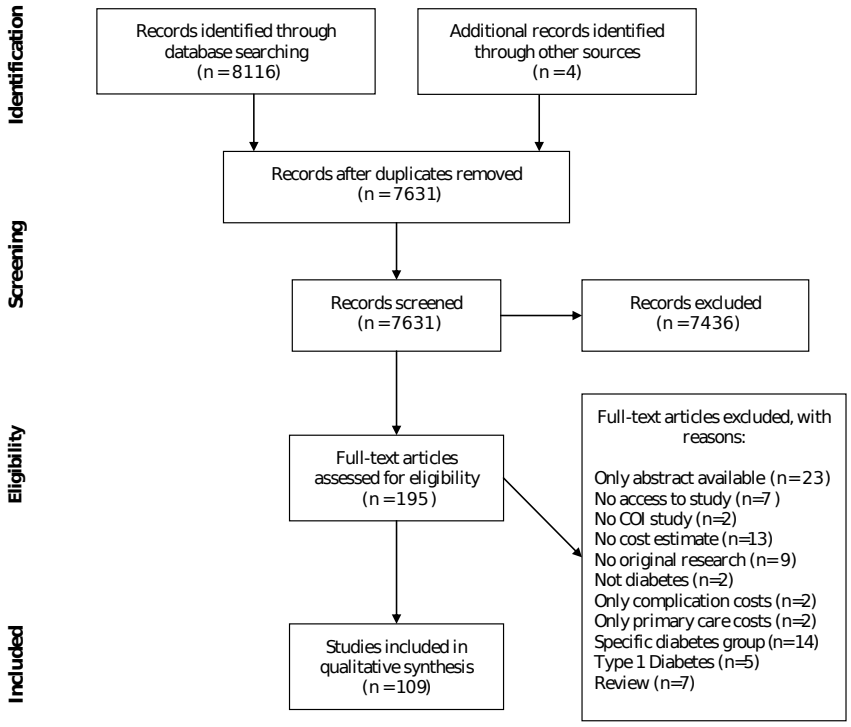
Studies were eligible if a monetary estimate of the direct and/or indirect costs of diabetes was presented in the results section or if studies provided an estimate of the impact of diabetes on labour market outcomes (employment chances, labour income, wages and lost work days). We did not exclude studies with a small sample size as this might have discriminated against studies in LMICs. Studies on types of diabetes explicitly different from type 2 diabetes were excluded. However, we included studies that did not explicitly mention the type of diabetes, given that type 2 diabetes accounts for about 90 % of all diabetes cases. Studies exclusively assessing the costs of diabetes complications or the costs of management strategies were excluded as were studies estimating the costs for specific groups with diabetes (e.g. costs for people with poorly controlled diabetes), since we were interested in the costs incurred to populations comprising the whole spectrum of people with type 2 diabetes. Editorials, reviews and studies for which the full text could not be retrieved or only an abstract was available were also excluded.

2.3 Data Extraction and Analysis

Data extraction was carried out by two investigators (TS and OA). After duplicates were removed, titles and abstracts were scanned by one researcher (TS) to identify studies suitable for a full text review. The process was checked by a second researcher (OA) on a random subsample of 2000 studies of the retrieved references. The full text was subsequently retrieved for the identified studies and they were reviewed by two researchers (TS and OA), with disagreements resolved by discussion. Finally, 109 studies were identified (see Figure 1) that fulfilled the inclusion criteria and data extraction was carried out using a pre-defined extraction table. Primary outcomes were the total costs, the direct costs,

and the indirect costs of type 2 diabetes and the respective per capita estimates of these outcomes, as well as the impact of type 2 diabetes on employment chances, income, wages and lost work days. Secondary outcomes comprised the methodology used to assess the monetary costs of type 2 diabetes, the range of cost factors included in the analysis, as well as the methodology used to assess the labour market impact of diabetes. Further extracted information included the year of publication, year of data collection, the time horizon, the country or region studied, the data source, sample size and age as well as information on whether the study distinguished between types of diabetes.

Figure 1: PRISMA flowchart.



We present the COI study results in per capita values to facilitate comparability across countries. For studies presenting overall population level estimates rather than per capita costs information, we calculated those costs, whenever possible, using the diabetes prevalence mentioned in the respective study. If no total cost estimate was presented but information on direct and indirect costs was available, then direct and indirect costs were added up to produce a total cost estimate. We converted costs into purchasing-power-parity (PPP) adjusted estimates, also called international dollars and henceforth denoted with the $ sign, in order to further increase comparability. Since some studies did not present the data in the country's local currency but in USA$ or some other major currency, we used the exchange rate given in the article to convert the estimates back into the local currency. If no exchange rate was provided in the study itself, the average exchange rate (midpoint exchange rate according to OANDA historical exchange rates - [http://www.oanda.com/currency/historical-rates/]) for the reported year. The PPP adjusted estimates for the year 2011 were then calculated using the Campbell and Cochrane

Economics Methods Group Evidence for Policy and Practice Information and Coordination Centre (CCEMG-EEPPI Centre) cost converter (Shemilt et al., 2010). For all additional analyses carried out in the following sections only studies for which a mean cost estimate was presented or could be calculated, were included. Further, in the case of a study presenting estimates for more than 1 year, only the estimate for the most recent year was used for the analysis. For studies presenting both incremental and total cost estimates, only the incremental cost estimate was taken into account.

Studies were further classified into two groups according to the level of economic development of the investigated country—(1) high-income and (2) LMICs (LMICs)—according to the historical World Bank income group classification of the respective country in the year that data collection for the respective study had taken place (World Bank, n.d.). Where necessary due to space constraints we used abbreviations for country names, as detailed in Table 7.

In order to explore the factors involved in the variation of direct costs reported in COI studies, we first plotted the direct per capita costs in relation to the gross-domestic-product (GDP) per capita of the respective country and provided an estimate of the relationship using linear regression. We then conducted an exploratory regression analysis, with the annual direct cost per patient as the dependent variable to investigate what other factors might explain the variation in direct cost estimates. The set of independent variables comprised (1) the estimation approach in each study, (2) the year of data used, (3) GDP per capita of the studied country in international dollars, (4) an indicator of whether the study was conducted in the USA, (5) an indicator of whether the study was deemed to be nationally representative, and (6) a variable indicating whether the study had explicitly taken diabetes-related complications into account. The year of the used data was considered because the development of social security systems and treatment methods may affect how the direct costs evolve over time. We categorized this variable into groups: studies using data from before 1995, 1995 to 1999, 2000 to 2004, 2005–2009 and 2010–2004. The dummy variable for studies on the USA was included to account for the generally higher healthcare expenditures in the USA compared which other HICs with similar per capita income levels (Laugesen and Glied, 2011). Accounting for national representativeness should cancel out any effects that might be driven by those studies that estimate costs for sub-national, regional- or city-level population samples. Including an estimator for diabetes complications should account for the possible underestimation of diabetes costs in studies excluding complications. We exclude country estimates extracted from multi-country studies in our preferred specification, as their inclusion would lead to an over-statement of the cost effect of the estimation method employed in the given multi-country study.

3 Results

Due to the differences in methodologies, we first present the findings on the identified COI studies and subsequently turn to studies on labour market outcomes.

3.1 COI studies on Type 2 Diabetes

3.1.1 Number of Studies

We identified a total of 86 relevant COI studies (see Table 8 for a detailed description of the included studies), of which 62 focused on HICs, 23 on LMICs, and one multi-country study covered both HICs and LMICs. Studies in LMICs increased over time, with the majority of the LMIC studies being published between 2007 and 2014. Six of the selected studies were multi-country studies, of which two (Kirigia et al., 2009; Smith-Spangler et al., 2012) did not provide detailed cost estimates for every country in the study and one did not provide a year for the estimated costs, so that we could not calculate estimates in international dollars (Boutayeb and Boutayeb, 2014). Therefore, we could not include these particular studies in our country-specific analysis.

3.1.2 Regional Distribution

In terms of geographic regions, most studies were carried out on countries in Latin America and the Caribbean (n=38) and Europe (n=37), followed by the USA and Canada (n=26), East Asia and Pacific (n=11), the Middle East and North Africa (n=5), South Asia (n=4), Sub-Saharan Africa (n=4) and Australia (n=1). The USA was the most studied country (n=19), followed by Canada (n=7) and Germany (n=5). Mexico (n=6) and China (n=4) were the most frequently studied LMICs.

3.1.3 Data Sources

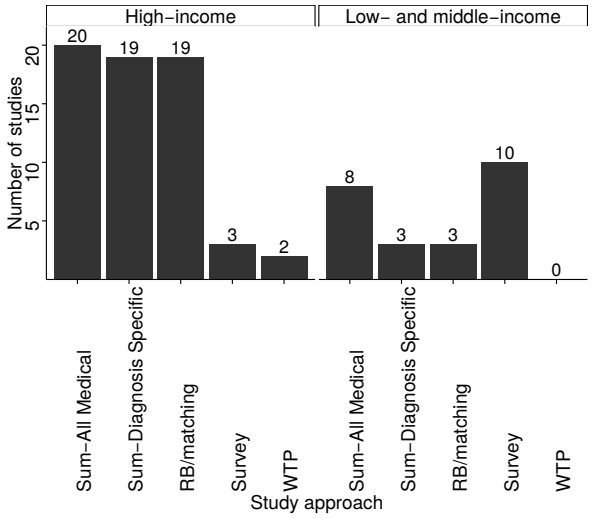
Especially in LMICs, self-administered surveys represented a popular method to retrieve data on the cost of diabetes. These were mostly limited regionally, i.e. to a city or hospital, and usually only representative of these regional diabetes populations but not of a national population. In HICs, databases of insurance and healthcare providers were the main source of information in most studies. These data tended to be representative either at a national or at some sub-national level. As a result, the size of the samples in HICs was mostly between 1,000 and several million. By contrast, studies in low- and lower-middle-income countries were generally characterized by smaller sample sizes, ranging from 35 (Suleiman et al., 2006) to about 2,433 (Yang et al., 2012) in the studies reviewed here.

3.1.4 Variation in Costing Approaches

As discussed in more detail in Text Box 1, a range of costing approaches can be found in the COI literature. Figure 2 shows that the most common costing method for the direct costs of diabetes in HICs was the sum-all medical approach for people with diabetes without using control groups (Arredondo and Barcelo, 2007; Arredondo, Zúñiga, and Parada, 2005; Arredondo and De Icaza, 2011; Arredondo and Zúñiga, 2004; Barceló et al., 2003; Bjegovic et al., 2007; Boutayeb and Boutayeb, 2014; Brandle et al., 2003; Camilo González et al., 2009; Chi et al., 2011; Condliffe et al., 2013; Horak, 2009; Jönsson, 2002; Kirigia et al., 2009; Lau et al., 2011; Lee et al., 2006; Lucioni et al., 2003; Maciejewski and Maynard, 2004; Martin et al., 2007; Morsanutto et al., 2006; Nakamura et al., 2008; Nolan et al., 2006; Ohinmaa et al., 2004; Oliva et al., 2004; Peele et al., 2002; Pohar,

Majumdar, et al., 2007; Redekop et al., 2002; Ringborg et al., 2008; Zhou et al., 2005). The disease-attributable costing approach (Abdulkadri et al., 2009; Ballesta et al., 2006; Bastida and Pagán, 2002; Buescher et al., 2010; Dall, Nikolov, et al., 2003; Davis et al., 2006; Honkasalo et al., 2014; Johnson et al., 2006; Lin et al., 2004; Mata et al., 2002; Rodríguez Bolaños et al., 2010; Simpson et al., 2003; Solli et al., 2010; Suleiman et al., 2006; Tunceli, Wade, et al., 2010) and the attributable-fraction approach were also used widely, though mainly in the USA (Bolin et al., 2009; Dall, Mann, et al., 2008; Dall, Zhang, et al., 2010; Dawson et al., 2002; Honeycutt et al., 2009; Lesniowska et al., 2014; Schmitt-Koopmann et al., 2004). The incremental cost approach was applied primarily in studies on HICs (Birnbaum et al., 2003; Bruno et al., 2012; Chodick et al., 2005; Durden et al., 2009; Esteghamati et al., 2009; Honeycutt et al., 2009; Köster, Ferber, et al., 2006; Köster, Huppertz, et al., 2011; Köster, Schubert, et al., 2012; Linden et al., 2009; Marchesini et al., 2011; Norlund et al., 2001; O'Connell et al., 2012; Pohar and Johnson, 2007; Ramsey et al., 2002; Ricordeau et al., 2003; Rodbard et al., 2010; Smith-Spangler et al., 2012; Trogdon and Hylands, 2008; Tunceli, Wade, et al., 2010; Wiréhn et al., 2008; Yang et al., 2012). For LMICs, the survey approach was the most used (Biorac et al., 2009; Chan et al., 2007; Chatterjee et al., 2011; Druss et al., 2001; Elrayah-Eliadarous et al., 2010; Javanbakht et al., 2011; Khowaja et al., 2007; Al-Maskari et al., 2010; Ramachandran et al., 2007; Tharkar et al., 2010; Wang, Fu, Pan, et al., 2009; Wang, Fu, Zhuo, et al., 2010; Wang, McGreevey, et al., 2009).

Figure 2: Number of COI studies, by costing approach and income group.



Notes: For LMICs no willingness to pay (WTP) study is counted, because the only study (Tharkar et al., 2010) presenting a WTP estimate for a LMIC used primarily a different approach to estimate costs, and the WTP estimate was only presented additionally. Therefore this study was not counted under WTP here. Two studies are counted twice as they give estimates for a sum-diagnosis specific and a RB/matching approach.

By contrast, almost all indirect cost assessments followed the same methodology, i.e. the human capital approach. This approach considers all forgone labour earnings of a patient or caregiver that are attributable to diabetes. A minority of three studies (Chang,

2010; Gyldmark and Morrison, 2001; Tharkar et al., 2010), estimated the indirect costs using the WTP approach, which tries to measure how much individuals would be willing to pay to reduce the risk of an illness (Segel, 2006), here diabetes (or certain complications associated with it). One of the studies included WTP estimates in addition to the direct and indirect costs measured by the human capital approach (Tharkar et al., 2010) but did not include the WTP estimate in the overall cost estimate, while the other two studies estimated exclusively the WTP (Chang, 2010; Gyldmark and Morrison, 2001).

3.1.5 Study Perspective

Studies also varied in their perspective, again compromising direct comparability of the cost estimates across studies. Overall, most studies either took a societal (n=32) or healthcare system perspective (n=48). The former generally takes into account the direct and indirect monetary costs that arise to society, including costs to the healthcare system, costs due to lost productivity and sometimes OOP costs (Segel, 2006). The latter was especially common in HICs where many studies assessed the cost of diabetes to private or public health insurances. In LMICs, studies often took the patient perspective (n=5), estimating OOP expenditures and in some cases productivity losses, directly arising to the diabetes patient.

Text box 1 COI methodologies

Methodologies for COI studies can broadly be categorized into two main categories:(1) estimating the total disease costs and (2) estimating the incremental costs (Akobundu et al., 2006). Studies can then be divided further according to the specific approach used for estimation. Our categorization builds on that by Akobundu et al. (2006) in their review of COI methodologies.

1. Total disease costs

   (a) Sum-All Medical: captures all medical expenditures of a person diagnosed with diabetes, irrespective of the relation of the expenditures with diabetes.

   (b) Sum-Diagnosis Specific: includes the costs that are related to diabetes. This can be done by using a disease-attributable costing approach, using administrative claims databases to identify the cost of diabetes by respective International Statistical Classification of Diseases and Related Health Problems (ICD) codes that link the expenditures to a primary or secondary diagnosis of diabetes as the reason for the healthcare utilization. Alternatively, a similar technique used at the population level is the attributable-fraction approach, where the relative contribution of, e.g., diabetes, to the risk of developing another disease (e.g. renopathy or cardiovascular disease) is used to determine how much of the costs of this disease can be attributed to diabetes.

   (c) Survey approach: while not specifically mentioned by Akobundu et al. (2006), for this review we create a separate category capturing studies using surveys of people with diabetes. This category differs from the two approaches a) and b) above in that estimations rely solely on the individual, reported experience of people with diabetes, without use of any diagnostic data at an aggregate level. The survey approach was also used as a separate category in the earlier review on diabetes COI studies by Ettaro et al. (2004).

2. Incremental disease costs

   There are two main approaches for the estimation of incremental medical costs:

   (a) Regression approach: a statistical technique which can account for observable differences between the group with diabetes and the control group (i.e. those without diabetes) to find—ideally—the independent effect of diabetes on healthcare costs. The differences typically accounted for are age, region and gender.

   (b) Matching approach: uses a control group to directly compare those with diabetes to those without diabetes after matching each person of the 'treatment' group to a 'similar' person of the control group, using various categories like age, region and gender to—again—find the independent effect of diabetes on healthcare cost (Akobundu et al., 2006).

All of the above approaches can be used in prevalence or an incidence based study. In the former case the costs of diabetes are estimated for a certain point in time, typically one year, while the latter approach estimates costs over a person's lifetime or several years, always starting with the point at which the disease is diagnosed. Both approaches may also be combined in studies estimating the future cost burden of type 2 diabetes by first taking a prevalence approach to calculate current costs and then using predictions about future diabetes incidence rates to arrive at an estimate of diabetes costs at a certain point in the future.

3.1.6 Costing Components

Of the 75 studies that reported the cost components they used to estimate direct costs, 72 took into account outpatient hospital visits, 70 inpatient hospital visits, 63 physician visits, 58 drug costs, 51 laboratory costs for diagnostic tests and check-ups, 37 equipment costs and 21 non-medical and transportation costs. A total of 46 studies had at least included the costs of hospital, outpatient and physician visits as well as drugs (see Table 9 for a detailed description of cost components used in each study).

3.1.7 Cost Estimates of Diabetes Using a Prevalence Approach

Two basic epidemiological approaches exist for the estimation of COI, and they are not directly comparable. The incidence approach follows people with diabetes, usually starting with their diagnosis at a common base year, estimating yearly costs for a sample of people at the same disease stage, finally giving an estimate of diabetes costs over a certain time period, such as from diagnosis to death or over a distinct period of, for example, 10 years. This approach can also document how costs of diabetes change and develop over the progression of the disease (Larg and Moss, 2011). By contrast, the prevalence approach estimates the costs of diabetes for a cross-section of people with diabetes at a certain point in time, normally a year, who are at different stages of the disease. It is most suitable for assessing the total economic burden of diabetes at a certain point in time. Due to this difference in time periods and the used data, the estimates of prevalence-based studies are not directly comparable with those of incidence-based studies. Hence, we present the cost estimates separately, starting with the prevalence approach.

Table 2 shows the range of direct cost estimates by estimation approach and income status. As can be observed, direct cost estimates varied widely, both between and within the different estimation approaches. Cost estimates for direct costs, irrespective of the costing method applied and the cost components included, ranged from $242 for Mexico Arredondo, Zúñiga, and Parada (2005) in 2010 to $11,917 for the USA Condliffe et al. (2013) in 2007. Also, studies from LMICs generally indicated smaller direct costs than studies from HICs.

For indirect costs, studies using the human capital approach estimated costs ranging from $45 for Pakistan (Khowaja et al., 2007) in 2006 to $16,914 for the Bahamas (Barceló et al., 2003) in 2000. Three studies estimated indirect costs by using the WTP approach and found costs ranging from $191 in a study on the WTP for a health insurance for type 2 diabetes in Denmark in 1993 (Gyldmark and Morrison, 2001), a WTP $4,004 per year for a cure of type 2 diabetes (Chang, 2010) in Taiwan and an annual payment of $4,737 to halt disease progression/prevent future complications of diabetes in India (Tharkar et al., 2010).

Societal costs of Type 2 Diabetes, which are estimated by studies combining direct and indirect costs, ranged from $544 in a study on the economic costs of diabetes in Iran (Esteghamati et al., 2009) in 2001 to $18,224 for the Bahamas (Barceló et al., 2003) in 2000.

In order to improve the cross-country comparability of the costs of diabetes we plotted the results from studies providing a direct per capita cost estimate against the GDP per capita estimate of the respective country (we limited this comparison to studies using

Table 1: Summary of direct costs by estimation approach and income status in international dollars $ (2011) for prevalence-based studies.

	High-income countries				Low- and middle-income countries			
	Sum-all medical costs	Sum-diagnosis specific	RB / matching	own survey	Sum-all medical costs	Sum-diagnosis specific	RB / matching	own survey
Min	1117	907	264	1495	242	662	443	456
Max	11917	9346	8306	5585	4129	4672	1136	3401
N	25[a]	19[a]	18	3	27[a]	5[a]	2	10

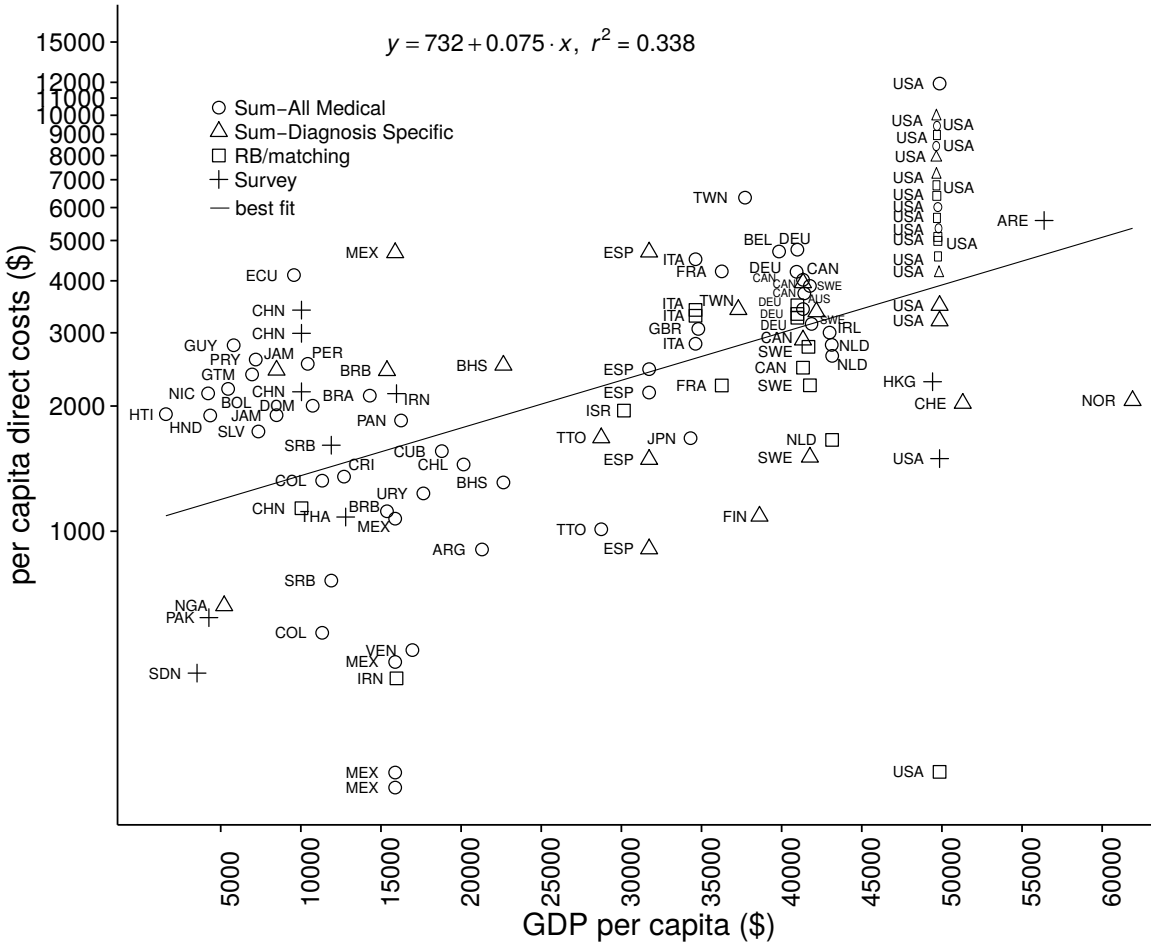
[a] Includes country estimates from multi-country studies; RB Regression based

samples representative of their entire population). Figure 3 confirms the expectation that costs do increase with economic wealth: GDP per capita explains about one-third of the variation in cost estimates (see r2 in Figure 3). Also, studies on the USA seem to estimate costs consistently higher than would be expected on the basis of its GDP per capita.

The USA, however, spend consistently more than what would be expected on the basis of its GDP per capita. Again, the wide variation in estimated costs for many countries underscores the point that the studies need to be contextualized and may not be directly comparable per se. On the whole—though by no means always—the matching and regression as well as the sum-diagnosis specific approaches appear to produce lower cost estimates than especially the total cost results, particularly so for HICs. In an inevitably crude attempt to quantitatively explore the driving factors behind the heterogeneity in cost estimates, we estimated a simple linear regression model with per capita direct costs as the dependent variable; explanatory variables included GDP per capita, the estimation approach employed by the study, the number of included cost components, a dummy for studies carried out in the USA, the year of data collection, the representativeness of the study and if the study included diabetes complications as explanatory variables. The results, displayed in Table 2, show a strong relationship between GDP per capita and expenditures for diabetes, with every additional international dollar in per capita GDP translating into an average increase in direct diabetes expenditures of about $0.04. The estimation approach is not found to matter significantly, nor is the year of study. Estimates from USA studies put the costs at over $3,000 higher (on average) than studies from other countries, indicating that costs in the USA may indeed be unusually high. The number of costing components and the inclusion of complications likely also explain some of the variance in estimates, although they are just below and above the 10 % significance level, respectively. Overall, the included independent variables explain about 56 % of the variation in direct cost estimates.

The sensitivity of the cost results to the estimation approach was also examined by two

Figure 3: GDP to direct costs ratio by estimation approach.



Notes: The line depicts the best fit based on the linear regression of direct costs on GDP per capita in international dollars.

Table 2: Relationship between direct costs and study characteristics (robust linear regression).

	Estimate	Std. Error
Constant	2133	1773.922
GDP per capita ($)	0.045**	0.017
Estimation Approach		
Sum-All medical (Ref.)		
Sum-Diagnosis Specific	−413.880	528.766
RB/matching	−719.868	526.896
Survey	−689.806	671.020
At least four costing components	702.966*	403.968
USA study	3111.067***	533.534
Year of study		
<1995 (Ref.)		
1995-1999	−1744.799	1632.498
2000-2004	−816.647	1586.966
2005-2009	−1021.685	1592.595
2010-2014	−2744.739	1839.689
Study representative	−598.670	409.070
Complications	666.803	414.727
R-squared adj.	0.559	
N	70	

Standard errors in parenthesis. Ref. reference category.
* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

studies that investigated the effect of different estimation techniques in diabetes COI studies. Honeycutt et al. (2009) compared the use of a regression-based and an attributable-fraction approach and found that the cost estimate of the former exceeded the latter by 43 %. Tunceli, Wade, et al. (2010) compared the matching and the diabetes (disease)-attributable costs approach and found a 14–29 % higher cost estimate using matching, depending on the used assumptions. Both studies concluded that an incremental cost approach results in a higher, and likely more exact, estimate of the direct costs of diabetes than disease-attributable approaches. The authors attributed this to the fact that a regression or matching approach can assign costs to diabetes that cannot be linked to diabetes otherwise. Those approaches are therefore in a position to account for all costs of co-morbidities caused by diabetes, while this is not automatically the case with the other approaches.

3.1.8 Direct and Indirect Costs of Diabetes

To assess the relative importance of direct and indirect costs across countries, we plotted direct against indirect costs from studies that provided both estimates and drew a 45°line depicting the equal share of direct and indirect costs (see Figure 4).

Most studies found a larger share for direct costs in comparison with indirect costs (observations above the 45°line in Figure 4). This is especially true for HICs, where only a study on Sweden (Bolin et al., 2009) found a larger share for indirect costs. For LMICs, a study on Colombia (Camilo González et al., 2009) found considerably higher indirect costs, as did the multi-country study of Barceló et al. (2003) and a study on various countries in the African region (Kirigia et al., 2009), which both found higher indirect costs for almost every country in the study and also on average for the entire regions, represented as the mean overall study estimate in Figure 4. Both studies used similar approaches to estimate costs, and indirect cost estimates were likely so high because evidence from only a few countries within the region were used as a basis for estimating indirect costs for every other country in the respective study. Further, the studies took the countries' per capita gross national product as a proxy for earnings, which might have led to an over-estimation of the indirect costs (Kirigia et al., 2009).

3.1.9 Studies Using the Incidence Approach

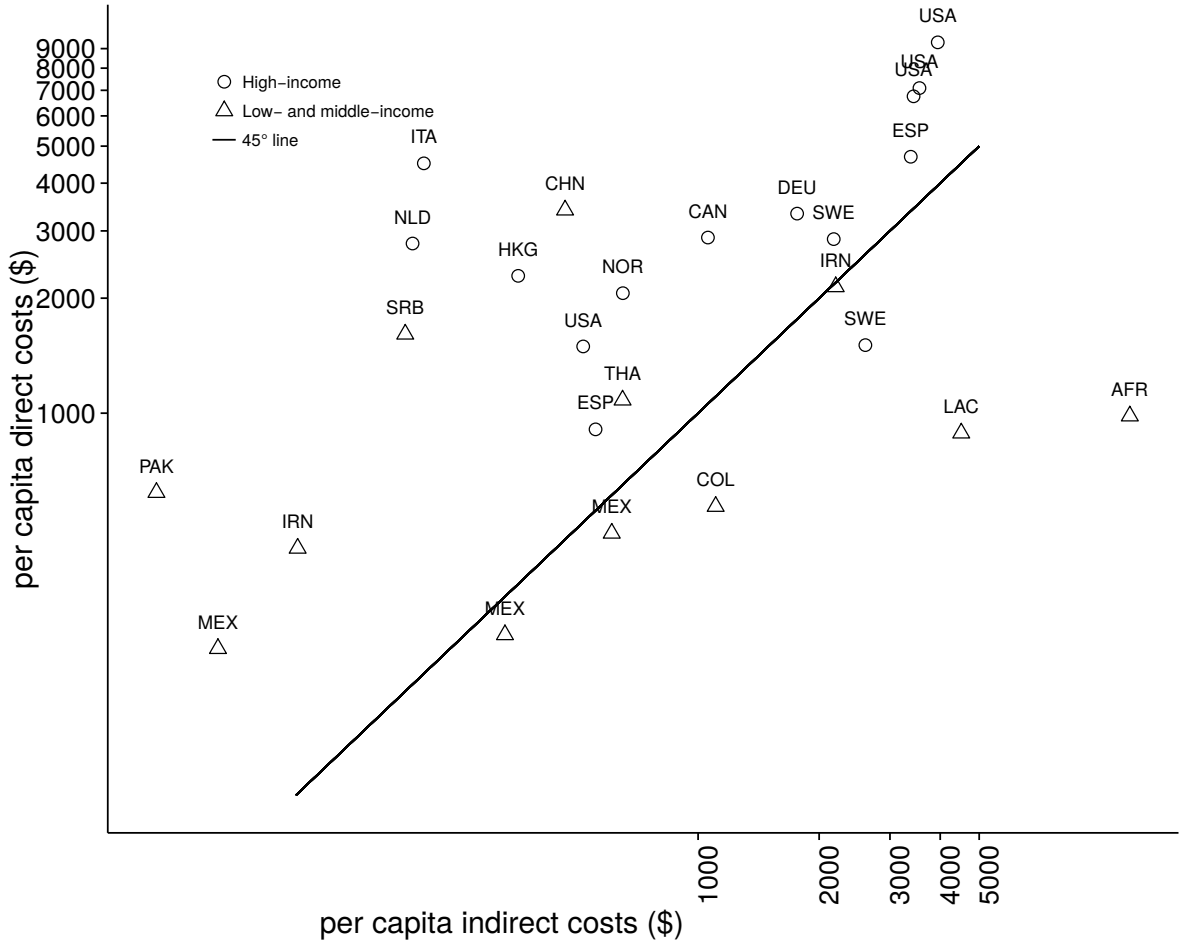
The four studies that used an incidence approach (see Table 3 estimated the cost of diabetes either over a person's lifetime (Birnbaum et al., 2003; Camilo González et al., 2009) or over a certain period after diagnosis Johnson et al. (2006) and Martin et al. (2007). Camilo González et al. (2009) modelled the lifetime (direct and indirect) costs of a typical diabetes patient in Colombia, arriving at a mean cost estimate of $54,000. The second study providing lifetime estimates by Birnbaum et al. (2003), estimated incremental lifetime healthcare costs for USA females with diabetes of $283,000.

Two studies followed patients over a limited time period and found different patterns in the development of Type 2 Diabetes-attributable healthcare costs. In Germany costs increased from $1634 in the first year after diagnosis to $4881 in the seventh year (Martin et al., 2007). In Canada, Johnson et al. (2006) found the highest costs in the year of diagnosis with $7635, up from $2755 the year prior to diagnosis. In the year after diagnosis costs decreased to $4273 and then only increased slightly to $4618 in year ten. In Germany and Canada, costs related to complications or hospital visits were the most important components and in Germany increased steadily over time. In Canada costs related to prescriptions increased the most.

3.1.10 Country level costs prediction studies

Four studies projected costs of diabetes over a certain period of time (Davis et al., 2006; Lau et al., 2011; Ohinmaa et al., 2004; Wang, McGreevey, et al., 2009), making assumptions about the future development of diabetes prevalence and population ageing (see Table 4). For Canada, a 1.7-fold increase from 2000 to 2016 (Ohinmaa et al., 2004) and a 2.4-fold increase from 2008 to 2035 in diabetes healthcare costs was estimated (Lau et al.,

Figure 4: Direct and indirect cost relation in studies estimating total costs of type 2 diabetes.



Notes: The 45°line depicts the points where direct and indirect costs would be equal. Above the line direct costs are higher than indirect costs and vice versa. For better visibility both coordinate axes are expressed in log scale

Table 3: Incidence studies on the costs of diabetes

Ref.	Country	Time horizon	Population	Approach	Results
Johnson et al. (2006)	Canada	1992–2001	Incidence T2D patients from Saskatchewan Health's administrative database in Canada	Sum-all medical	Highest total healthcare costs at year of diagnosis with CAN$7343 ($7635), then increased from a low of CAN$3880 ($4034) 3 years after diagnosis to CAN$4441 10 years thereafter ($4618).
Camilo González et al. (2009)	Colombia	32 years	Hypothetical average Columbian T2D patient	Sum-all medical	Total lifetime costs (32 year period) of average diabetes patient, including direct and indirect costs, 57.565 million Colombian pesos ($54,351).
Martin et al. (2007)	Germany	1995–2003	Newly diagnosed T2D patients from randomly drawn practices across Germany	Sum-all medical	EUR 1,288 ($1635) for the first treatment year after diabetes diagnosis and increased to EUR 3845 ($4880) in the seventh year.
Birnbaum et al. (2003)	United States	1997–1998	Women employed by nationwide operating company and hypothetical women above age 64 receiving Medicare	RB/matching	$282973 incremental lifetime direct healthcare costs, using incidence-based, steady-state methodology.

2011). Taking a health care system perspective, both studies found that the estimated increase would be mostly driven by an ageing population. For Australia, Davis et al. (2006) estimated a 2.5- to 3.4-fold increase in diabetes attributable healthcare costs from 2000 to 2051, depending on the underlying assumptions about population ageing and diabetes prevalence rates. For China, Wang, McGreevey, et al. (2009) extrapolated total costs of diabetes from the year 2007 to 2030, estimating the costs of diabetes to increase 1.8-fold, solely accounting for the expected increase in prevalence.

Table 4: Country level costs prediction studies

Ref.	Country	Population	Approach	Time horizon	Results
Davis et al. (2006)	Australia	Australian population	Sum diagnosis Specific	2000–2051	If age and sex specific prevalence remains unchanged a 2.5-fold increase; if age and sex specific prevalence allowed to change as well a 3.4-fold increase.
Ohinmaa et al. (2004)	Canada	Canadian population	Sum-all medical costs	2000–2016	1.7-fold increase.
Lau et al. (2011)	Canada	Four Alberta Health and Wellness databases	Sum-all medical costs	2008–2035	2.4-fold increase.
Wang, McGreevey, et al. (2009)	China	In patients and outpatients in 20 hospitals	Own survey	2007 and 2030 (projection)	Increase from $73 billion in 2007 to $132 billion in 2030 (1.8 fold increase).

3.2 The Impact of Diabetes on Employment Chances and Productivity

Besides studies that determined the cost of diabetes by costing related expenditures, another body of research has investigated —using econometric techniques—the impact of diabetes on 'productivity', a term used here to comprise outcomes including employment probabilities and lost work days and income or earnings. A recent study systematically reviewed evidence on the impact of diabetes on the ability to work, focusing on studies

assessing the impact of diabetes on early retirement, lost work hours, absenteeism and presenteeism (Breton et al., 2013). We focused particularly on studies exploring the impact of diabetes on employment probabilities and earnings—both issues that were not covered in the mentioned review—and we took a more detailed look at the empirical challenges posed by the issue of endogeneity (see the Appendix for a more detailed discussion of endogeneity).

Tables 5 and 6 synthesize the relevant information from the 22 identified studies on the effect of diabetes on employment and other labour market outcomes. Almost all studies were conducted on HICs, mainly the USA (n=13) and European countries (n=4). Only one study focused on a LMIC. investigating the effect of diabetes on labour income in China.

3.2.1 Employment Chances

Most studies examined the impact of diabetes on employment probability (n=17), applying a range of econometric techniques. These have evolved over time, and more recent studies took into account the possibility that diabetes might be endogenous: it is conceivable that especially personal traits such as motivation and drive could influence the propensity to develop type 2 diabetes as well as a persons' job market opportunities. Further, being employed or unemployed could also lead to changes in lifestyles, due to changes in income, stress or leisure time, that could themselves affect the chances of developing diabetes (Brown, Pagan, et al., 2005). Of the studies that tried to account for this problem (Brown, Pagan, et al., 2005; Harris, 2009; Latif, 2009; Lin, 2011; Minor, 2011; Zhang et al., 2009), the majority used an instrumental variable (IV) technique. This approach allows for the consistent estimation of the effect of diabetes on employment if a variable can be found that is causally related to diabetes without affecting the employment chances through any other unobserved pathway apart from its effect on diabetes. (see Text Box in Online Resource 2). In the case of type 2 diabetes all studies used the family history of diabetes as an IV to exploit the fact that the development of type 2 diabetes is much more likely for individuals whose biological parents have also had diabetes. It is argued that, while controlling for education, age and other observable demographic and socioeconomic factors (e.g. wealth, regional and ethnic differences and the number of children in the household), having a family member with diabetes should not affect the person's employment status or other labour market outcomes, while strongly predicting the onset of type 2 diabetes.

Table 5: Studies estimating the relationship between diabetes and employment (2001 – 2014)

Ref	Survey year	Country	Age	Effect on employment	
				Males	Females
Harris (2009)	1999-2000	Australia	>24	Exogenous: 10.8 percentage points reduction to be in labour force; endogenous: 7.1 percentage points reduction and test indicates endogeneneity.	Exogenous: 10 percentage points to be in labour force; endogenous: Nine percentage points reduction and test indicates endogeneneity.
Zhang et al. (2009)	2001, 2004-2005	Australia	18-64	50-64: 11.5 percentage points less likely to be in labour force; 18-49: 3.9 percentage points less likely, all effects increase when other chronic diseases are present.	No significant effect for diabetes alone; significant negative effect if other chronic diseases are present.
Latif (2009)	1998	Canada	15-64	Exogenous: 19 percentage points less likely to be employed; endogenous: not significant and positive and test indicates endogeneity.	Exogenous: 17 percentage points less likely to be employed, endogenous: not significant and positive and test indicates exogeneity.
Kraut et al. (2001)	1983-1990	Canada	18-64	With complications 2 times less likely to be in labour force; no significant effect on employment for those in labour force.[a]	
Norlund et al. (2001)	1992-1993	Sweden	>24	14.2 percentage points higher retirement rate (22.9 compared to 8.7).[a]	

Ref	Survey year	Country	Age	Effect on employment	
				Males	Females
Alavinia and Burdorf (2008)	2004	Sweden, Denmark, Netherlands, Germany, Austria, Switzerland, France, Italy, Spain, Greece	50-65	For whole dataset: no effect of diabetes on being unemployed, but increased odds ratio of 1.33 on being retired. No information on effects by country.[a]	
Lin (2011)	2005	Taiwan	45-64	Exogenous: 9 percentage points less likely to be employed; endogenous: 19 percentage points less likely to be employed; test on whole sample indicates endogeneity.	Exogenous: 11 percentage points less likely to be employed, endogenous: not significant and negative.
Brown, Pagan, et al. (2005)		United States	>44	Exogenous: 7.4 percentage points less likely to be employed; endogenous: 10.6 percentage points less likely but test indicates exogeneity.	Exogenous: 7.5 percentage points less likely to be employed; Endogenous: no significant effect found and test indicates endogeneity.
Minor (2011)	2006	United States	>19 at diagnosis		Exogenous: 25.2 percentage points less likely to be employed, endogenous: 45.1 percentage points less likely to be employed.

Ref	Survey year	Country	Age	Effect on employment	
				Males	Females
Vijan et al. (2004)	1992-2000	United States	51-61	More likely to be retired in 1992 (adjusted OR 1.3). Over 8 years follow up spent 0.14 incremental years in retirement.[a]	
Bastida and Pagán (2002)	1996-1997	United States	>44	7.5 percentage points less likely to be employed.	No significant effect on employment chances found.
Brown, Perez, et al. (2011)	2008	United States	35-64	Diabetes negatively related to employment (5 percentage points reduction); better diabetes management (HbA1c) positively affects employment probabilities; HbA1c lowering of 10% increases employment probability by 0.44 percentage points.	No significant effect on employment chances found.
Tunceli, Bradley, et al. (2005)	1992,1994	United States	51-61	9 percentage points less likely to work without complications controlled for, with complications controlled for 7.1 percentage points less likely.	5.9 percentage points less likely to work without complications controlled for, with complications controlled for 4.4 percentage points less likely but not significant.
Tunceli, Zeng, et al. (2009)	1997-2005	United States	20-44 and 45-64	20-44: proportion with work limitations 3.1% higher; 45-64: proportion not working is 8.1% higher; the proportion work disabled is 3.4% higher; proportion with work limitations is 5.7% higher (all compared to similar age group without diabetes).[a]	

Ref	Survey year	Country	Age	Effect on employment	
				Males	Females
Valdmanis et al. (2001)	1990-1995	United States		Unemployment rate for persons with diabetes was 16% compared with 3% among matched comparison group.[a]	
Ng et al. (2001)	1989	United States	>29 at diagnosis	3.6% less likely of being employed (exogenous), 12% for those with complications.[a]	
Minor (2013)	1979-2010	United States	>14	Average reduction of employment probability of 28 percentage points; strongest employment penalty in first 5 years after diagnosis.	Average reduction of employment probability of 36 percentage points; strongest employment penalty in first 15 years after diagnosis.

[a] No gender differentiation in study

Because IV estimation has worse asymptotic properties than single equation regression results when endogeneity is not an issue, studies tested for the existence of endogeneity to determine which results to rely on for inference (Brown, Pagan, et al., 2005; Latif, 2009; Lin, 2011; Minor, 2011). Interestingly, the reviewed studies found diabetes to be endogenous for either males (Latif, 2009) or females (Brown, Pagan, et al., 2005; Minor, 2011), but never for both. Further, the use of an IV sometimes increased the estimated effect(Lin, 2011; Minor, 2011) whereas in other cases the effect turned insignificant (Brown, Pagan, et al., 2005; Latif, 2009). As a result, no unambiguous conclusions can be drawn as to how endogeneity affects diabetes and whether or not it causes biased estimates. Most of the relevant studies also explored whether accounting for body mass index (BMI) or other diabetes-related chronic conditions would substantially alter the result and found this not to be the case (Brown, Pagan, et al., 2005; Latif, 2009; Minor, 2013).

Overall, studies more commonly found a significant adverse impact of diabetes on males, ranging from no effect in Canada (Latif, 2009) to a 19 percentage point reduction in Taiwan (Lin, 2011). Conversely, no effect was found for women in Taiwan (Lin, 2011), Australia (Zhang et al., 2009) or for Mexican Americans in Texas (Brown, Pagan, et al., 2005). However, a 45 % decrease in employment chances was observed for women in the USA (Minor, 2011). Extending the scope and looking at how diabetes duration affected labour market outcomes, using panel data from the USA, one study found that the main adverse effect on employment chances materialized within the first 5 years after diagnosis for men and 11–15 years after diagnosis for women (Minor, 2013).

3.2.2 Productivity

For earnings, no effect was found for Mexican-American men in Texas (Bastida and Pagán, 2002), while the highest loss was found for women in the USA ($21392 per year) (Minor, 2011). Again looking at diabetes duration, a wage penalty was only found for USA men 6–10 years after diagnosis, reducing their wage by about 18 percentage points (Minor, 2013). The only study on a non-HIC, China, tried to tease out the psychological effect of a diabetes diagnosis on subsequent labour income, finding a reduction of 22 % in income for males, but not for females. Further, those with an HbA1c between 8–10 % experienced the most severe income penalty (29 %). The study further showed that the adverse effect of a diabetes diagnosis was concentrated among the poorest third of the study population (Liu and Zhu, 2014). Another study investigated the effect on earning losses for caregivers of people with diabetes in the United Kingdom (UK), finding a reduction of $2,609 per year, while the person with diabetes experienced a loss of $1,744 per year (Holmes et al., 2003). For income, a reduction of $6,250 per year was found for older USA adults who had been followed between the years 1992 and 2000 (Vijan et al., 2004). In terms of lost workdays and work hours due to diabetes, the effects ranged from no impact on lost work days on older people (Vijan et al., 2004) and females in the USA (Minor, 2011) to 3.2 lost work days in a USA population within a 2-week period if complications were present (Ng et al., 2001).

Table 6: Studies estimating the relationship between diabetes and other productivity outcomes (2001 – 2014)

Ref.	Survey year	Country	Age	Effect on other productivity outcomes	
				Males	Females
Kraut et al. (2001)	1983–1990	Canada	18–64	Effect on earnings only when complications are present: reduced to 72% of total income of controls.a	
Liu and Zhu (2014)	2009, 2011	China	not given	16.3% decrease in annual income; strongest effect for those in lower income quintiles.	16.3% decrease in annual income; strongest effect for those in lower income quintiles.
Herquelot et al. (2011)	1989–2007	France	Male 40–50, females 35–50 in 1989	1.7 HR to transition from employed to disabled, 1.6 HR to be retired, 7.3 HR to be dead; between age 35 and 60 each person with diabetes lost 1.1 years of time in workforce.[a]	

Ref.	Survey year	Country	Age	Effect on other productivity outcomes	
				Males	Females
Leijten et al. (2014)	2010–2013	Netherlands	45–64	Diabetes reduced work ability measured using Work Ability Index (WAI) by 2%. No significant effect on productivity was found.[a]	
Norlund et al. (2001)	1992–1993	Sweden	>24	9.4 more sick days.[a]	
Holmes et al. (2003)	1999	United Kingdom	<65	GBP 869 lost earnings per year with diabetes; GBP 1300 for carers of people with diabetes.[a]	
Minor (2011)	2006	United States	>19 at diagnosis		Exogenous: $2865 loss in earnings per year, Endogenous: $19655; Exogenous: 2 working hours less per week, no significant effect on missed workdays per year, endogenous: no significant effect on working hours or workdays missed.
Vijan et al. (2004)	1992–2000	United States	51–61	Lost income of $50004 from 1992–2000 per capita or $6250 per year, for whole USA population of same age $85.6 billion or $10.7 billion per year; people with diabetes more likely to have taken sick days in 1992 (adjusted OR 1.3).[a]	
Collins et al. (2005)	2002	United States	working age	No significant effect on work days.[a]	
Bastida and Pagán (2002)	1996–1997	United States	>44	No significant effect on earnings.	Women with diabetes earn 84% less.

Ref.	Survey year	Country	Age	Effect on other productivity outcomes	
				Males	Females
Brown, Perez, et al. (2011)	2008	United States	35–64	Wages reduced by 0.74% due to diabetes; for every 10% reduction in A1C wages rise by 0.62 %. A1C >8 was related to decreasing wages.	No significant effect of diabetes on female earnings; no effect of blood sugar management for women, A1C levels just below 6 to just above 7 were related to lower wages.
Lenneman et al. (2011)	2005–2009	United States	>16	Lost earnings per year of $2146.[a]	
Tunceli, Bradley, et al. (2005)	1992, 1994	United States	51–61	No significant effect on number of work days.	2.5 more lost workdays per year.
Valdmanis et al. (2001)	1990–1995	United States		71% of the persons with diabetes had an annual income of less than $20000 compared with 59% of the matched respondents.[a]	
Ng et al. (2001)	1989	United States	>29 at diagnosis	No significant effect on work days for T2D, for those with complications 3.2 days lost within two weeks	
Brown, Estrada, et al. (2005)	NA	United States	>45	For every dollar of labor income lost by adults with diabetes, a further income reduction of $0.48 occurs in the community. Total output reduction for upper bound estimate is $300 million for the local economy.[a]	

Ref.	Survey year	Country	Age	Effect on other productivity outcomes	
				Males	Females
Minor (2013)	1979–2010	United States	>14	no general effect of type 2 diabetes on wages; some evidence of wage penalty of about 18% 6–10 years after diagnosis	No strong evidence found for wage penalty for females

[a] No gender differentiation in study

In terms of the methodology used, these studies tended to rarely account for endogeneity, and they mostly used standard regression or matching methods to estimate the impact of diabetes. Three studies (Bastida and Pagán, 2002; Brown, Perez, et al., 2011; Minor, 2011) corrected for the possibility of a sample selection bias, to account for systematic differences between the working population and the overall population. Only one study additionally applied IV methods and found diabetes to be endogenous, so that its effects on earnings were dramatically understated using naive regression results (Minor, 2011). For working hours and days missed due to illness, the same study found no indication of endogeneity. Only one study applied an approach other than IV to account for endogeneity, using a difference-in-difference model and exploiting a recent diagnosis of diabetes, which was the result of the collection of biomarkers in the survey used, as a natural experiment to measure how income developed between those who were newly diagnosed and those without diabetes in the years following diagnosis (Liu and Zhu, 2014).

4 Discussion

The objectives of this systematic review were to identify new evidence on the economic impact of type 2 diabetes that emerged since 2001 and extend the scope of the review by including studies on the labour market impact of diabetes. We identified studies from a great variety of countries, with large differences in cost estimates across and within countries.

4.1 General Findings and Developments Since the 2004 Review of Diabetes COI Studies

An obvious development since the last review is the emergence of COI studies on LMICs. The economic burden related to diabetes found in these studies indicated a strong direct impact on those affected by diabetes. This is reflected in the substantial burden of OOP treatment costs incurred by patients (Arredondo and Barcelo, 2007; Chatterjee et al., 2011; Elrayah-Eliadarous et al., 2010; Esteghamati et al., 2009; Khowaja et al., 2007; Ramachandran et al., 2007; Smith-Spangler et al., 2012; Suleiman et al., 2006; Tharkar

et al., 2010; Wang, Fu, Pan, et al., 2009; Wang, Fu, Zhuo, et al., 2010), with considerable proportions of the annual income being spent on diabetes care. This relative cost burden was generally higher for people with relatively lower household incomes (Khowaja et al., 2007; Ramachandran et al., 2007; Tharkar et al., 2010). Health insurance coverage had some protective effects against OOP expenditures, but mainly for those with higher incomes, while the poor often lacked coverage (Khowaja et al., 2007; Ramachandran et al., 2007; Tharkar et al., 2010). Once people were covered by health insurance their risk of incurring catastrophic expenditures decreased significantly (Smith-Spangler et al., 2012). An important cost factor that was predominantly investigated in studies on LMICs were non-medical costs for transportation, informal healthcare or food which were found to considerably add to the experienced diabetes cost burden (Chatterjee et al., 2011; Esteghamati et al., 2009; Tharkar et al., 2010; Wang, Fu, Pan, et al., 2009; Wang, McGreevey, et al., 2009).

In terms of the costing methodology applied in COI studies, the number of studies estimating the excess costs of diabetes increased since the Ettaro et al. (2004) review. Those studies either used regression analysis or matching to adjust for the differences between people with diabetes and those without, accounting at least for age and gender, but often also for other socioeconomic, geographic and demographic differences. Other widely used approaches to estimate direct healthcare costs from the perspective of the healthcare system or private insurance included the disease-attributable and—slightly less frequently—the attributable-fraction approach. For cost assessment in LMICs, studies often either estimated total healthcare costs or carried out self-administered surveys. While Ettaro et al. (2004) suggested an increased use of disease-attributable approaches to arrive at more exact estimates of the costs of diabetes, the evidence found in this review indicates that using an incremental cost approach via matching or regression analysis could provide more accurate results, due to its ability to capture costs otherwise not directly traceable to diabetes. Nonetheless, the use of the estimation technique always hinges on the availability of appropriate data, with regression or matching analyses requiring information on people without diabetes to be used as a control group. Therefore the estimation approach needs to be tailored to the available data.

Compared with the evidence reviewed by Ettaro et al. (2004), the field has generally advanced with respect to the analysis of costs in different ethnic and age groups. Two studies investigated differences between racial groups in the USA, showing that while ethnic minorities spend less on diabetes healthcare than Whites, this difference seems to be mainly based on differences in access to care between Whites and Blacks or Hispanics (Buescher et al., 2010; Lee et al., 2006). In terms of age, studies found an increase in healthcare costs with age as well as with, in some cases, the duration of diabetes. A recurring problem was that many studies did not distinguish diabetes types, making it difficult to exactly attribute the costs to the respective diabetes types.

To explore the reasons for the wide heterogeneity in direct cost estimates across studies, we performed a regression analysis, which indicated that an important determinant for the cost variation across countries could be the economic wealth of the country (proxied by GDP per capita), similar to what was found in a review of indirect costs of various chronic diseases (Zhao et al., 2013), possibly due to differences in the availability and affordability of diabetes care between HICs and LMICs (Cameron, Ewen, et al., 2009;

Cameron, Roubos, et al., 2011).

Further, studies on the USA seem to estimate consistently higher costs than studies on other countries, even when accounting for differences in GDP per capita. The higher direct costs of diabetes estimated for the USA are in line with the generally higher healthcare expenditures in the USA compared with countries with similar income levels, and could be the result of exceptionally high service fees (Laugesen and Glied, 2011) and prices paid in the USA healthcare system (Lorenzoni et al., 2014; Squires, 2012).

Because of the small sample size on which our analysis was based, these results must be interpreted with caution, and other factors could still be important. For instance, other evidence suggests that different costing approaches have a considerable effect on diabetes cost estimates (Honeycutt et al., 2009; Tunceli, Wade, et al., 2010). Furthermore, the perspective taken, different data sources and populations investigated and decisions on the cost components included are likely important in explaining within-country heterogeneity. In particular, the inclusion of diabetes complications and decisions about which complication(s) to include, as well as the extend to which costs for these diseases are attributable to diabetes, can significantly affect the results. Not all studies in the review provide extensive information about how they include complications and some do not include them at all.

Finally, the quality of the data used could have affected the cost estimates. Many studies in LMICs relied on self-reported data from small household surveys, limiting their generalizability and leading their results to be prone to recall bias. Further, these studies often identified people with diabetes via their use of healthcare institutions, which excluded a potentially important section of the population in LMICs unable to access formal care, possibly leading to an overestimation of the average diabetes-related costs.

4.2 Labour market studies

Turning to the effects of diabetes on the labour market, the existing studies showed, almost consistently, with the exception of Canada (Latif, 2009) and one study on the USA (Minor, 2013), that the employment probabilities of men were affected more adversely by the disease than those of women. However, while most studies have tried to tentatively explain these gender differences, the reasons for this have not been investigated in depth. The studies also showed that, when interpreting this research, it is important to consider whether a study has tried to account for unobservable factors or reverse causality, as otherwise the results might be misleading. Nonetheless, all studies using IV techniques used similar instruments to achieve identification, providing scope for further research using different identification strategies to further explore how endogeneity might affect the results. What has been apparent is the lack of research on labour market outcomes of diabetes in LMICs, with only one study investigating the effect of diabetes on labour income in China (Liu and Zhu, 2014). This deficit might be due to a limited availability of suitable data sources containing sufficient information to allow for a similar investigation of the topic.

The potential for rich, good-quality data sources to aid the investigation of the economic impact of diabetes can be illustrated by the several studies that used data from the Lower Rio Grande Valley in Texas. These studies demonstrate the evolution of methodology and data from the use of single equation regression models (Bastida and Pagán, 2002)

to the use of IV methods (Brown, Pagan, et al., 2005) and—finally—biometric data on blood glucose values (Brown, Perez, et al., 2011). While the first two methods allowed the investigation of the general effect of diabetes on employment chances, the latter was able to assess the impact according to how diabetes was managed by the patient, as proxied by the measured biomarkers. The study found that the main adverse effect was due to having diabetes regardless of how it was managed and that improvements in management only had minor positive effects. The authors concluded that investments in the prevention of diabetes would likely be more effective than improved diabetes management.

The latter study and the study by Liu and Zhu (2014) also show how biometric data (e.g. blood glucose values) can be used to arrive at a deeper understanding of the economic effects of diabetes. This information makes it possible to investigate the impact of diabetes according to the severity of the disease and also allows for the consideration of previously undiagnosed people with diabetes, increasing the policy relevance of the research.

4.3 Comparison of COI and Labour Market Studies: Common Themes and Lessons Learned

The results of both fields, COI and labour market studies, show a considerable adverse impact of diabetes in terms of costs to society, health systems, individuals and employers and in terms of a reduction in the productive workforce and productivity in general. Both research strands particularly indicate that the adverse effects of diabetes increase with diabetes duration as well as with the severity of the disease, judged by the high complication costs estimated in COI studies and the larger employment and income penalties for those with a longer disease duration or higher blood glucose levels.

Nonetheless, several lessons can be learned for each field from advancements in the other field. Future COI studies would, for instance, benefit from the more frequent use of biomarker data. This would allow for a more precise analysis of the costs of diabetes according to the severity of the disease and help inform researchers and policy makers about the possible economic effects of achieving certain treatment goals, e.g., a reduction in blood glucose values.

Also, and in contrast to the labour market outcomes literature, the endogeneity problem has hitherto not been addressed in any form in studies estimating direct healthcare or productivity costs, despite it being an equally important challenge in this domain. A possible bias could arise if some people developed diabetes as a result of an unobserved accident or illness, likely resulting in an overestimation of the costs. Endogeneity could also be introduced if people with diabetes became poorer as a result of the disease and consequently were not able to spend as much on their treatment as they would like to, leading to an underestimation of the true monetary cost of diabetes. Furthermore, an endogeneity bias would be introduced if diabetes was correlated with poverty so that diabetes prevalence would be disproportionately high in subgroups with less resources and consequently less access to care. This would lead to an underestimation of the healthcare costs of diabetes. Endogeneity in COI studies has recently been addressed for the estimation of healthcare costs of obesity, suggesting that direct costs would have been underestimated, had the study not accounted for endogeneity (Cawley and Meyerhoefer, 2012). It appears that, on the basis of the studies identified in our review, a similar—worthwhile—approach

could and should be applied to the case of Type 2 Diabetes.

Yet the labour market studies also stand to gain from adopting certain approaches that are more common in COI studies. To date, only few labour market studies have used the incidence approach found for COI studies to follow people with diabetes over a certain time period from their diagnosis onwards, in order to further explore how the effect of diabetes on employment and productivity measures develops over time.

Some further recommendations may be derived for future COI and labour market studies on diabetes:

1. For COI studies the estimation of incremental costs—wherever possible—appears to be most suitable for diabetes, as it more accurately accounts for costs of co-morbidities and for less obviously related disease costs (Honeycutt et al., 2009; Tunceli, Wade, et al., 2010). More information that can guide researchers in their choice of methods already exists and should be referred to when performing a COI study (Akobundu et al., 2006).

2. If possible, the use of convenience samples of people with diabetes visiting a health care institution should be avoided, particularly in LMICs, as it excludes those not able or willing to visit a clinic for treatment due to economic reasons, leaving out a potentially important proportion of diabetes patients.

3. The interpretation of the COI results always hinges on the amount of information provided about, among others, the aim of the study, the perspective adopted and the cost components included as well as the estimation approach used. A discussion of how these choices might affect the estimates should also be part of every COI study. Researchers should therefore consult available guidance from the literature that sets out what information should ideally be included in a COI study (Larg and Moss, 2011) to increase the transparency and usability of their research.

4. For labour market studies more evidence from LMICs is needed. There is scope for for exploring existing household datasets from LMICs that contain information on diabetes (Seuring et al., 2014). In some cases, panel data are (or may come) available, which would allow the investigation of the effects of diabetes over time as well as to improve the degree of causal inference by controlling for unobserved heterogeneity.

5. As for labour market studies, other ways of achieving identification should be explored to reduce the reliance on IV methods using the family history of diabetes as the sole instrument. The increasing richness of information provided in recent data sets could be used to this effect, also taking into account other quasi-experimental econometric methods (Craig et al., 2012).

4.4 Limitations

A possible limitation of this review is the decision to refrain from excluding studies based on certain quality criteria, such as study design, costing methodology, sample size or reporting standards. This might have resulted in the inclusion of lower quality studies

with less reliable estimates, compromising the comparability across countries, particularly between LMICs and HICs, as study designs differed considerably. On the other hand our overarching objective was to ensure a truly globally comprehensive overview of the literature on the economic impact of diabetes, including evidence from LMICs, which, for reasons often beyond the control of the researchers, may have been of limited quality and thus would have been excluded, had we applied stringent quality benchmarks. Further, any attempt to apply a quality threshold would have faced the challenge of dealing with the absence of a formal checklist to follow in critically appraising the quality of COI studies. Rather than interpreting it as a limitation, we see the identification and synthesis of LMIC studies as a unique added value of this review, when compared to the Ettaro et al. (2004) review.

Notably, we also abstained from any language restrictions, which would have particularly excluded evidence from Spanish speaking and Eastern European countries. Taken together, these factors have resulted in a large number of included studies, allowing for an (albeit exploratory) statistical investigation of the heterogeneity in diabetes cost estimates as a complement to the narrative analysis. We therefore feel that the advantages of refraining from too stringent inclusion criteria more than outweigh the possible negative consequences of including potentially lower-quality studies.

Further, our search was limited to studies after the year 2000. While for COI studies a previous review covered the literature until 2000, this is not the case for the literature on labour market effects of diabetes and we therefore cannot exclude the possibility of having missed some relevant (if old) studies.[1]

5 Conclusion

This review has provided an updated and considerably expanded picture of the literature on the global economic impact of type 2 diabetes. The results show a considerable impact of diabetes in terms of costs to society, health systems, individuals and employers and in terms of a reduction in the productive workforce and productivity in general. Studies on the costs of diabetes now provide evidence from HICs as well as LMICs, using a variety of study designs to estimate the costs of diabetes. The evidence indicates a particularly strong and direct economic impact of type 2 diabetes on people's livelihoods in lower-income settings. Studies on labour market outcomes so far have been confined, almost exclusively, to HICs, leaving space for further studies in LMICs to provide additional evidence of the effect of diabetes in these countries. An issue not yet covered in diabetes COI studies—in striking contrast to labour market outcome studies—has been the possible bias introduced by endogeneity, providing an opportunity for advancing research in this area.

[1] We have checked the references of our included labour market studies for any relevant studies published before 2001. We could find only one relevant study from 1998 investigating how employment chances and family income were affected by diabetes in the USA, comparing samples from 1976, 1988 and 1992 and finding significant adverse effects of diabetes on employment chances but not on family income (Kahn, 1998). The effect for women decreased somewhat between 1976 and 1992, while the effect increased for men. The study did not account for the possible endogeneity of diabetes nor selection bias when estimating the effects on income.

Acknowledgments The work of MS on this paper was partially funded by the Centre for Diet and Activity Research (CEDAR), a UK CRC Public Health Research Centre of Excellence. Funding from the British Heart Foundation, Cancer Research UK, Economic and Social Research Council (MRC), Medical Research Council, the National Institute for Health Research, and the Wellcome Trust, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged.

Author Contributions TS, OA and MS planned the work and finalized the manuscripts. TS carried out the data base search, extracted, analysed and interpreted the data and produced the draft of the manuscript. OA also performed data extraction and contributed to the production of the first draft. MS oversaw the development of the work, contributed to the various drafts of the manuscript and provided guidance. TS is the guarantor for the overall content.

A What is endogeneity?

Endogeneity is a statistical problem that occurs in regression models if the assumptions about the flow or direction of causality are incorrect. If endogeneity is ignored, it could be that claims about causality between two variables or the magnitude of the effect are false. In general, one can only be certain about a causal relationship of the effect of x on y if the following three conditions are met (Antonakis et al., 2012):

- y follows x temporally
- y changes as x changes (and this relationship is statistically significant)
- no other causes should eliminate the relation between x and y.

There are three major causes of endogeneity that violate the conditions above.

1. Omitted variables When a regression is run to determine the causal effect of variable x on variable y, but there are unobserved variables that affect variables x or x and y simultaneously, the estimated effect of x on y will be biased. For the case of type 2 diabetes and employment chances, there is the danger that, e.g., personal traits like ambition, which are hard to observe, could influence the probability of developing type 2 diabetes through their effect on a person's lifestyle, but they could also simultaneously affect the chances of employment through their influence on a person's determination to find work or to perform well at work. If we are not able to control for this, then our estimate of the effect of diabetes on employment chances might, at least partially, represent the effect of personal traits on employment chances. As a result, our estimate of the effect of diabetes is biased and does not represent the true size of the relationship between the two variables.

2. Simultaneity Simultaneity is present, if our outcome variable y and our variable of interest x influence each other simultaneously, so that y not only is affected by x but x is also affected by y. In the case of type 2 diabetes and labour market outcomes, not only diabetes could influence employment chances or work related income, but

also resulting changes in lifestyle due to employment or an increase in income could affect the probabilities of developing diabetes. Due to an increase in income people could change their diet or change towards a less active lifestyle which in turn would make them more likely to develop type 2 diabetes.

3. Measurement error Measurement errors occur when the independent variable x is imprecisely measured. Here this would be the case if people in a survey did not remember if they have been diagnosed with type 2 diabetes and gave a wrong answer.

There are several solutions to the problem of endogeneity, but only using instrumental variable (IV) techniques has the potential to deal with all three causes of endogeneity at once. Endogeneity is a problem, because the variable of interest, here diabetes, is correlated with the error term of the estimated model, which includes all omitted variables as well as the effect of y on x and if measurement error is present, the true values. To do this, one needs to find a suitable instrument that needs to fulfil the following conditions:

- it has to be causally related to the endogenous variable x and
- it should not be correlated to the dependent variable y other than through its correlation with x.

This instrument is then used in a first regression to obtain predicted values of the problematic endogenous regressor. Because the instrument is not correlated with the error term, these predicted values of the endogenous variable will be uncorrelated as well and can then be used in a second regression to predict the dependent variable y. The estimated coefficients of this second stage can then be regarded as consistent estimates.

In the case of type 2 diabetes and labour market outcomes, an instrument has to predict the development of diabetes without being otherwise causally related to any of the labour market outcomes, be it employment chances, wages or some other measure of productivity. The instrument of choice so far has been the family history of diabetes. It has been shown that a considerable part of the risk of developing type 2 diabetes is hereditary (Hemminki et al., 2010; Herder and Roden, 2011; The Interact Consortium, 2013). This fact is exploited when the instrument is used and it is assumed that this is the only pathway through which a family history of diabetes affects a person's diabetes risk, and also that, e.g., parental diabetes does not affect the person's labour market outcomes directly.

The most common estimation techniques for the estimation of IV regressions are the linear IV model and the bivariate probit model. The latter is often deemed more apt for models where both the outcome as well as the instrumental variable are binary, so either 0 or 1, which is the case for employment as an outcome variable as well as diabetes family history as an instrument. Nonetheless, there is some discussion in the econometrics literature regarding the best method to estimate these cases, as it also has been argued that because the linear IV technique does not depend on the assumption of normality of the error terms, in contrast to the bivariate probit model, its results are more reliable in the case of non-normality, but can sometimes lead to imprecise estimators which can no longer be interpreted meaningfully (Chiburis et al., 2012). Both methods can be found in the reviewed papers.

B Country codes

Table 7: Country Codes

Country	Country code	Country	Country code
35 developing countries	LMIC	Jamaica	JAM
Argentina	ARG	Japan	JPN
Australia	AUS	Latin America and Caribbean	LAC
Bahamas	BHS	Mexico	MEX
Barbados	BRB	Netherlands	NLD
Belgium	BEL	Nicaragua	NIC
Bolivia	BOL	Nigeria	NGA
Brazil	BRA	Norway	NOR
Canada	CAN	Pakistan	PAK
Chile	CHL	Panama	PAN
China	CHN	Paraguay	PRY
Colombia	COL	Peru	PER
Costa Rica	CRI	Serbia	SRB
Cuba	CUB	Spain	ESP
Czech Republic	CZE	Sudan	SDN
Denmark	DNK	Sweden	SWE
Dominican Republic	DOM	Switzerland	CHE
Ecuador	ECU	Taiwan	TWN
El Salvador	SLV	Thailand	THA
Europe	EUR	The Bahamas, Barbados, Jamaica, Trinidad and Tobago	CARICOM
France	FRA	Trinidad and Tobago	TTO
Germany	DEU	United Arab Emirates	ARE
Guatemala	GTM	United Kingdom	GBR
Guyana	GUY	United States	USA
Haiti	HTI	Uruguay	URY
Honduras	HND	Venezuela	VEN
Hong Kong	HKG	WHO African Region	AFR
India	IND		
Iran, Islamic Rep.	IRN		
Ireland	IRL		
Israel	ISR		
Italy	ITA		

C Tables

Table 8: COI study characteristics and cost estimates

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Smith-Spangler et al. (2012)	2002–2003	35 LMIC	121051	General pop.	Patient	RB/M	$				3 at 50th percentile to 157 at 95th percentile	3.40 at 50th percentile to 178 at 95th percentile		
Boutayeb and Boutayeb (2014)	NA	Various Arab countries	NA	General pop.	Healthc. system	SAM	USD				UDD 529[j]			
Barceló et al. (2003)	2000	ARG	1250300	General pop.	Societal	SAM	ARS	16547	1130	15416[b]	597[a]	904[a]	8145[a]	12330[a]
Davis et al. (2006)	2000–2051	AUS	1294	General pop.	Healthc. system	SDS	AUD		1514 (2000), 2282 (2051)		3496[a] (2000)	3379[a] (2000)		
Barceló et al. (2003)	2000	BHS	12800	General pop.	Societal	SAM	BSD	43	25.2	16	1605	2507	1009	1575
Abdulkadri et al. (2009)	2001	BHS	10435	General pop.	Societal	SDS	BSD	233	17	216[b]	836[a]	1310[a]	10789[a]	16914[a]
Abdulkadri et al. (2009)	2001	BRB	28438	General pop.	Societal	SDS	BBD	75	69.2	5	2455	2433	204	202
Barceló et al. (2003)	2000	BRB	23300	General pop.	Societal	SAM	BBD	307	26	281[b]	1099[a]	1117[a]	11880[a]	12076[a]
Jönsson (2002)	1999	BEL	735 patients	General pop.	Healthc. system	SAM	EUR		1561		3295	4704		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Jönsson (2002)	1999		7000 (overall)	General pop.	Healthc. system	SAM	EUR				2834	Not possible because no country specific estimate		
Barceló et al. (2003)	2000	BOL	153900	General pop.	Societal	SAM	BOB	901	338	563[b]	3435[a]	2199[a]	5717[a]	3659[a]
Barceló et al. (2003)	2000	BRA	4532600	General pop.	Societal	SAM	BRL	54892	9598	45294[b]	1595[a]	2118[a]	1595[a]	9993[a]
Lau et al. (2011)	2008–2035	CAN	147498 with diabetes	Four Alberta Health and Wellness databases	Healthc. system	SAM	CAD		5934 (2007); 20032 (2035)		4563[a]	4023[a]		
Pohar, Majumdar, et al. (2007)	1993–2001	CAN	57774	Saskatchewan Canadians (excluding Indians)	Healthc. system	SAM	CAD				large urban: 3563 (1993), 3454 (2001), small urban:3321 (1993), 3427(2001), rural:3368 (1993), 3289 (2001)	large urban: 2665 (1993), 3591 (2001), small urban: 3453 (1993), 3563 (2001), rural: 3502 (1993), 3420 (2001)		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Pohar and Johnson (2007)	2001	CAN	5284 (Indians) + 41630 (general pop.) with diabetes, 11692 (Indians) + 98680 (general pop.) without diabetes	Registered Indians according to the Indian Act	Healthc. system	RB/M	CAD				Excess costs: Indians 2227, General pop. 2378 (total costs with diabetes: 3,622 for Indians/ 3253 in general pop., controls: 1,395 for Indians/ 875 for general pop.)	Excess costs: Indians 2316, General pop. 2473: (total costs with diabetes: 3766 for Indians/ 3382 in general pop., controls: 1450 for Indians/ 910 for general pop.)		
Barceló et al. (2003)	2000	CHL	496500	General pop.	Societal	SAM	CLP	5890	719	5171[b]	320601[a]	1447[a]	2307131[a]	10416[a]
Wang, Fu, Zhuo, et al. (2010)	2007	CHN	1478	T2D patients in these Chinese hospitals	Healthc. system	Survey	RMB				4564 (median), 7926 (mean)	1246 (median), 2164 (mean)		
Wang, McGreevey, et al. (2009)	2007 and 2030 (projection)	CHN	2040	Inpatients and outpatients with DM in 20 hospitals	Societal	Survey	RMB	72916 (2007), 132472 (2030)	67946 (2007), 123187 (2030)	4982 (2007), 9058 (2030)	11555	3401	1586	467

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Yang et al. (2012)	2009–2010	CHN	1232 (diabetes), 1201 (no diabetes)	General pop.	Healthc. system	RB/M	RMB				4135 (3.38 times greater than controls)	1136 (3.38 times greater than controls)		
Wang, Fu, Pan, et al. (2009)	2007	CHN	2054	T2D patients in these Chinese hospitals	Healthc. system	Survey	RMB				4800 (median), 10164 (mean)	1412 (median), 2991 (mean)		
extcite-Gonzalez2009b	32 years	COL	NA	Hypothetical average Columbian type 2 DM patient	Societal	SAM	COP	5.3	1.8	3.5	611750	570	1187000	1106
Barceló et al. (2003)	2000	COL	937700	General pop.	Societal	SAM	COP	7737	1241	6496[b]	923826[a]	1323[a]	4836001[a]	6928[a]
Barceló et al. (2003)	2000	CRI	154900	General pop.	Societal	SAM	CRC	1026	210	817[b]	192194[a]	1353[a]	749278[a]	5274[a]
Barceló et al. (2003)	2000	CUB	592400	General pop.	Societal	SAM	CUP	1721	923	798[b]	1219[a]	1558[a]	1054[a]	1347[a]
Horak (2009)	2007	CZE		Insured in healthcare system (63.1% of pop.)	Healthc. system	SAM	CHK		190					
Gyldmark and Morrison (2001)	1993	DNK	948	General pop.	Societal	WTP	DKK						1128 (mean), 300 (median)	191 (mean), 51 (median)

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Barceló et al. (2003)	2000	DOM	254100	General pop.	Societal	SAM	DOP	1410	509	901[b]	14580[a]	2003[a]	25801[a]	3545[a]
Barceló et al. (2003)	2000	ECU	267300	General pop.	Societal	SAM	USD	2830	1104	1727[b]	873[a]	4129[a]	1366[a]	6460[a]
Barceló et al. (2003)	2000	SLV	219400	General pop.	Societal	SAM	SVC	1385	381	1004[b]	626[a]	1737[a]	1650[a]	4577[a]
Honkasalo et al. (2014)	2005–2010	FIN	1890 with T2D	People with T2D in two cities in Finland	Healthc. system	SDS	EUR				1038	1087		
Ricordeau et al. (2003)	1998, 2000	FRA	704423 (1998), 1145603 (2000) with diabetes	Metropolitan France	Healthc. system	RB/M	EUR		2784 (1998), 3268 (2000)		1529 (1998), 1655 (2000)	2107 (1998), 2241 (2000)		
Jönsson (2002)	1999	FRA	751 patients	General pop.	Healthc. system	SAM	EUR		5478		3064	4214		
Jönsson (2002)	1999	DEU	809 patients	General pop.	Healthc. system	SAM	EUR		1653		3576	4752		
Köster, Ferber, et al. (2006)	2001	DEU	306736 (26971 with diabetes)	General pop.	Societal	RB/M	EUR		Excess: 19364 (total: 40650)		Excess 2507 (total 5262)	Excess: 3329 (total: 6987)	Excess 1328 (total: 5019)	Excess: 1763 (total: 6664)
Köster, Huppertz, et al. (2011)	2000–2007	DEU	320000 (2000) to 275000 (2007)	AOK Hessen	Healthc. system	RB/M	EUR		17299 (2000), 25614 (2007)		2400 (2000), 2605 (2007)	3493 (2007), 3218 (2000)		
Martin et al. (2007)	1995–2003	DEU	3268	Newly diagnosed T2D patients	Healthc. system	SAM	EUR				3210	4075		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Köster, Schubert, et al. (2012)	2000–2009	DEU	not given, only DM patients stated (30472)	AOK Hessen	Healthc. system	RB/M	EUR		21230 (2000), 26226 (2009)		2779 (2000), 2611 (2009)	3471 (2000), 3261 (2009)		
Barceló et al. (2003)	2000	GTM	368700	General pop.	Societal	SAM	GTQ	2535	878	1657[b]	6131[a]	2382[a]	11572[a]	4495[a]
Barceló et al. (2003)	2000	GUY	28400	General pop.	Societal	SAM	GYD	141	80	62[b]	131041[a]	2800[a]	102135[a]	2182[a]
Barceló et al. (2003)	2000	HTI	79500	General pop.	Societal	SAM	HTG	249	152	97[b]	12782[a]	1912[a]	8175[a]	1223[a]
Barceló et al. (2003)	2000	HND	193000	General pop.	Societal	SAM	HNL	772	366	405[b]	8750[a]	1898[a]	9680[a]	2100[a]
Chan et al. (2007)	2004	HKG	147	T2D patients attending the DM outpatient clinic at a public hospital	Societal	Survey	USD				11638	2288	1817[e]	357[e]
Ramachandran et al. (2007)	1998, 2005	IND	556 with T2D (urban=309, rural= 247)	T2D patients in India	Patient	Survey	INR				Median values: 10000 (urban), 6260 (rural)	Median values: 773 (urban), 484 (rural)		
Tharkar et al. (2010)	2009	IND	718	Diabetes patients in Chennai city	Societal	Survey	INR		268		25391 (median)	1557 (median)	4970 (median)	305 (median)

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Javanbakht et al. (2011)	2009	IRN	4500	Diabetes patients from Tehran and Fars province	Societal	Survey	IRR	9611[h]	5187[h]	4420[h]	8358592	2142	8578816	2199
Esteghamati et al. (2009)	2004, 2005	IRN	710 (T2D), 904 (controls)	Pop. in Teheran	Societal	RB/M	IRR	401 (Teheran); 2117[h] (Iran)	327 (Teheran); 1727[h] (Iran)	74 (Teheran), 390[h] (Iran)	876622 (Teheran)	443 (Teheran)	200146 (Teheran)	101 (Teheran)
Nolan et al. (2006)	1999	IRL	701	T2D patients of four Irish hospitals	Healthc. system	SAM	EUR				2469	2867		
Chodick et al. (2005)	2001	ISR	24632	Insured patients in HMO	Healthc. system	RB/M	ILS		433		6002 (2001), 3926 (1999)	1950 (2001), 1275 (1999)		
Lucioni et al. (2003)	1998	ITA	1263	T2D patients from randomly drawn practices across Italy	Societal	SAM	EUR	8289[d]	7930	359	2991	4588	135[ac]	208[ac]
Bruno et al. (2012)	2003–2004	ITA	33792 (diabetes) and 863123 (no diabetes)	Turin pop.	Healthc. system	RB/M	EUR				2465 (3361 (diabetes), 896 (no diabetes)	3328 (4537 (diabetes), 1210 (no diabetes)		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Morsanutto et al. (2006)	2001–2002	ITA	299	T2D patients who visited a diabetologic center in Italy (DC)	Healthc. system	SAM	EUR				1910	2823		
Marchesini et al. (2011)	2006	ITA	311979	People with DM at 22 local health districts	Healthc. system	RB/M	EUR				2589	3296		
Abdulkadri et al. (2009)	2001	JAM	186036	General pop.	Societal	SDS	JMD	556	454	102	44647	2439	10046	549
Barceló et al. (2003)	2000	JAM	181400	General pop.	Societal	SAM	JMD	1037	345	693[a]	32251[a]	1901[a]	64787[a]	3818[a]
Nakamura et al. (2008)	1990–2001	JPN	4535	Community-dwelling in Shiga	Healthc. system	SAM	JPY				189060 (diabetes), 99900 (non-diabetes)	1674 (diabetes), 884 for (non-diabetes)		
Barceló et al. (2003)	2000	LAC	Diabetes prevalence of 15.2 million	Pop. from all countries in Latin America and Caribbean	Societal	SAM	USD	82304	13529	68774[b]	703[a]	887[a]	3576[a]	4512[a]
Barceló et al. (2003)	2000	MEX	3738000	General pop.	Societal	SAM	MXN	30677	4006	26671[b]	4994[a]	1072[a]	33249[a]	7135[a]

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Arredondo, Zúñiga, and Parada (2005)	2004, 2006	MEX	951417 estimated cases	All users of health care in public institutions	Societal	SAM	MXN	290[d]	229	61k	1472[a]	242[a]	386[a]	64[a]
Arredondo and De Icaza (2011)	2010	MEX	Whole pop.	Population demanding services at Mexican healthcare institutions for T2D	Societal	SAM	MXN	1066	470	596	4016[a]	485[a]	5090[a]	610[a]
Arredondo and Barcelo (2007)	2005	MEX	Whole pop.	General pop.	Patient	SAM	MXN		284 OOP expenditures (52% of overall expenditures)					
Arredondo and Zúñiga (2004)	2003, 2005	MEX	Whole pop.	General pop. using public healthcare institutions	Societal	SAM	MXN	532 (2005)	235 (2005)	297 (2005)	1467[a] (2005)	263[a] (2005)	1852[a] (2005)	331[a] (2005)
Rodríguez Bolaños et al. (2010)	2002, 2004	MEX	497	IMSS insured	Healthc. system	SDS	MXN		661 (2004)		35622[a] (2004)	4672[a] (2004)		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Redekop et al. (2002)	1998	NLD	1371 with T2D	T2D patients in the Netherlands	Societal	SAM	NLG	1014[d]	953	61	4023	2780	282[a]	195[a]
Linden et al. (2009)	2000–2004	NLD	2.5 million (641200 with diabetes)	Dutch people with diabetes	Healthc. system	SDS	EUR		571 (2000), 1063 (2004)		974 (2000), 1283 (2004)	1259 (2000), 1658 (2004)		
Jönsson (2002)	1999	NLD	909 patients	General pop.	Healthc. system	SAM	EUR		671		1827	2761		
Barceló et al. (2003)	2000	NIC	136100	General pop.	Societal	SAM	NIO	442	292	150[b]	7922[a]	2145[a]	4082[a]	1105[a]
Suleiman et al. (2006)	July 2003–June 2004	NGA	35	Diabetes patients in outpatient clinic in Nigeria	Patient	SDS	NGN				29366	662		
Solli et al. (2010)	2005	NOR	4.6 million from register data of entire pop.	General pop.	Societal	SDS	NRK	319	242	76	20492[a]	2061[a]	5067[a]	650[a]
Khowaja et al. (2007)	2006	PAK	345	Diabetes patients in Karachi	Societal	Survey	PKR				11580[f]	620[f]	840[e]	45[e]
Barceló et al. (2003)	2000	PAN	120500	General pop.	Societal	SAM	PAB	926	222	704[b]	866[a]	1846[a]	2741[a]	5840[a]
Barceló et al. (2003)	2000	PRY	94300	General pop.	Societal	SAM	PYG	738	244	495[b]	2661903[a]	2587[a]	5397747[a]	5245[a]

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Barceló et al. (2003)	2000	PER	606800	General pop.	Societal	SAM	PEN	5627	1533	4094[b]	2890[a]	2526[a]	7717[a]	6746[a]
Lesniowska et al. (2014)	2009	POL	Whole pop.	All Polish diabetes patients	Healthc. system	SAM	RSD	3396	1910	1486				
Biorac et al. (2009)	2007	SRB	99	T2D patients in health centre in Svilajnac	Societal	Survey	RSD	7579[h]			47865	1610	5548	187
Bjegovic et al. (2007)	2002	SRB	360433 people with T2D in Serbia	Serbian T2D patients	Healthc. system	SAM	RSD		280		12457[a]	761[a]		
Mata et al. (2002)	1998	ESP	1004	Diabetes patients from 29 primary healthcare centres	Healthc. system	SDS	EUR				771	1488		
Ballesta et al. (2006)	1999	ESP	517	People with DM in region of Cadiz	Societal	SDS	EUR				2560	4690	1844	3379
Oliva et al. (2004)	2002	ESP	1675304 to 2010365 depending on assumed prevalence	Diabetes patients in National Health System	Healthc. system	SAM	EUR		4010 (6% prev.)–4461 (5% prev.)		1290 (6% prev.)–1476 (5% prev.)	2155 (6% prev.)–2466 (5% prev.)		
Jönsson (2002)	1999	ESP	1004 patients	General pop.	Healthc. system	SAM	EUR		3679		1305	2453		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Bastida, Aguilar, et al. (2002)	1998	ESP	Whole pop. (exact number not given)	Canary Island pop. with diabetes	Societal	SDS	Pts (pre Euro)	75	47	28	78240	907	47928[b]	556[b]
Elrayah-Eliadarous et al. (2010)	2005	SDN	822	Patients with T2D in Khartoum state in Sudan	Patient	Survey	USD				438	456		
Bolin et al. (2009)	1987 and 2005	SWE	Whole pop.	General pop.	Societal	SDS	SEK	499 (1987), 1045 (2005)	223 (1987), 383 (2005)	276 (1987), 662 (2005)	12102 (1987), 12287 (2005)	1484 (1987), 1507 (2005)	15000[a] (1987), 21253[a] (2005)	1840[a] (1987), 2606[a] (2005)
Norlund et al. (2001)	1993	SWE	70786 (1677 with diabetes)	Southern Sweden	Societal	RB/M	SEK				19411	2855	14777	2174
Wiréhn et al. (2008)	2005	SWE	415990 (19226 with diabetes)	Whole Östergötland population	Healthc. system	RB/M	EUR				18293	2243		
Jönsson (2002)	1999	SWE	773 patients	General pop.	Healthc. system	SAM	SEK		929		24927	3319		
Ringborg et al. (2008)	2004	SWE	8230	Diabetes patients in Uppsala county	Healthc. system	SAM	SEK				33210	3888		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Schmitt-Koopmann et al. (2004)	1998	CHE	1479	T2D patients from randomly drawn practices across Switzerland	Healthc. system	SDS	CHF		561		3004	2030		
Lin et al. (2004)	1998–1999	TWN	20757185 (in 1998), 21089859 (in 1999)	People with DM in National Health Insurance	Healthc. system	SDS	TWD				62617 (1998), 60775 (1999)	3499 (1998), 3396 (1999)		
Chang (2010)	2006–2007	TWN	498	Diabetes patients in outpatient clinics in northern Taiwan	Societal	WTP	TWD			4003			68118	4004
Chi et al. (2011)		TWN	16094	Elderly with DM in Taiwan	Healthc. system	SAM			51		111982	6338		
Chatterjee et al. (2011)	2008	THA	475	Diabetes patients treated in district hospital	Societal	Survey	TWD				17638	1082	10569	649

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Barceló et al. (2003)	2000	TTO	71300	Pop. from all countries in Latin America and Caribbean	Societal	SAM	TTD	540	72	468[b]	3358[a]	1011[a]	21780[a]	6560[a]
Abdulkadri et al. (2009)	2001	TTO	135093	General pop.	Societal	SDS	TTD	852	227	625	5722	1677	15797	4628
Al-Maskari et al. (2010)	2004	ARE	150	Diabetes patients in Al-Ain District	Healthc. system	Survey	AED				no complication: 5906, with complications: 20774, overall: 16115	no complications: 2047, with complications: 7199, overall: 5585		
Jönsson (2002)	1999	GBR	756 patients	General pop.	Healthc. system	SAM	GBP		244		1558	3065		
Dall, Zhang, et al. (2010)	2007	USA	Diabetes prevalence of 16.5 million	General pop.	Societal	SDS	USD	167862	111257	56604	6414	6751	3263	3434
Buescher et al. (2010)	1998	USA	127991	Medicaid pop.	Healthc. system	SDS	USD		540		4098	4221		
Dall, Nikolov, et al. (2003)	2002	USA	Diagnosed DM prevalence of 12.1 million	General pop.	Societal	SDS	USD	161896	112947	48948	7601[a]	9346[a]	3294[a]	4050[a]

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Druss et al. (2001)	1996	USA	23200	General pop.	Societal	Survey	USD	78518	13768	4771	1097	1495	380[ac]	518[ac]
Durden et al. (2009)	2000, 2005	USA	21592 (2000), 127254 (2005)	Employees of large, privately-insured companies	Healthc. system	RB/M	USD				7365 (2000), 7327 (2005)	8349 (2000), 8306 (2005)		
Trogdon and Hylands (2008)	2000–2004	USA	3790 (diabetes), 42413 (no diabetes)	General pop.	Healthc. system	RB/M	USD				5035[i]	5708[i]		
Brandle et al. (2003)	2000	USA	1364	People with T2D enrolled in managed care programs	Healthc. system	SAM	USD				3715 (median)	4747 (median)		
O'Connell et al. (2012)	2005	USA	32052	American Indians in and around Phoenix, Arizona	Healthc. system	RB/M	USD				5542	6282		
Peele et al. (2002)	1996	USA	20937 with diabetes	Employed DM patients	Healthc. system	SAM	USD		126		4430 (17.9% OOP)	6039 (17.9% OOP)		
Rodbard et al. (2010)	2006	USA	3551 (diabetes), 8686 (no diabetes)	General pop.	Patient	RB/M	USD				233	264		

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Honeycutt et al. (2009)	1998–2003	USA	96873 (5289 had diabetes)	General pop.	Healthc. system	SDS and RB/M	USD		61958 (regression), 43452 (attributable fraction)		4240 (regression), 2980 (attributable fraction)	4966(regression), 3490 (attributable fraction)		
Maciejewski and Maynard (2004)	1998	USA	429918	USA veterans	Healthc. system	SAM	USD		2214		3888[a]	5150[a]		
Birnbaum et al. (2003)	1997–1998	USA	3759 (diabetes), 3759 (without diabetes)	Employed and retired women	Healthc. system	RB/M	USD				5.500 for women <age 65 per year, 25000 for women >= age 65 per year, 233000 lifetime costs	6680[f]or women <age 65 per year, 30362 for women >= age 65 per year, 282973 lifetime costs		
Zhou et al. (2005)	10 year follow up	USA	1223 with T2D	People with DM in Michigan	Healthc. system	SAM	USD				7100 (undiscounted per year over 10 year period)	9072 (undiscounted per year over 10 year period)		
Dall, Mann, et al. (2008)	2007	USA	Diagnosed DM prevalence of 17.5 million	General pop.	Societal	SDS	USD	185682	123788	62108	6649	7095	3328	3552

Ref.	Horizon	Country	Sample size	Population	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)
Tunceli, Wade, et al. (2010)	2007	USA	256245 (T2D), 256223 (controls)	Non-institutionalized adults	Healthc. system	SDS and RB/M	USD				Matching: 4217, Disease attributable: 3002	Matching: 4500, Disease attributable: 3204		
Condliffe et al. (2013)	2007	USA	7514 with diabetes	USA pop. with positive healthcare expenditures in survey	Healthc. system	SAM	USD				11167[g]	11917[g]		
Ramsey et al. (2002)	1998	USA	8748 diabetes patients, 8748 matched controls	Employees of large, privately-insured companies	Employer	RB/M	USD				3842	5021	568	743
Lee et al. (2006)	2000	USA	984 with DM (540 white, 210 African American, 234 Hispanic)	White, African Americans and Hispanics in the USA	Healthc. system	SAM	USD				6616 (6887 if white, 6162 if African American, 5647 if Hispanic)	8453 (8799 if white, 7873 if African American, 7215 if Hispanic)		
Barceló et al. (2003)	2000	URY	119000	General pop.	Societal	SAM	UYU	1202	147	1055[b]	9619[a]	1233[a]	69171[a]	8867[a]
Barceló et al. (2003)	2000	VEN	610800	General pop.	Societal	SAM	VEF	4820	317	4503[b]	342[a]	518[a]	2100[a]	7373[a]
Kirigia et al. (2009)	2005	WHO African region	7020000	General pop.	societal	SAM	USD	28610	9090	19520	876	983	10556	11845

Ref.	Horizon	Country	Sample size	Popula-tion	Perspective	Approach	LCU	Aggregate costs (mill. $)			Per capita costs			
								Total	Direct	Indirect	Direct (LCU)	Direct ($)	Indirect (LCU)	Indirect ($)

DM Diabetes Mellitus Healthc. System Healthcare system LCU Local currency unit Pop. Population Prev. Prevalence Ref. Reference RB/M regression based/matching SAM Sum-all medical SDS Sum-diagnosis specific.

[b] [a] Own calculation dividing presented aggregate cost estimate by number of people with diabetes in study. Total and direct cost estimates were presented in paper and indirect costs calculated, but not explicitly stated. We calculated indirect costs by deducting the presented direct costs estimate from the presented total costs estimate to arrive at an indirect costs estimate.

[c] Calculated the number of people with diabetes by dividing the aggregated direct costs and the per capita direct costs estimate as presented in the study.

[d] Calculated total costs of diabetes for papers summing up direct and indirect costs.

[e] Calculated per capita indirect costs deducting direct from total cost estimate presented in study.

[f] Costs originally presented per visit, to arrive at yearly costs had to multiply costs per visit by number of visits per year.

[g] Per capita direct costs were presented for different groups of diabetics, calculated average costs for person with diabetes by summing up and weighting costs people with diabetes + hypertension, people with diabetes + obesity, people with diabetes + obesity + hypertension.

[h] The study assumes sample would be nationally representative.

[i] Study only reported the adjusted incremental cost ratio of 2.39 compared to the average healthcare expenditures of people without diabetes of USA$3630. To calculate the incremental costs of a person with diabetes we multiplied the average healthcare expenditures of people without diabetes by the given cost ratio .

Table 9: COI study costing components

Ref.	Country (year of cost data)	Hospital Visits	Outpatient Visits	Physician Visits	Drugs	Laboratory	Equipment	Non-medical	Other Costs	Two main cost contributors
Smith-Spangler et al. (2012)	LMIC (2002-2003)	No breakdown of costs provided								
Kirigia et al. (2009)	AFR (2000-2005)	x	x	x	x	x	x	x	x	No exact information on share in expenditures is available
Davis et al. (2006)	AUS (1993-1996)	x	x	x	x	x	x			No exact information on share in expenditures is available
Lau et al. (2011)	CAN (1995-2007)	x	x	x						Hospital, physician
Pohar, Majumdar, et al. (2007)	CAN (1993-2001)	x	x	x	x	x	x			Hospital, medication
Ohinmaa et al. (2004)	CAN (1996)	x	x	x	x	x	x			Hospital, medication
Dawson et al. (2002)	CAN (1998)	x	x	x	x	x				No exact information on share in expenditures is available
Johnson et al. (2006)	CAN (1992-2001)	x	x	x	x					Hospital
Simpson et al. (2003)	CAN (1991-1996)	x	x	x	x					Hospital, prescription drugs
Pohar and Johnson (2007)	CAN (1991-2001)	x	x	x						Hospital
Wang, Fu, Zhuo, et al. (2010)	CHN (2007)	x	x	x				x		Complications, insulin therapy
Wang, McGreevey, et al. (2009)	CHN (2007)	x	x					x		Hospital, outpatient visits
Yang et al. (2012)	CHN (2009-2010)	x	x	x	x	x	x			Hospital, medication

Ref.	Country (year of cost data)	Hospital Visits	Outpatient Visits	Physician Visits	Drugs	Laboratory	Equipment	Non-medical	Other Costs	Two main cost contributors
Wang, Fu, Pan, et al. (2009)	CHN (2007)	x	x	x	x	x	x	x		No exact information on share in expenditures available
Camilo González et al. (2009)	COL (2007)	No breakdown of costs provided								
Horak (2009)	CZE (2007)	x	x	x	x	x	x			Hospital, medication
Honkasalo et al. (2014)	FIN (2005-2010)	x	x	x	x	x	x			
Ricordeau et al. (2003)	FRA (1998,2000)	x	x	x				x		Hospital, medication
Köster, Ferber, et al. (2006)	DEU (2001)	x	x	x	x	x	x	x		Hospital, medication
Köster, Huppertz, et al. (2011)	DEU (2000-2007)	x	x	x	x	x	x	x	x	Hospital, other services (medical devices, remedies, professional home nursing, transportation)
Martin et al. (2007)	DEU (1995-2003)	x	x	x	x	x	x			No exact information on share in expenditures available
Köster, Schubert, et al. (2012)	DEU (2000-2009)	x	x	x	x	x	x	x	x	Hospital, medication
Jönsson (2002)	EUR (1999)	x	x	x	x	x	x	x		Hospital, medication
Chan et al. (2007)	HKG (2004)	x	x	x	x	x	x	x	x	Hospital, outpatient clinic visits
Ramachandran et al. (2007)	IND (2005)	x	x	x	x	x	x			Hospital/surgery, medication
Tharkar et al. (2010)	IND (2009)	x	x	x				x		Hospital, medication
Javanbakht et al. (2011)	IRN (2009)	x	x	x	x	x	x	x	x	Complications, medication
Esteghamati et al. (2009)	IRN (2004;2005)	x	x	x	x	x	x	x		Hospital, medication and devices
Nolan et al. (2006)	IRL (1999-2000)	x	x	x	x	x				Hospital, ambulatory/drug costs
Chodick et al. (2005)	ISR (1999-2001)	x	x	x	x					Medication and lab/diagnostics

Ref.	Country (year of cost data)	Hospital Visits	Outpatient Visits	Physician Visits	Drugs	Laboratory	Equipment	Non-medical	Other Costs	Two main cost contributors
Lucioni et al. (2003)	ITA (1999)	x	x	x	x	x				Hospital, drugs
Bruno et al. (2012)	ITA (August 2003-July 2004)	x	x		x	x				Hospital, drugs
Morsanutto et al. (2006)	ITA (Jan 2001-Aug 2002)	x		x	x	x				Hospital, drugs
Marchesini et al. (2011)	ITA (1997-2006)	x		x	x	x	x			Hospital, drugs
Nakamura et al. (2008)	JPN (1990-2001)	No breakdown of costs provided								
Barceló et al. (2003)	LAC (2000)	x	x	x	x					Medication, complications
Arredondo, Zúñiga, and Parada (2005)	MEX (1989-2003)	x	x	x	x	x				No exact information on share in expenditures available
Arredondo and De Icaza (2011)	MEX (1990-2008)	x	x	x	x	x				Medication, complications
Arredondo and Zúñiga (2004)	MEX (1989-2002)	x	x	x	x	x				Drugs, complications
Arredondo and Barcelo (2007)	MEX (2002-2004)	x	x	x	x	x				Drugs, complications
Rodríguez Bolaños et al. (2010)	MEX (2002-2004)	x	x	x	x	x	x		x	Hospital, administrative costs
Redekop et al. (2002)	NLD (1998)	x	x	x	x	x	x	x		Hospital, medication
Linden et al. (2009)	NLD (2000-2004)	x			x					Hospital, medication
Suleiman et al. (2006)	NGA (2003-2004)		x		x	x	x	x	x	Drugs, diagnostic tests
Solli et al. (2010)	NOR (2005)	x	x	x	x		x		x	Drugs, medical devices
Khowaja et al. (2007)	PAK (2006)		x		x	x		x		Medicine cost, laboratory costs

Ref.	Country (year of cost data)	Hospital Visits	Outpatient Visits	Physician Visits	Drugs	Laboratory	Equipment	Non-medical	Other Costs	Two main cost contributors
Lesniowska et al. (2014)	POL (2005-2009)	x	x	x	x	x	x			Medication, primary care
Biorac et al. (2009)	SRB (2007)	x	x	x	x	x	x			Medication, medical services (incl. ambulatory and hospital costs)
Bjegovic et al. (2007)	SRB (2002)		x	x	x	x	x			No exact information on share in expenditures available
Mata et al. (2002)	ESP (1998-1999)	x	x	x	x	x	x			Drugs, hospital
Ballesta et al. (2006)	ESP (1999)	x	x	x	x		x		x	Medication, hospital
Oliva et al. (2004)	ESP (2002)	x	x	x						Hospital, medication
Bastida, Aguilar, et al. (2002)	ESP (1998)	x	x	x	x	x				Hospital, medication
Elrayah-Eliadarous et al. (2010)	SDN (2005)		x		x	x				Outpatient clinic, drugs
Bolin et al. (2009)	SWE (1987 and 2005)	x	x		x					Hospital, drugs
Norlund et al. (2001)	SWE (1992-1993)	x	x	x				x		Hospital, home help hours
Wiréhn et al. (2008)	SWE (2005)	x	x	x						Hospital, medication
Ringborg et al. (2008)	SWE (2000-2004)	x	x		x	x	x			Hospital, outpatient visits
Schmitt-Koopmann et al. (2004)	CHE (1998-1999)	x	x	x						Hospital, medication
Lin et al. (2004)	TWN (1998-1999)	x	x	x	x	x				No exact information on share in expenditures available
Chi et al. (2011)	TWN (2000)	x	x							Outpatient visits

Ref.	Country (year of cost data)	Hospital Visits	Outpatient Visits	Physician Visits	Drugs	Laboratory	Equipment	Non-medical	Other Costs	Two main cost contributors
Chatterjee et al. (2011)	THA (2007-2008)	x	x		x	x		x	x	Informal care, hospitalizations
Abdulkadri et al. (2009)	CARICOM (2001)	x	x	x	x	x				Medication and lab/diagnostics
Al-Maskari et al. (2010)	ARE (2004-2005)	x	x	x	x	x				Hospital (information on other cost components not presented)
Dall, Zhang, et al. (2010)	USA (2007)	x	x	x	x	x	x	x	x	No exact information on share in expenditures available
Ramsey et al. (2002)	USA (1998)	x	x	x	x	x	x		x	Inpatient, outpatient
Buescher et al. (2010)	USA (1998)	x	x	x	x	x	x	x	x	Physician visits, hospital
Dall, Nikolov, et al. (2003)	USA (1998-2000)	x	x	x	x	x	x			Institutional care (nursing home stays, hospital), outpatient care
Druss et al. (2001)	USA (1996)	No breakdown of costs provided. Only self reported healthcare cost estimate.								
Durden et al. (2009)	USA (2000, 2005)	x	x	x	x	x	x			Hospital, outpatient services
Trogdon and Hylands (2008)	USA (2000-2004)	No breakdown of costs provided. Only self reported healthcare cost estimate.								
Brandle et al. (2003)	USA (2000-2001)	x	x		x	x				No exact information on share in expenditures is available
O'Connell et al. (2012)	USA (2004-2005)	x	x	x						Hospital, medication
Peele et al. (2002)	USA (1996)	x	x	x		x				No exact information on share in expenditures available
Rodbard et al. (2010)	USA (2006)	No breakdown of costs provided.								

Ref.	Country (year of cost data)	Hospital Visits	Outpatient Visits	Physician Visits	Drugs	Laboratory	Equipment	Non-medical	Other Costs	Two main cost contributors
Honeycutt et al. (2009)	USA (1998-2003)	x	x	x	x	x	x			No exact information on share in expenditures available
Maciejewski and Maynard (2004)	USA (1998)	x	x							Hospital
Birnbaum et al. (2003)	USA (1997-1998)	No breakdown of costs provided. Only self reported healthcare cost estimate.								
Zhou et al. (2005)	USA (2000)	x	x	x	x	x	x			No exact information on share in expenditures available
Dall, Mann, et al. (2008)	USA (2006)	x	x	x						Hospital, medication
Tunceli, Wade, et al. (2010)	USA (2006-2007)	x	x	x						Hospital, medication
Condliffe et al. (2013)	USA (2004-2007)	No breakdown of costs provided.								
Lee et al. (2006)	USA (2000)		x	x				x	x	Medication, ambulatory

References

Abdulkadri, A. O., Cunningham-Myrie, C., and Forrester, T. (2009). "Economic Burden of Diabetes and Hypertension in CARICOM States." *Social and Economic Studies* 58 (3-4), 175–197.

Akobundu, E., Ju, J., Blatt, L., and Mullins, C. D. (2006). "Cost-of-illness studies : a review of current methods." *PharmacoEconomics* 24 (9), 869–90.

Alavinia, S. M. and Burdorf, A. (2008). "Unemployment and retirement and ill-health: a cross-sectional analysis across European countries." *International Archives of Occupational and Environmental Health* 82 (1), 39–45. DOI: http://dx.doi.org/10.1007/s00420-008-0304-6.

Antonakis, J., Bendahan, S., Jacquart, P., Lalive, R., and Day, D. V. (2012). "Causality and endogeneity: problems and solutions." *The Oxford Handbook of Leadership and Organizations*. January. Oxford.

Arredondo, A. and Barcelo, A. (2007). "The economic burden of out-of-pocket medical expenditures for patients seeking diabetes care in Mexico." *Diabetologia* 50 (11), 2408–2409.

Arredondo, A., Zúñiga, A., and Parada, I. (2005). "Health care costs and financial consequences of epidemiological changes in chronic diseases in Latin America: evidence from Mexico." *Public health* 119 (8), 711–720. DOI: 10.1016/j.puhe.2005.01.009.

Arredondo, A. and De Icaza, E. (2011). "Costs of diabetes in Latin America: Evidences from the Mexican case." *Value in Health*. Costos de la Diabetes en America Latina: Evidencias del Caso Mexicano 14 (5 Suppl 1), S85–88. DOI: 10.1016/j.jval.2011.05.022.

Arredondo, A. and Zúñiga, A. (2004). "Economic consequences of epidemiological changes in diabetes in middle-income countries: The Mexican case." *Diabetes Care* 27 (1), 104–109.

Ballesta, M., Carral, F., Olveira, G., Girón, J. A., and Aguilar, M. (2006). "Economic cost associated with type II diabetes in Spanish patients." *The European journal of health economics* 7 (4), 270–5. DOI: 10.1007/s10198-006-0367-9.

Barceló, A., Aedo, C., Rajpathak, S., and Robles, S. (2003). "The cost of diabetes in Latin America and the Caribbean." *Bulletin of the World Health Organization* 81 (1), 19–27.

Bastida, E. and Pagán, J. A. (2002). "The impact of diabetes on adult employment and earnings of Mexican Americans: findings from a community based study." *Health economics* 11 (5), 403–413. DOI: 10.1002/hec.676.

Bastida, J. L., Aguilar, P. S., and Gonzalez, B. D. (2002). "The social and economic cost of diabetes mellitus." *Atencion primaria / Sociedad Española de Medicina de Familia y Comunitaria*. Los costes socioeconomicos de la diabetes mellitus 29 (3), 145–150.

Biorac, N., Jakovljević, M., Stefanović, D., Perović, S., and Janković, S. (2009). "[Assessment of diabetes mellitus type 2 treatment costs in the Republic of Serbia]." *Vojnosanitetski pregled. Military-medical and pharmaceutical review* 66 (4), 271–276.

Birnbaum, H., Leong, S., and Kabra, A. (2003). "Lifetime medical costs for women: Cardiovascular disease, diabetes, and stress urinary incontinence." *Women's Health Issues* 13 (6), 204–213. DOI: 10.1016/j.whi.2003.07.001. URL: http://www.ncbi.nlm.nih.gov/pubmed/14675789%20http://ovidsp.ovid.com/ovidweb.cgi?T=JS%7B%

5C&%7DPAGE=reference%7B%5C&%7DD=emed6%7B%5C&%7DNEWS=N%7B%5C&%7DAN=2003507923.

Bjegovic, V., Terzic, Z., Marinkovic, J., Lalic, N., Sipetic, S., and Laaser, U. (2007). "The burden of type 2 diabetes in Serbia and the cost-effectiveness of its management." *The European journal of health economics: HEPAC: health economics in prevention and care* 8 (2), 97–103. DOI: 10.1007/s10198-006-0012-7.

Bolin, K., Gip, C., Mörk, A.-C., and Lindgren, B. (2009). "Diabetes, healthcare cost and loss of productivity in Sweden 1987 and 2005—a register-based approach." *Diabetic Medicine* 26 (9), 928–934. DOI: 10.1111/j.1464-5491.2009.02786.x.

Boutayeb, A. and Boutayeb, W. (2014). "Estimation of the direct cost of diabetes in the Arab region." *Mediterranean Journal of Nutrition and Metabolism* 7 (1), 21–32. DOI: 10.3233/MNM-140002.

Brandle, M., Zhou, H., Smith, B. R. K., Marriott, D., Burke, R., Tabaei, B. P., Brown, M. B., and Herman, W. H. (2003). "The direct medical cost of type 2 diabetes." *Diabetes care* 26 (8), 2300–2304.

Breton, M.-C., Guénette, L., Amiche, M. A., Kayibanda, J.-F., Grégoire, J.-P., and Moisan, J. (2013). "Burden of diabetes on the ability to work: a systematic review." *Diabetes care* 36 (3), 740–9. DOI: 10.2337/dc12-0354.

Brown, H. S., Estrada, J. K., Hazarika, G., and Bastida, E. (2005). "Diabetes and the Labor Market: The community-wide economic cost in the Lower Rio Grande Valley." *Diabetes Care* 28 (12), 2945–2947. DOI: 10.2337/diacare.28.12.2945.

Brown, H. S., Pagan, J. A., and Bastida, E. (2005). "The Impact of Diabetes on Employment: Genetic IVs in a Bivariate Probit." *Health Economics* 14 (5), 537–544. DOI: 10.1002/hec.942.

Brown, H. S., Perez, A., Yarnell, L. M., Pagan, J. A., Hanis, C. L., Fischer-Hoch, S. P., and McCormick, J. B. (2011). "Diabetes and employment productivity: does diabetes management matter?" *The American journal of managed care* 17 (8), 569–576.

Bruno, G., Picariello, R., Petrelli, A., Panero, F., Costa, G., Cavallo-Perin, P., Demaria, M., and Gnavi, R. (2012). "Direct costs in diabetic and non diabetic people: the population-based Turin study, Italy." *Nutrition, metabolism, and cardiovascular diseases : NMCD* 22 (8), 684–90. DOI: 10.1016/j.numecd.2011.04.007.

Buescher, P. A., Whitmire, J. T., and Pullen-Smith, B. (2010). "Medical care costs for diabetes associated with health disparities among adult Medicaid enrollees in North Carolina." *North Carolina medical journal* 71 (4), 319–324.

Cameron, A., Ewen, M., Ross-Degnan, D., Ball, D., and Laing, R. (2009). "Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis." *The Lancet* 373 (9659), 240–249. DOI: 10.1016/S0140-6736(08)61762-6.

Cameron, A., Roubos, I., Ewen, M., Mantel-Teeuwisse, A. K., Leufkens, H. G. M., and Laing, R. O. (2011). "Differences in the availability of medicines for chronic and acute conditions in the public and private sectors of developing countries." *Bulletin of the World Health Organization* 89 (6), 412–421. DOI: 10.2471/BLT.10.084327.

Camilo González, J., Walker, J. H., Einarson, T. R., and González, J. C. (2009). "Cost-of-illness study of type 2 diabetes mellitus in Colombia." *Revista panamericana de salud pública = Pan American journal of public health* 26 (1), 55–63.

Cawley, J. and Meyerhoefer, C. (2012). "The medical care costs of obesity: An instrumental variables approach." *Journal of Health Economics* 31 (1), 219–230. DOI: 10.1016/j.jhealeco.2011.10.003. arXiv: arXiv:1011.1669v3.

Chan, B. S. W., Tsang, M. W., Lee, V. W. Y., and Lee, K. K. C. (2007). "Cost of Type 2 Diabetes mellitus in Hong Kong Chinese." *International journal of clinical pharmacology and therapeutics* 45 (8), 455–468.

Chang, K. (2010). "Comorbidities, quality of life and patients' willingness to pay for a cure for type 2 diabetes in Taiwan." *Public health* 124 (5), 284–294. DOI: 10.1016/j.puhe.2010.02.019.

Chatterjee, S., Riewpaiboon, A., Piyauthakit, P., Riewpaiboon, W., Boupaijit, K., Panpuwong, N., and Archavanuntagul, V. (2011). "Cost of diabetes and its complications in Thailand: a complete picture of economic burden." *Health & social care in the community* 19 (3), 289–298. DOI: 10.1111/j.1365-2524.2010.00981.x.

Chi, M.-j., Lee, C.-y., and Wu, S.-c. (2011). "The prevalence of chronic conditions and medical expenditures of the elderly by chronic condition indicator (CCI)." *Archives of gerontology and geriatrics* 52 (3), 284–289. DOI: 10.1016/j.archger.2010.04.017.

Chiburis, R. C., Das, J., and Lokshin, M. (2012). "A practical comparison of the bivariate probit and linear IV estimators." *Economics Letters* 117 (3), 762–766. DOI: 10.1016/j.econlet.2012.08.037.

Chodick, G., Heymann, A. D., Wood, F., and Kokia, E. (2005). "The direct medical cost of diabetes in Israel." *The European journal of health economics : HEPAC : health economics in prevention and care* 6 (2), 166–71. DOI: 10.1007/s10198-004-0269-7.

Collins, J. J., Baase, C. M., Sharda, C. E., Ozminkowski, R. J., Nicholson, S., Billotti, G. M., Turpin, R. S., Olson, M., and Berger, M. L. (2005). "The Assessment of Chronic Health Conditions on Work Performance, Absence, and Total Economic Impact for Employers." *Journal of Occupational and Environmental Medicine* 47 (6), 547–557. DOI: 10.1097/01.jom.0000166864.58664.29.

Condliffe, S., Link, C. R., Parasuraman, S., and Pollack, M. F. (2013). "The effects of hypertension and obesity on total health-care expenditures of diabetes patients in the United States." *Applied Economics Letters* 20 (7), 649–652. DOI: 10.1080/13504851.2012.727966. URL: http://www.tandfonline.com/doi/abs/10.1080/13504851.2012.727966.

Craig, P., Cooper, C., Gunnell, D., Haw, S., Lawson, K., Macintyre, S., Ogilvie, D., Petticrew, M., Reeves, B., Sutton, M., and Thompson, S. (2012). "Using natural experiments to evaluate population health interventions: new Medical Research Council guidance." *Journal of epidemiology and community health* 66 (12), 1182–6. DOI: 10.1136/jech-2011-200375. URL: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3796763%7B%5C&%7Dtool=pmcentrez%7B%5C&%7Drendertype=abstract.

Dall, T., Mann, S., Zhang, Y., Martin, J., Chen, Y., Hogan, P., and Petersen, M. (2008). "Economic costs of diabetes in the U.S. In 2007." *Diabetes care* 31 (3), 596–615. DOI: 10.2337/dc08-9017.

Dall, T., Nikolov, P., and Hogan, P. (2003). "Economic costs of diabetes in the US in 2002." *Diabetes care* 26 (3), 917–932.

Dall, T. M., Zhang, Y., Chen, Y. J., Quick, W. W., Yang, W. G., and Fogli, J. (2010). "The economic burden of diabetes." *Health Affairs* 29 (2), 297–303. DOI: 10.1377/hlthaff.2009.0155.

Davis, W. A., Knuiman, M. W., Hendrie, D., and Davis, T. M. E. (2006). "The obesity-driven rising costs of type 2 diabetes in Australia: projections from the Fremantle Diabetes Study." *Internal medicine journal* 36 (3), 155–161. DOI: 10.1111/j.1445-5994.2006.01014.x.

Dawson, K. G., Gomes, D., Gerstein, H., Blanchard, J. F., and Kahler, K. H. (2002). "The economic cost of diabetes in Canada, 1998." *Diabetes care* 25 (8), 1303–7.

Druss, B., Marcus, S., and Olfson, M. (2001). "Comparing the national economic burden of five chronic conditions." *Health Affairs* 20 (6), 233–241.

Durden, E. D., Alemayehu, B., Bouchard, J. R., Chu, B.-C., and Aagren, M. (2009). "Direct health care costs of patients with type 2 diabetes within a privately insured employed population, 2000 and 2005." *Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine* 51 (12), 1460–1465. DOI: 10.1097/JOM.0b013e3181c2bb31.

Elrayah-Eliadarous, H., Yassin, K., Eltom, M., Abdelrahman, S., Wahlström, R., and Ostenson, C.-G. (2010). "Direct costs for care and glycaemic control in patients with type 2 diabetes in Sudan." *Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association* 118 (4), 220–5. DOI: 10.1055/s-0029-1246216.

Esteghamati, A., Khalilzadeh, O., Anvari, M., Meysamie, A., Abbasi, M., Forouzanfar, M., and Alaeddini, F. (2009). "The economic costs of diabetes: a population-based study in Tehran, Iran." *Diabetologia* 52 (8), 1520–1527. DOI: 10.1007/s00125-009-1398-4.

Ettaro, L., Songer, T. J., Zhang, P., and Engelgau, M. M. (2004). "Cost-of-illness studies in diabetes mellitus." *PharmacoEconomics* 22 (3), 149–164. DOI: 10.2165/00019053-200422030-00002.

Gyldmark, M. and Morrison, G. C. (2001). "Demand for health care in Denmark: results of a national sample survey using contingent valuation." *Social Science and Medicine* 53 (8), 1023–1036.

Harris, A. (2009). "Diabetes, Cardiovascular Disease and Labour Force Participation in Australia: An Endogenous Multivariate Probit Analysis of Clinical Prevalence Data." *Economic Record* 85 (271), 472–484. DOI: 10.1111/j.1475-4932.2009.00572.x.

Hemminki, K., Li, X., Sundquist, K., and Sundquist, J. (2010). "Familial Risks for Type 2 Diabetes in Sweden." *Diabetes Care* 33 (2), 293–297. DOI: 10.2337/dc09-0947.

Herder, C. and Roden, M. (2011). "Genetics of type 2 diabetes: pathophysiologic and clinical relevance." *European Journal of Clinical Investigation* 41 (6), 679–692. DOI: 10.1111/j.1365-2362.2010.02454.x.

Herquelot, E., Guéguen, A., Bonenfant, S., and Dray-Spira, R. (2011). "Impact of diabetes on work cessation: data from the GAZEL cohort study." *Diabetes care* 34 (6), 1344–9. DOI: 10.2337/dc10-2225.

Holmes, J., Gear, E., Bottomley, J., Gillam, S., Murphy, M., and Williams, R. (2003). "Do people with type 2 diabetes and their carers lose income? (T2ARDIS-4)." *Health policy* 64 (3), 291–296.

Honeycutt, A. A., Segel, J. E., Hoerger, T. J., and Finkelstein, E. A. (2009). "Comparing cost-of-illness estimates from alternative approaches: an application to diabetes." *Health services research* 44 (1), 303–320. DOI: 10.1111/j.1475-6773.2008.00909.x.

Honkasalo, M. T., Linna, M., Sane, T., Honkasalo, A., and Elonheimo, O. (2014). "A comparative study of two various models of organising diabetes follow-up in public primary health care - the model influences the use of services, their quality and costs." *BMC health services research* 14, 26. DOI: 10.1186/1472-6963-14-26.

Horak, P. (2009). "[Pharmacoeconomy of diabetes mellitus–trends in the Czech Republic]." *Vnitr Lek* 55 (4), 331–340.

Hu, F. B. (2011). "Globalization of diabetes: the role of diet, lifestyle, and genes." *Diabetes care* 34 (6), 1249–57. DOI: 10.2337/dc11-0442.

International Diabetes Federation (2014). *Diabetes Atlas 2014 Update*. 6th ed. International Diabetes Federation.

Javanbakht, M., Baradaran, H. R., Mashayekhi, A., Haghdoost, A. A., Khamseh, M. E., Kharazmi, E., and Sadeghi, A. (2011). "Cost-of-illness analysis of type 2 diabetes mellitus in Iran." *PloS one* 6 (10), e26864. DOI: 10.1371/journal.pone.0026864.

Johnson, J. A., Pohar, S. L., and Majumdar, S. R. (2006). "Health care use and costs in the decade after identification of type 1 and type 2 diabetes: a population-based study." *Diabetes care* 29 (11), 2403–2408. DOI: 10.2337/dc06-0735.

Jönsson, B. (2002). "Revealing the cost of Type II diabetes in Europe." *Diabetologia* 45 (7), S5–12. DOI: 10.1007/s00125-002-0858-x.

Kahn, M. (1998). "Health and labor market performance: the case of diabetes." *Journal of Labor Economics* 16 (4), 878–899.

Khowaja, L. A., Khuwaja, A. K., and Cosgrove, P. (2007). "Cost of diabetes care in out-patient clinics of Karachi, Pakistan." *BMC health services research* 7, 189. DOI: 10.1186/1472-6963-7-189.

Kirigia, J. M., Sambo, H. B., Sambo, L. G., and Barry, S. P. (2009). "Economic burden of diabetes mellitus in the WHO African region." *BMC international health and human rights* 9, 6. DOI: 10.1186/1472-698X-9-6.

Köster, I., Ferber, L. von, Ihle, P., Schubert, I., and Hauner, H. (2006). "The cost burden of diabetes mellitus: the evidence from Germany–the CoDiM study." *Diabetologia* 49 (7), 1498–1504. DOI: 10.1007/s00125-006-0277-5.

Köster, I., Huppertz, E., Hauner, H., and Schubert, I. (2011). "Direct costs of diabetes mellitus in Germany - CoDiM 2000-2007." *Experimental and Clinical Endocrinology and Diabetes* 119 (6), 377–385. DOI: 10.1055/s-0030-1269847.

Köster, I., Schubert, I., and Huppertz, E. (2012). "Follow up of the CoDiM-Study: Cost of diabetes mellitus 2000-2009." *Deutsche Medizinische Wochenschrift*. Fortschreibung der KoDiM-Studie: Kosten des Diabetes mellitus 2000-2009 137 (19), 1013–1016. DOI: 10.1055/s-0032-1304891.

Kraut, A., Walld, R., Tate, R., and Mustard, C. (2001). "Impact of diabetes on employment and income in Manitoba, Canada." *Diabetes care* 24 (1), 64–68.

Larg, A. and Moss, J. R. (2011). "Cost-of-illness studies: a guide to critical evaluation." *PharmacoEconomics* 29 (8), 653–71. DOI: 10.2165/11588380-000000000-00000. URL: http://www.ncbi.nlm.nih.gov/pubmed/21604822.

Latif, E. (2009). "The impact of diabetes on employment in Canada." *Health Economics* 18 (5), 577–589. DOI: 10.1002/hec.1390.

Lau, R. S., Ohinmaa, A., and Johnson, J. A. (2011). "Predicting the Future Burden of Diabetes in Alberta from 2008 to 2035." *Canadian Journal of Diabetes* 35 (3), 274–281. DOI: 10.1016/S1499-2671(11)53011-4.

Laugesen, M. J. and Glied, S. a. (2011). "Higher fees paid to US physicians drive higher spending for physician services compared to other countries." *Health affairs (Project Hope)* 30 (9), 1647–56. DOI: 10.1377/hlthaff.2010.0204.

Lee, J.-A., Liu, C.-F., and Sales, A. E. (2006). "Racial and ethnic differences in diabetes care and health care use and costs." *Preventing chronic disease* 3 (3), A85.

Leijten, F. R. M., Heuvel, S. G. van den, Ybema, J. F., Beek, A. J. van der, Robroek, S. J. W., and Burdorf, A. (2014). "The influence of chronic health problems on work ability and productivity at work: a longitudinal study among older employees." *Scandinavian journal of work, environment & health* 40 (5), 473–82. DOI: 10.5271/sjweh.3444.

Lenneman, J., Schwartz, S., Giuseffi, D. L., and Wang, C. (2011). "Productivity and health: an application of three perspectives to measuring productivity." *Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine* 53 (1), 55–61. DOI: 10.1097/JOM.0b013e3182029110.

Lesniowska, J., Schubert, A., Wojna, M. M., Skrzekowska-Baran, I., Fedyna, M., Leśniowska, J., Schubert, A., Wojna, M. M., Skrzekowska-Baran, I., and Fedyna, M. (2014). "Costs of Diabetes and Its Complications in Poland." *The European journal of health economics*. ISPOR 14th Annual European Congress Madrid Spain. Conference Start: 20111105 Conference End: 20111108 15 (6), 653–660. DOI: 10.1007/s10198-013-0513-0.

Lin, S. (2011). "Estimating the impact of diabetes on employment in Taiwan." *Economics Bulletin* 31 (4), 3089–3102.

Lin, T., Chou, P., Tsai, S.-T., Lee, Y.-C., and Tai, T.-Y. (2004). "Predicting factors associated with costs of diabetic patients in Taiwan." *Diabetes research and clinical practice* 63 (2), 119–125.

Linden, M. W. van der, Plat, A. W., Erkens, J. A., Emneus, M., and Herings, R. M. C. (2009). "Large impact of antidiabetic drug treatment and hospitalizations on economic burden of diabetes mellitus in The Netherlands during 2000 to 2004." *Value in health* 12 (6), 909–14. DOI: 10.1111/j.1524-4733.2009.00506.x.

Liu, X. and Zhu, C. (2014). "Will knowing diabetes affect labor income? Evidence from a natural experiment." *Economics Letters* 124 (1), 74–78. DOI: 10.1016/j.econlet.2014.04.019.

Lorenzoni, L., Belloni, A., and Sassi, F. (2014). "Health-care expenditure and health policy in the USA versus other high-spending OECD countries." *Lancet* 384 (9937), 83–92. DOI: 10.1016/S0140-6736(14)60571-7. URL: http://www.ncbi.nlm.nih.gov/pubmed/24993914.

Lucioni, C., Garancini, M. P., Massi-Benedetti, M., Mazzi, S., and Serra, G. (2003). "The costs of type 2 diabetes mellitus in Italy: A CODE-2 sub-study." *Treatments in Endocrinology* 2 (2), 121–133.

Maciejewski, M. and Maynard, C. (2004). "Diabetes-related utilization and costs for inpatient and outpatient services in the Veterans Administration." *Diabetes Care* 27 (SUPPL.2), B69–B73.

Marchesini, G., Forlani, G., Rossi, E., Berti, A., and De Rosa, M. (2011). "The direct economic cost of pharmacologically-treated diabetes in Italy-2006. The ARNO observatory." *Nutrition, metabolism, and cardiovascular diseases : NMCD* 21 (5), 339–46. DOI: 10.1016/j.numecd.2009.10.009.

Martin, S., Schramm, W., Schneider, B., Neeser, K., Weber, C., Lodwig, V., Heinemann, L., Scherbaum, W. A., and Kolb, H. (2007). "Epidemiology of complications and total treatment costs from diagnosis of Type 2 diabetes in Germany (ROSSO 4)." *Experimental and clinical endocrinology & diabetes* 115 (8), 495–501. DOI: 10.1055/s-2007-981470.

Al-Maskari, F., El-Sadig, M., and Nagelkerke, N. (2010). "Assessment of the direct medical costs of diabetes mellitus and its complications in the United Arab Emirates." *BMC public health* 10 (1), 679. DOI: 10.1186/1471-2458-10-679.

Mata, M., Antoñanzas, F., Tafalla, M., and Sanz, P. (2002). "[The cost of type 2 diabetes in Spain: the CODE-2 study]." *Gaceta sanitaria / S.E.S.P.A.S* 16 (6), 511–520.

Minor, T. (2011). "The effect of diabetes on female labor force decisions: new evidence from the National Health Interview Survey." *Health economics* 20 (12), 1468–1486. DOI: 10.1002/hec.1685.

— (2013). "An investigation into the effect of type I and type II diabetes duration on employment and wages." *Economics and human biology* 11 (4), 534–44. DOI: 10.1016/j.ehb.2013.04.004.

Moher, D., Liberati, A., Tetzlaff, J., and Altman, D. G. (2009). "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement." *PLoS medicine* 6 (7), e1000097. DOI: 10.1371/journal.pmed.1000097.

Morsanutto, A., Berto, P., Lopatriello, S., Gelisio, R., Voinovich, D., Cippo, P. P., and Mantovani, L. G. (2006). "Major complications have an impact on total annual medical cost of diabetes: results of a database analysis." *Journal of Diabetes and its Complications* 20 (3), 163–169. DOI: 10.1016/j.jdiacomp.2005.06.011.

Nakamura, K., Okamura, T., Kanda, H., Hayakawa, T., Murakami, Y., Okayama, A., and Ueshima, H. (2008). "Medical expenditure for diabetic patients: a 10-year follow-up study of National Health Insurance in Shiga, Japan." *Public health* 122 (11), 1226–1228. DOI: 10.1016/j.puhe.2007.12.004.

Ng, Y. C., Philip, J., and Johnson, J. (2001). "Productivity Losses Associated With Diabetes in the U.S." *Diabetes Care* 24 (2), 257–261. DOI: 10.2337/diacare.24.2.257.

Nolan, J. J., O'Halloran, D., McKenna, T. J., Firth, R., and Redmond, S. (2006). "The cost of treating type 2 diabetes (CODEIRE)." *Irish medical journal* 99 (10), 307–310.

Norlund, A., Apelqvist, J., Bitzén, P. O., Nyberg, P., and Scherstén, B. (2001). "Cost of illness of adult diabetes mellitus underestimated if comorbidity is not considered." *Journal of Internal Medicine* 250 (1), 57–65.

O'Connell, J. M., Wilson, C., Manson, S. M., and Acton, K. J. (2012). "The costs of treating American Indian adults with diabetes within the Indian Health Service." *American journal of public health* 102 (2), 301–308. DOI: 10.2105/AJPH.2011.300332.

Ohinmaa, A., Jacobs, P., Simpson, S., and Johnson, J. (2004). "The projection of prevalence and cost of diabetes in Canada: 2000 to 2016." *Canadian Journal of Diabetes* 28 (2), 116–123.

Oliva, J., Lobo, F., Molina, B., and Monereo, S. (2004). "Direct health care costs of diabetic patients in Spain." *Diabetes care* 27 (11), 2616–2621.

Peele, P. B., Lave, J. R., and Songer, T. J. (2002). "Diabetes in employer-sponsored health insurance." *Diabetes care* 25 (11), 1964–1968.

Pohar, S. L. and Johnson, J. A. (2007). "Health care utilization and costs in Saskatchewan's registered Indian population with diabetes." *BMC health services research* 7, 126. DOI: 10.1186/1472-6963-7-126.

Pohar, S. L., Majumdar, S. R., and Johnson, J. A. (2007). "Health Care Costs and Mortality for Canadian Urban and Rural Patients with Diabetes: Population-Based Trends from 1993-2001." *Clinical Therapeutics* 29 (6 PART 1), 1316–1324. DOI: 10.1016/j.clinthera.2007.07.001.

Ramachandran, A., Ramachandran, S., Snehalatha, C., Augustine, C., Murugesan, N., Viswanathan, V., Kapur, A., and Williams, R. (2007). "Increasing expenditure on health care incurred by diabetic subjects in a developing country: a study from India." *Diabetes care* 30 (2), 252–256. DOI: 10.2337/dc06-0144.

Ramsey, S., Summers, K. H., Leong, S. A., Birnbaum, H. G., Kemner, J. E., and Greenberg, P. (2002). "Productivity and medical costs of diabetes in a large employer population." *Diabetes care* 25 (1), 23–29. URL: http://www.ncbi.nlm.nih.gov/pubmed/11772896%20http://ovidsp.ovid.com/ovidweb.cgi?T=JS%7B%5C&%7DPAGE=reference%7B%5C&%7DD=emed5%7B%5C&%7DNEWS=N%7B%5C&%7DAN=11772896%20http://ovidsp.ovid.com/ovidweb.cgi?T=JS%7B%5C&%7DPAGE=reference%7B%5C&%7DD=emed5%7B%5C&%7DNEWS=N%7B%5C&%7DAN=2005342883.

Redekop, W. K., Koopmanschap, M. A., Rutten, G. E. H. M., Wolffenbuttel, B. H. R., Stolk, R. P., and Niessen, L. W. (2002). "Resource consumption and costs in Dutch patients with type 2 diabetes mellitus. Results from 29 general practices." *Diabetic medicine: a journal of the British Diabetic Association* 19 (3), 246–253.

Ricordeau, P., Weill, A., Vallier, N., Bourrel, R., Schwartz, D., Guilhot, J., Fender, P., and Allemand, H. (2003). "The prevalence and cost of diabetes in metropolitan France: What trends between 1998 and 2000?" *Diabetes and Metabolism* 29 (5), 497–504.

Ringborg, A., Martinell, M., Stålhammar, J., Yin, D. D., and Lindgren, P. (2008). "Resource use and costs of type 2 diabetes in Sweden - estimates from population-based register data." *International journal of clinical practice* 62 (5), 708–716. DOI: 10.1111/j.1742-1241.2008.01716.x.

Rodbard, H. W., Green, A. J., Fox, K. M., and Grandy, S. (2010). "Impact of type 2 diabetes mellitus on prescription medication burden and out-of-pocket healthcare expenses." *Diabetes research and clinical practice* 87 (3), 360–365. DOI: 10.1016/j.diabres.2009.11.021.

Rodríguez Bolaños, R. d. L. Á., Reynales Shigematsu, L. M., Jiménez Ruíz, J. A., Juárez Márquezy, S. A., Hernández Ávila, M., and R., D. l. A. R. B. (2010). "Direct costs of medical care for patients with type 2 diabetes mellitus in Mexico: Micro-costing analysis." *Revista Panamericana de Salud Publica/Pan American Journal of Public*

Health. Costos directos de atencion medica en pacientes con diabetes mellitus tipo 2 en Mexico: analisis de microcosteo 28 (6), 412–420.

Schmitt-Koopmann, I., Schwenkglenks, M., Spinas, G. A., and Szucs, T. D. (2004). "Direct medical costs of type 2 diabetes and its complications in Switzerland." *European journal of public health* 14 (1), 3–9.

Segel, J. E. (2006). "Cost-of-Illness Studies — A Primer." *RTI-UNC Center of Excellence in Health Promotion Economics*.

Seuring, T., Goryakin, Y., and Suhrcke, M. (2014). "The impact of diabetes on employment in Mexico." *CHE Research Paper*. CHE Research Paper (100).

Shemilt, I., Thomas, J., and Morciano, M. (2010). "A web-based tool for adjusting costs to a specific target currency and price year." *Evidence and Policy* 6 (1), 51–59. DOI: 10.1332/174426410X482999.

Simpson, S. H., Corabian, P., Jacobs, P., and Johnson, J. A. (2003). "The cost of major comorbidity in people with diabetes mellitus." *Canadian Medical Association Journal* 168 (13), 1661–1667.

Smith-Spangler, C. M., Bhattacharya, J., and Goldhaber-Fiebert, J. D. (2012). "Diabetes, its treatment, and catastrophic medical spending in 35 developing countries." *Diabetes care* 35 (2), 319–326. DOI: 10.2337/dc11-1770.

Solli, O., Jenssen, T., and Kristiansen, I. S. (2010). "Diabetes: cost of illness in Norway." *BMC endocrine disorders* 10, 15. DOI: 10.1186/1472-6823-10-15.

Squires, D. A. (2012). "Explaining High Health Care Spending in the United States: An International Comparison of Supply, Utilization, Prices, and Quality The." 10 (May), 1–14.

Suleiman, I., Fadeke, O., and Okubanjo, O. (2006). "Pharmacoeconomic Evaluation of Anti-Diabetic Therapy in A Nigerian Tertiary Health Institution." *Annals of African Medicine* 5 (3), 132–137.

Tharkar, S., Devarajan, A., Kumpatla, S., and Viswanathan, V. (2010). "The socioeconomics of diabetes from a developing country: A population based cost of illness study." *Diabetes Research and Clinical Practice* 89 (3), 334–340. DOI: 10.1016/j.diabres.2010.05.009.

The Interact Consortium (2013). "The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: the EPIC-InterAct study." *Diabetologia* 56 (1), 60–9. DOI: 10.1007/s00125-012-2715-x.

Trogdon, J. G. and Hylands, T. (2008). "Nationally representative medical costs of diabetes by time since diagnosis." *Diabetes care* 31 (12), 2307–2311. DOI: 10.2337/dc08-1375.

Tunceli, K., Bradley, C. J., Nerenz, D., Williams, L. K., Pladevall, M., and Elston Lafata, J. (2005). "The impact of diabetes on employment and work productivity." *Diabetes care* 28 (11), 2662–2667.

Tunceli, K., Zeng, H., Habib, Z. A., and Williams, L. K. (2009). "Long-term projections for diabetes-related work loss and limitations among U.S. adults." *Diabetes research and clinical practice* 83 (1), e23–25. DOI: 10.1016/j.diabres.2008.11.004.

Tunceli, O., Wade, R., Gu, T., Bouchard, J. R., Aagren, M., and Luo, W. (2010). "Cost of diabetes: comparison of disease-attributable and matched cohort cost estimation methods." *Current medical research and opinion* 26 (8), 1827–34. DOI: 10.1185/03007995.2010.488544.

Valdmanis, V., Smith, D. W., and Page, M. R. (2001). "Productivity and economic burden associated with diabetes." *American journal of public health* 91 (1), 129–30.

Vijan, S., Hayward, R. A., and Langa, K. M. (2004). "The impact of diabetes on workforce participation: results from a national household sample." *Health services research* 39 (6 Pt 1), 1653–69. DOI: 10.1111/j.1475-6773.2004.00311.x.

Wang, W., Fu, C. W., Pan, C. Y., Chen, W., Zhan, S., Luan, R., Tan, A., Liu, Z., and Xu, B. (2009). "How do type 2 diabetes mellitus-related chronic complications impact direct medical cost in four major cities of urban China?" *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research* 12 (6), 923–9. DOI: 10.1111/j.1524-4733.2009.00561.x.

Wang, W., Fu, C., Zhuo, H., Luo, J., and Xu, B. (2010). "Factors affecting costs and utilization of type 2 diabetes healthcare: a cross-sectional survey among 15 hospitals in urban China." *BMC health services research* 10. DOI: 10.1186/1472-6963-10-244.

Wang, W., McGreevey, W. P., Fu, C., Zhan, S., Luan, R., Chen, W., and Xu, B. (2009). "Type 2 diabetes mellitus in China: a preventable economic burden." *The American journal of managed care* 15 (9), 593–601.

Wiréhn, A.-B., Andersson, A., Ostgren, C. J., and Carstensen, J. (2008). "Age-specific direct healthcare costs attributable to diabetes in a Swedish population: a register-based analysis." *Diabetic medicine : a journal of the British Diabetic Association* 25 (6), 732–7. DOI: 10.1111/j.1464-5491.2008.02444.x.

World Bank. *World Bank Analytical Classifications*. URL: http://siteresources.worldbank.org/DATASTATISTICS/Resources/OGHIST.xls.

Yang, W., Zhao, W., Xiao, J., Li, R., Zhang, P., Kissimova-Skarbek, K., Schneider, E., Jia, W., Ji, L., Guo, X., Shan, Z., Liu, J., Tian, H., Chen, L., Zhou, Z., Ji, Q., Ge, J., Chen, G., and Brown, J. (2012). "Medical care and payment for diabetes in China: enormous threat and great opportunity." *PloS one* 7 (9), e39513. DOI: 10.1371/journal.pone.0039513.

Zhang, X., Zhao, X., and Harris, A. (2009). "Chronic Diseases and Labour Force Participation in Australia." *Journal of Health Economics* 28 (1), 91–108.

Zhao, F.-L., Xie, F., Hu, H., and Li, S.-C. (2013). "Transferability of indirect cost of chronic disease: a systematic review and meta-analysis." *PharmacoEconomics* 31 (6), 501–8. DOI: 10.1007/s40273-013-0053-6. URL: http://www.ncbi.nlm.nih.gov/pubmed/23620212.

Zhou, H., Isaman, D. J. M., Messinger, S., Brown, M. B., Klein, R., Brandle, M., and Herman, W. H. (2005). "A computer simulation model of diabetes progression, quality of life, and cost." *Diabetes care* 28 (12), 2856–2863.