The global economic burden of diabetes in adults aged 20–79 years: a cost-of-illness study

Christian Bommer, Esther Heesemann, Vera Sagalova, Jennifer Manne-Goehler, Rifat Atun, Till Bärnighausen, Sebastian Vollmer

Summary

Background Differences in methods and data used in past studies have limited comparisons of the cost of illness of diabetes across countries. We estimate the full global economic burden of diabetes in adults aged 20–79 years in 2015, using a unified framework across all countries. Our objective was to highlight patterns of diabetes-associated costs as well as to identify the need for further research in low-income regions.

Methods Epidemiological and economic data for 184 countries were used to estimate the global economic burden of diabetes, regardless of diabetes type. Direct costs were derived using a top-down approach based on WHO general health expenditure figures and prevalence data from the 2015 International Diabetes Federation Diabetes Atlas. Indirect costs were assessed using a human-capital approach, including diabetes-associated morbidity and premature mortality.

Findings We estimate the global cost of diabetes for 2015 was US$1·31 trillion (95% CI 1·28–1·36) or 1·8% (95% CI 1·8–1·9) of global gross domestic product (GDP). Notably, indirect costs accounted for 34·7% (95% CI 34·7–35·0) of the total burden, although substantial variations existed both in the share and the composition of indirect costs across countries. North America was the most affected region relative to GDP and also the largest contributor to global absolute costs. However, on average, the economic burden as percentage of GDP was larger in middle-income countries than in high-income countries.

Interpretation Our results suggest a substantial global economic burden of diabetes. Although limited data were available for low-income and middle-income countries, our findings suggest that large diabetes-associated costs are not only a problem in high-income settings but also affect poorer world regions.

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Introduction

A large body of literature has quantified the economic burden of diabetes at the country level. Cost-of-illness studies typically include direct and indirect costs of diabetes. Direct costs comprise all expenditures for the treatment of diabetes, including medication, hospital stays, and treatment of complications.[1] Indirect costs are defined as productivity or production losses associated with morbidity and premature mortality.[2] Prominent examples of cost-of-illness studies are the cost estimates provided by the American Diabetes Association for the US population: the total burden for 2012 was estimated to be US$245 billion,[3] taking increased health expenditure and productivity losses due to diabetes into consideration. In this analysis, indirect costs accounted for 28% of the total costs of diabetes, highlighting the significance of labour market effects for the total economic burden. Evidence of high economic costs, however, is not only limited to developed countries. For example, Seuring and colleagues[2] analysed the results of 86 cost-of-illness studies published between 2001 and 2014 and found evidence for a substantial economic burden in low-income and middle-income countries (LMICs), with annual direct costs ranging from INT$242 to $4129 (international dollars; 2011 purchasing power parity) per capita and indirect costs ranging from INT$45 to $16 914 per capita.[2]

Comparing cost-of-illness studies both within and across countries is challenging because the costs included in the calculations and the methods used to assess costs vary widely in the existing literature. Ettaro and colleagues[1] reviewed three decades of primarily US-based cost-of-illness studies and found large discrepancies between studies using differing methods. Similarly, studies[4,5] comparing different costing approaches have illustrated the sensitivity of results to methodological choices.

Few cost-of-illness studies have aimed to quantify the economic burden of diabetes at the regional level. Barceló and colleagues[6] estimated a total economic burden for Latin America and the Caribbean of US$65·22 billion in 2000. Indirect costs, evaluated by forgone earnings, constituted 82% of the total costs. In another study[7] in the region the economic burden of diabetes and hypertension for the Bahamas, Barbados, Jamaica, and Trinidad and Tobago was quantified and the total costs of diabetes ranged from 0·5% to 5·2% of gross domestic product (GDP). For the WHO African Region in 2005, Kirigia and colleagues[8] estimated the cost of diabetes per patient was INT$3633 (using 2005 purchasing power parity), adding up to a total burden of INT$25·51 billion. The share of indirect costs in the study by Kirigia and colleagues[8] was 68%, which is slightly lower than what was found by Barceló and colleagues[6] for Latin America and the Caribbean.

Research in context

Evidence before this study

We started our literature search by screening studies about the economic costs or labour market consequences of diabetes discussed in a systematic review by Seuring and colleagues. We further searched Google Scholar for articles published before Dec 20, 2016, that either included only the search term "cost(s) of diabetes" alone or the search term "diabetes" in combination with "absenteeism", "presenteeism", "sick leave", "sick days", "disability days", "work days", "workdays", "productivity", "labo(u)r market", "labo(u)r supply", "indirect cost(s)", "economic cost(s)", "economic burden", "cost burden", "cost of illness", "wage(s)", "earning(s)", "labo(u)r income", "labo(u)r force", "workforce", "work force", "employment", "unemployment", "direct cost(s)", "direct expenditure", or "health expenditure" in the title. We then repeated the above search procedure in PubMed and extended the search to titles and abstracts. Last, we searched for labour market studies cited in relevant cost-of-illness studies identified by the above search, because labour market studies have frequently been used to motivate assumptions for the calculation of indirect costs. 53 labour market studies were identified for high-income countries but only eight studies estimated the labour market consequences of diabetes in low-income and middle-income countries. Additionally, eight cost-of-illness studies aimed to compare the costs of diabetes between countries or world regions.

Added value of this study

To our knowledge, this study is the first to estimate the global costs of diabetes, including both direct and indirect components and to draw comparisons between world regions and countries. Our analysis differs from that in previous studies by building on a large set of labour market studies to motivate assumptions made for the estimation of indirect costs. The study further improves existing direct cost estimates provided by the International Diabetes Federation using a range of patient-level health expenditure ratios derived from the identified literature.

Implication of all the available evidence

This study shows that diabetes imposes an economic burden not only in HICs but also in many LMICs. The global dimension of the problem suggests that adequately addressing diabetes requires increased efforts from the international community. However, data limitations make it difficult to precisely gauge the economic burden of diabetes in many LMICS and further research is necessary to improve knowledge about economic costs of diabetes in understudied regions.

In addition to these regional studies, a small number of studies[9–11] provide cost calculations for the global level. The 2015 version of the International Diabetes Federation's (IDF) Diabetes Atlas[9] estimated global health expenditure due to diabetes to be US$673 billion or INT$795 billion (2011 purchasing power parity). Furthermore, a study from the NCD Risk Factor Collaboration[10] calculated global direct costs of INT$825 billion (2011 purchasing power parity) for 2014, almost 60% of which arose in LMICs. Bloom and colleagues[11] reported estimates of the global direct and indirect economic burden of diabetes, but they did not provide a detailed breakdown of costs by country or world region and did not consider all relevant productivity losses for calculation of indirect costs.

See Online for appendix

We aimed to estimate the full global economic burden of diabetes by taking into consideration both direct costs and production losses due to morbidity or premature mortality. We applied the same method and cost definition for each country to allow a regional breakdown and ranking of countries by economic costs.

Methods

Prevalence and deaths due to diabetes

As a basis for cost calculations, we used estimates for the prevalence of diabetes and number of deaths due to diabetes, regardless of diabetes type, for adults aged 20–79 years disaggregated by sex and 10-year age groups from the 2015 IDF Diabetes Atlas.[9] Due to data limitations, estimates were not available for individuals outside this age range for most countries, which is why we restricted our analysis to adults. This study covers 184 countries from all World Bank regions. For comparison purposes, we used prevalence and mortality data from the 2015 Global Burden of Disease (GBD) Study,[12] truncating the GBD estimates to the same age range as in the 2015 IDF Diabetes Atlas. By contrast with the IDF data, GBD estimates do not distinguish between the prevalence of diabetes in rural and urban areas or diagnosed and undiagnosed diabetes, which is why we gave preference to IDF estimates. When making use of GBD data, we assumed the same share of undiagnosed and rural people with diabetes as reported by the IDF. Prevalence estimates and number of diabetes-associated deaths by country are in the appendix (pp 3–7).

Health expenditure ratios and labour market effects

Building on the methods of the IDF Diabetes Atlas,[13] we used a top-down approach to quantify direct costs, requiring assumptions to be made regarding age group-specific and sex-specific health expenditure for people with diabetes relative to people without diabetes. Similarly, the calculation of indirect costs involved assumptions about the labour market consequences of diabetes for male and female individuals of different age groups. We defined these labour market effects as lost work days due to sickness (absenteeism), reduced productivity while working (presenteeism), and dropout from the labour force because of disability. Additionally, we considered lost production potential due to premature mortality to be part of the indirect costs.

We did a comprehensive systematic review of past studies on the health expenditure of people with diabetes versus those without (henceforth cost ratio studies) as well as the labour market consequences of the disease for affected individuals. The advantage of this approach is that it provides an extensive account of the available evidence and lends transparency to the process of selecting assumptions. A detailed account of all review and literature assessment stages is in the appendix (pp 14–46). First, we excluded studies with a high risk of bias due to insufficient reporting of methods or results, suspected conflicts of interest, inadequate sampling design, unsuitable outcome definitions, or severe methodological limitations in their statistical analyses. Second, we ranked the remaining studies by statistical approach, sample quality, age of data, and sample size or precision. The ranking was done separately for two major World Bank income groups because we suspected cost ratios and labour market effects would differ substantially between high-income countries (HICs) and LMICs.

To derive cost ratios, we selected studies based on their ranking in each group. The highest ranked study[13] for HICs was conducted in North America and was used to inform assumptions about age group-specific and sex-specific cost ratios for this income group. Because the second-ranked study[14] was from a different World Bank region (Europe) but was assessed to have a similar quality, albeit only providing results by age group or by sex, it was used to derive separate assumptions for Europe. By contrast, only one study,[15] from China, in the group of LMICs reported age group-specific results and hence served as a basis for cost ratio assumptions for all LMICs. However, because the study for LMICs provided separate cost ratios for rural and urban areas (albeit not stratified by sex), we were able to derive adjustment factors to reflect differential health care access in rural and urban areas in LMICs. Additionally, to allow for stratification across World Bank regions, we derived adjustment factors for the Middle East and North Africa as well as South Asia from two remaining studies[16,17] in the group of LMICs. Last, all cost ratios for HICs and LMICs were readjusted to account for generally low cost ratios for people with undiagnosed diabetes, because prior diagnosis is a necessary prerequisite for costly specialised diabetes treatment. The adjustment factors were based on results by Bächle and colleagues[18] who estimated age-adjusted and sex-adjusted cost ratios for people with undiagnosed versus diagnosed diabetes using data from the Heinz Nixdorf Recall study, a population-based cohort study from three cities in northwest Germany. The use of adjustment factors for the derivation of cost ratios is summarised in figure 1 and further explained in the appendix (pp 30–36).

We assumed cost ratios in HICs ranged from 1·08 to and 4·32 for men and from 1·17 to and 3·88 for women. By contrast, in LMICs, where stratification was done by rural versus urban location rather than by sex, we assumed cost ratios between 1·14 and 9·07 in urban areas and between 1·00 and 4·83 in rural areas. A detailed summary of the resulting cost ratios is reported in the online appendix (p 36).

By contrast with the derivation of cost ratios, no adjustment factors were used to derive labour market assumptions. Instead, we selected the highest ranked labour market study for each outcome (ie, presenteeism, absenteeism, and labour-force dropout) by income group. We deviated from this rule only in the case of absenteeism in LMICs because the four ranked studies were all from different World Bank regions, had sufficient quality to justify inclusion, and we suspected substantial regional disparities in labour markets within this group. Unfortunately, no such stratification could be implemented for presenteeism and labour-market dropout because all LMIC studies were from Latin America and the Caribbean.

Labour-force dropout was assessed on the basis of studies investigating the employment probability shortfall of people with diabetes compared with those without diabetes. To obtain percentage effects on labour-force dropout, we set the observed marginal effects in relation to the study-specific labour-force participation rate, assuming that the proportion of unemployed is the same among those with and without diabetes. The outcome in selected absenteeism studies was the number of sick days over various time periods, which we extrapolated to 1 year. Presenteeism was measured on the basis of self-assessed productivity loss during a given time-period expressed as a percentage. Because no such

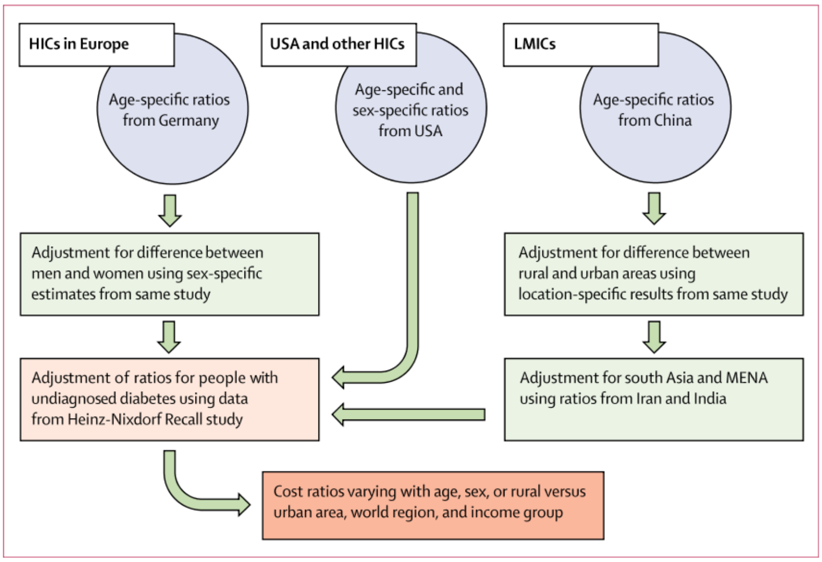

Figure 1: **Derivation of cost ratios for calculation of direct costs**
Data for Germany are from Köster and colleagues;[14] for USA are from the International Diabetes Federation;[13] for China are from Yang and colleagues;[15] for Iran are from Esteghamati and colleagues;[16] and for India are from Sharma and colleagues.[17] HICs=high-income countries. LMICs=low-income and middle-income countries. MENA=Middle East and North Africa.

study could be identified for LMICs, we interpreted the relative shortfall in hourly wages of people with diabetes compared with those without diabetes as a proxy for productivity shortfall provided that the selected studies were adequately adjusted for education and socio-economic status.

Evidence for the labour market effects of undiagnosed diabetes is still inconclusive—we only identified two relevant studies, which had contradictory results (appendix p 37). We therefore conservatively assumed that people with undiagnosed diabetes incur no absenteeism, presenteeism, or labour-market dropout attributable to their condition.

We provide a full overview of the assumed labour market effects for people diagnosed with diabetes in the appendix (p 37). To summarise, based on the review of labour market studies, absenteeism in HICs was assumed to vary by age group and sex from 2·1 to 4·3 days per year. In LMICs located in sub-Saharan Africa, Middle East and North Africa, or South Asia the available evidence did not allow stratification by age group or sex; however, regional estimates used to derive assumptions vary between 2·8 days and 8·6 days per year for all age groups. For the remaining LMICs, we assumed men were absent 1·9 days per year due to diabetes and women absent 10·2 days per year. The shortfall in productivity due to diabetes-associated presenteeism was assumed to be 0·3% in HICs and between 0·6% and 1·0% in LMICs. Lastly, the labour force participation shortfall of diabetics in HICs was assumed to be 12·6% for men and 25·2% for women. For LMICs, the estimates were further stratified by age groups with assumptions ranging from 1·1% to 1·2% participation shortfall for individuals aged 20–39 years and between 13·2% and 17·4% participation shortfall for individuals aged 40–65 years. Lack of stratification by age for HICs could result in an overestimation of costs for young age groups. The effect on total estimates is, however, limited, because on average only 10% of people with diabetes in HICs fall into the affected age groups (20–39 years).

To verify that our results were not driven by our study ranking, we did an additional meta-analysis using all available studies per stratum without high risk of bias (appendix pp 37–46). Because most studies in LMICs were not ranked within the same region (except for labour-force dropout), the meta-analysis was mainly done for studies conducted in HICs. Overall, we obtained similar assumptions about the labour market effects of diabetes.

Calculation of direct costs

We estimated direct costs of diabetes by deriving health expenditure due to diabetes from aggregate health data, applying the expenditure ratios for people with diabetes versus those without diabetes. The formula for the estimation of direct costs due to diabetes for age group *a*, sex *s*, and location *l* (ie, rural or urban) extends a previous approach used in the 2006 IDF Diabetes Atlas[13] and is given by:

$$D_{asl} = \frac{N_{asl}C_{asl}\,[(R^{DD}_{asl}-1)P^{DD}_{asl} + (R^{UD}_{asl}-1)P^{UD}_{asl}]}{P^{DD}_{asl}(R^{DD}_{asl}-1) + P^{UD}_{asl}(R^{UD}_{asl}-1) + 1}$$

in which

C_{asl}

denotes group-specific per capita health expenditure,

P^{DD}_{asl}

denotes prevalence of diagnosed diabetes, and

P^{UD}_{asl}

denotes prevalence of undiagnosed diabetes.

N_{asl}

denotes population in each group. Age-specific, sex-specific, and location-specific cost ratios are denoted by

R^{DD}_{asl}

for people with diagnosed diabetes, and

R^{UD}_{asl}

for people with undiagnosed diabetes. Male and female population data by age group, sex, and rural versus urban location were derived from UN Population Division data, assuming that the share of urban population was constant across age groups and sexes, because no age group-specific and sex-specific population data were available for rural and urban regions separately.[19,20] Because group-specific per capita health expenditure is not known for the vast majority of countries, health expenditure had to be derived by age, sex, and location from the total health expenditure reported by WHO.[21] Similar to methods used in the IDF Diabetes Atlas,[13] we assumed that a fraction of per capita health expenditure varies with age-specific and sex-specific mortality rates, while the remainder is constant across age groups. A full description of this method, along with details on adjustments made to correct for differences in access to health care in rural and urban areas, high child mortality in many LMICs, and sharply increasing mortality rates in older age groups, are in the appendix (pp 47–49).

Calculation of indirect costs

We defined indirect costs as the economic burden caused by production losses due to premature mortality and morbidity (absenteeism, presenteeism, and labour-force dropout). Production losses to premature mortality were obtained by multiplying the number of deaths attributed to diabetes with the discounted number of years lost until retirement at 65 years, using a discount factor of 3%

per year. As in previous studies,[6,8] we assigned future discounted lost production due to death to the year when the affected person died. In turn, production losses due to reduced labour force participation were calculated by multiplying the number of people with diabetes by the labour force participation shortfall of people with diabetes relative to those without diabetes. By contrast with Barceló and colleagues,[6] we did not distinguish between permanent and temporary disability when calculating labour-force dropout costs. Consequently, we ignored earnings in future years as far as disability is concerned, allowing for the possibility for disabled diabetics to re-enter the labour force in the next year after adequate treatment, changes in lifestyle, or requalification. A key advantage of this approach is that we avoid double counting because we do not need to know whether individuals were already disabled in the past. Finally, production losses due to presenteeism and absenteeism were obtained by multiplying the productivity shortfall or the excess sick days of people with diabetes compared with those without diabetes by the number of people with diabetes still assumed to be in the labour force after those dropping out were subtracted (appendix pp 49–52).

The economic value (2015 US$) of production losses due to mortality, presenteeism, and labour-market dropout was assessed based on annual wages, while absenteeism costs were based on daily wages. For HICs, we used 2014 Organisation for Economic Co-operation and Development (OECD) wage data, which we projected to 2015 based on past growth rates.[22] In view of the scarcity of reliable wage data from LMICs, we multiplied the GDP per labour force member with the labour ratio (ie, the share of total income that is comprised of labour income) as a proxy for wages when OECD data were not available. This proxy closely mimics true OECD wages and is therefore likely to provide an acceptable second-best solution for non-OECD countries (appendix pp 12–13). Data for 2014 GDP workforce size per country were taken from the World Development Indicators and extrapolated to 2015 using the average annual growth rate between 2000 and 2014.[23] Data for labour share were obtained from Karabarbounis and Neiman,[24] and consisted of estimates for 106 countries within our sample. For all available countries, we used the latest year (2005 or later in 92% of available countries). To all other countries, we assigned subregional averages or extrapolated from neighbouring countries (appendix pp 8–11). To derive daily wages, we divided the OECD data or wage proxy by 261 working days.

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all of the data and the final responsibility to submit for publication.

Results

Descriptive statistics for the main input data used in this study are in table 1. Countries are grouped by their respective World Bank Region. The sample consists of 184 countries representing 7·27 billion people. The worldwide prevalence of diabetes in adults (20–79 years) was 8·8% (according to IDF data). Summary statistics by country are in the appendix (pp 3–7).

Using IDF prevalence and mortality data, we estimate the global economic burden of diabetes in 2015 at US$1·31 (95% CI 1·28–1·36) trillion or 1·8% (95% CI 1·8–1·9) of world GDP. Notably, 34·7% (95% CI 34·7–35·0) of the overall burden is due to indirect costs of diabetes, with the average fraction varying from 40·0% in HICs to 33·5% in LMICs. Figure 2 shows the share of indirect costs attributed to the four causes we considered: labour-force dropout, absenteeism, presenteeism, and mortality.

Accordingly, labour-force dropout (48·5%) and mortality (45·5%) are the major contributors to indirect costs, followed by absenteeism (3·9%), and presenteeism (2·1%). Splitting the sample into income groups reveals a strong heterogeneity in the composition of indirect

	Number of countries	GDP† (US$ billion)	Population (million)*	Annual wage (SD; US$)‡	Prevalence of diabetes (20–79 years)§	Number of diabetes-associated deaths (20–65 years)§
Means (SD)						
Sub-Saharan Africa	47	33·47 (82·38)	21·06 (31·72)	1251·30 (1632·61)	4·1% (4·1%)	6276·67 (9830·05)
East Asia and Pacific	26	783·23 (2227·60)	85·68 (269·50)	10 931·15 (16 292·21)	9·6% (4·9%)	46 874·80 (156 447·60)
Europe and Central Asia	49	407·12 (743·43)	18·40 (27·99)	23 231·54 (23 114·27)	8·4% (2·5%)	5757·22 (14 145·43)
Latin America and the Caribbean	32	168·02 (374·31)	19·65 (42·00)	6884·58 (4306·89)	10·1% (2·8%)	6540·72 (15 776·69)
Middle East and North Africa	20	162·15 (174·62)	20·97 (25·57)	9402·67 (8581·28)	10·6% (3·7%)	6914·44 (11 733·19)
North America	2	9748·77 (11 594·05)	178·86 (202·11)	54 319·29 (5603·73)	11·1% (2·4%)	63 710·13 (79 552·77)
South Asia	8	333·26 (710·09)	217·98 (447·63)	1752·72 (1737·84)	7·1% (1·7%)	110 464·30 (239 229·2)
Totals						
Worldwide	184	72 668·96	7269·01	..	8·8%	3 154 578·30

*United Nations.[19] †World Development Indicators,[23] GDP data estimated for 2015 based on past growth rates. ‡World Development Indicators,[23] Organization for Economic Cooperation and Development (OECD),[22] Karabarbounis and Neiman;[24] wage is OECD wage data or GDP per workforce member times the labour share. §International Diabetes Federation,[9] estimated on the basis of age groups provided by Diabetes Atlas.

Table 1: **Sample characteristics**

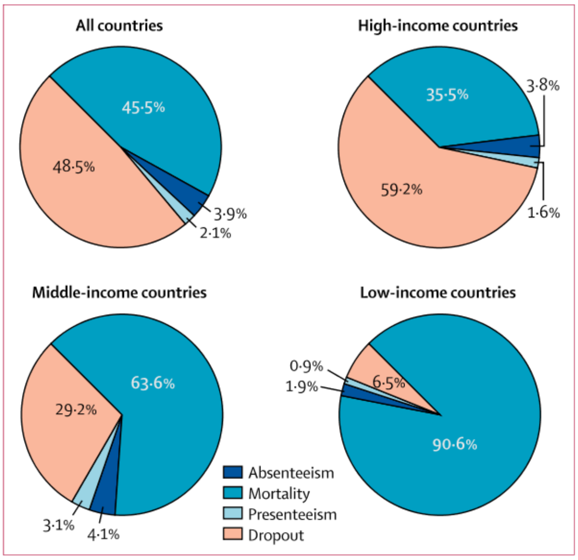

Figure 2: Composition of global indirect diabetes-associated costs

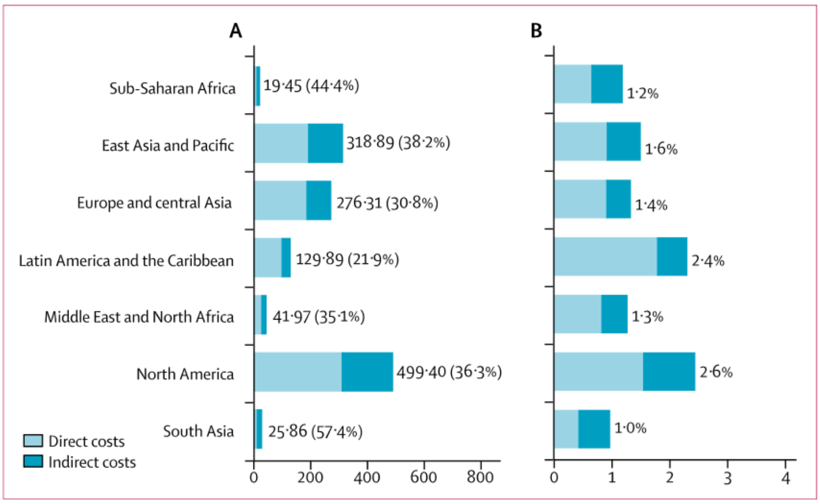

Figure 3: Economic burden in 2015 by World Bank region
(A) Costs in US$ billion; data in parentheses are the percentages attributable to indirect costs. (B) Costs in percentage of gross domestic product.

	High-income countries	Middle-income countries	Low-income countries
Number of countries	53	102	29
Absolute burden (US$ billion)			
Direct costs	510·70 (495·15–528·53)	344·69 (326·30–367·71)	1·57 (1·44–1·92)
Indirect costs	293·66 (284·93–308·33)	160·20 (150·74–176·65)	0·95 (0·87–1·15)
Total costs	804·36 (780·19–836·03)	504·89 (477·41–544·16)	2·51 (2·32–3·05)
Mean costs as a percentage of GDP			
Direct costs	0·7% (0·7–0·8)	1·2% (1·2–1·3)	0·4% (0·4–0·5)
Indirect costs	0·5% (0·5–0·5)	0·5% (0·5–0·6)	0·3% (0·2–0·3)
Total costs	1·2% (1·2–1·3)	1·8% (1·7–1·8)	0·7% (0·7–0·8)

Data for absolute burden are totals. All numbers in parentheses are 95% CI.

Table 2: Absolute and relative costs for diabetes by World Bank income group

costs. Notably, morbidity-associated factors dominate in HICs, whereas middle-income countries and especially low-income countries incur most of the indirect burden from premature mortality.

Across global regions, substantial variation exists in the magnitude of the economic burden of diabetes (figure 3). North America has the highest absolute economic burden (US$499·40 billion), and is also the most affected region relative to its total GDP (2·6%). Sub-Saharan Africa is the least affected region in absolute terms (US$19·45 billion) and south Asia in relative terms (1·0%). Regional differences also exist in the composition of total costs. For example, indirect costs are the highest contributor to economic burden in south Asia (57·4%) but amount to only a fifth of total costs in Latin America and the Caribbean (21·9%).

To investigate the economic burden of diabetes at the country-level, we grouped countries by income classification showing both absolute and relative costs (table 2). By contrast with the regional analysis, relative costs are defined here as the unweighted average of country-level costs in percent of GDP. HICs contribute by far the most to the global economic burden with a total of US$804·36 billion (1·2% of GDP), of which $293·66 billion are indirect cost components. By contrast, relative to GDP, middle-income countries are substantially more affected than HICs with an average burden of 1·8% of GDP. Low-income countries bear the lowest burden with an average of 0·7% of GDP. Country-level results for total, direct, and indirect costs as percentage of GDP along with direct cost estimates as percentage of total health expenditure, in absolute terms as well as by individual with diabetes (age 20–79 years), are in the appendix (pp 53–61).

When using GBD data as an alternative source for prevalence and mortality estimates, the global economic burden of diabetes declines to US$1·06 trillion or 1·5% of world GDP. This reduction is mainly driven by a decline in indirect costs (US$253·21 billion using GBD data *vs* $454·81 billion using IDF data) by contrast with much smaller changes for direct costs (US$ 811·35 billion *vs* $856·95 billion). A key reason for this difference is the substantially lower mortality estimates in most countries when comparing GBD data with those provided by the IDF. Detailed cost estimates by country are in the appendix (pp 62–70).

We further investigated how the results changed when labour market assumptions were derived from a meta-analysis rather than based on the selection of highly ranked studies (appendix pp 71–74). The global burden of diabetes was nearly identical to the main analysis when using this alternative approach (US$1·29 trillion or 1·8% of global GDP).

Discussion

Our analysis showed a substantial global burden of diabetes, reaching 1·8% of world GDP, with 34·7% of this burden attributable to indirect costs. Notably, North America is most affected both in terms of absolute burden and percentage of GDP, but total costs are large relative to GDP in all world regions.

This study extends previous direct cost estimates from the IDF by providing validation for age group-specific, sex-specific, and location-specific health expenditure estimates and by allowing cost ratios between people with diabetes and people without diabetes to vary across countries, age groups, and sexes, as well as between rural and urban areas.[9] To our knowledge, this study is the first of its type to explicitly distinguish between diagnosed and undiagnosed diabetes when estimating direct costs. As a result, the estimates provided in this study differ from those presented in the 2015 IDF Diabetes Atlas.[9] These differences are most salient in LMICs, to which we applied substantially higher cost ratios than those used in the IDF calculations: for example, we estimated per-patient costs of diabetes (defined as direct costs divided by the number of people with diabetes) in China to be about 3 times as high as those provided in the IDF Diabetes Atlas (US$1291·25 *vs* $466·00). Similarly, we found direct costs of US$3327·25 per patient in Brazil—substantially higher than the IDF estimate for this country (US$1527·40). Furthermore, expressed in terms of international dollars and deflated to the year 2014, our estimate for the global direct economic burden of diabetes substantially exceeds that of the NCD Risk Factor Collaboration, at INT$1267·70 billion versus $825 billion. This difference can be explained by the use of different data sources and methods. Notably, we derived direct costs using a top-down approach similar to that of the IDF Diabetes Atlas, whereas the NCD Risk Factor Collaboration used country-level per capita cost estimates from a systematic review.[10]

Our indirect cost estimates suggest that not only direct health expenditure but also missed production opportunities due to diabetes pose an enormous economic burden for the world economy: these missed production opportunities amount to 0·6% of world GDP. Therefore a large potential payoff exists for societies when resources are invested into the reduction of indirect costs.

The methodology used in this article for calculating indirect costs might overstate the economic burden by also estimating indirect costs for the unemployed. Alternative methods such as the friction-cost approach are more conservative;[25] however, the approach used in this article was chosen because only estimating indirect costs for employed people with diabetes would have the disadvantage that, holding all other factors equal, increasing unemployment would result in reduced economic burden of diabetes, making it difficult to accurately track changes in indirect costs over time. Therefore, we think it is more reasonable to base the estimation of indirect costs on a human-capital approach and to interpret the economic burden as potential costs in the presence of high unemployment rates.

An important limitation of our study is the lack of reliable prevalence and mortality estimates for a number of LMICs because a large proportion of the estimates provided by the IDF are based on extrapolations rather than original data.[9] Similarly, detailed country-level estimates are scarce for both cost ratios used for the calculation of direct costs and labour market effects of diabetes, making it necessary to derive assumptions for a diverse range of different countries from a small number of studies. Country-level comparisons, especially for LMICs, should therefore be interpreted with caution.

Furthermore, presenteeism estimates in this article are subject to the limitation that none of the assessed studies used a direct measure of productivity. Wage differentials used as a proxy for productivity in LMICs might at least partially be the result of discrimination. Similarly, self-assessed productivity could be a flawed measure of presenteeism because people with diabetes might understate true productivity losses to avoid stigmatisation.

More research is needed on the effect of undiagnosed diabetes on the labour market because, especially in countries with very limited access to health care, people with undiagnosed diabetes might differ substantially from those covered by existing studies, potentially facing a higher risk of complications. Finally, identification of causal labour market effects is challenging, in view of the number of important comorbidities of diabetes, such as obesity, or unobserved confounders. Although the selection criteria applied in the literature review underlying this study accounted for self-selection when possible, the estimated total costs of diabetes might nevertheless overlap in part with the economic burden of obesity or other conditions causing diabetes.

Our study contributes to the literature about the growing global economic burden of diabetes. We show that although direct costs of illness are certainly an important driver of the overall costs, the contribution of indirect costs is also important. Across world regions, however, the share of indirect costs varies widely, ranging from about one fifth to almost three fifths of total economic burden. This variation probably reflects not only different epidemic patterns but also the trade-off between direct and indirect costs that is implicit in health systems investments in the diabetes response. Increasing spending on diabetes prevention and treatment—ie, direct costs—might reduce the indirect costs of the disease. As a result, the total economic burden of diabetes would decrease, as long as the investments in the diabetes response are less costly than the economic consequences they help to avoid. The exact dynamics of this trade-off are unclear, however, and further research is needed to explicitly model the net effect of diabetes-related investments.

Contributors

The authors jointly conceived the study. CB, EH, VS, and SV conceptualised the study and developed the analytical strategy. CB, EH, and VS did the literature review and procured the data. CB wrote the first draft of the paper and did the statistical analysis. All authors contributed to the interpretation of the results and writing.

Declaration of interests

We declare no competing interests.

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