Availability and affordability of essential medicines for diabetes across high-income, middle-income, and low-income countries: a prospective epidemiological study

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Summary

Background Data are scarce on the availability and affordability of essential medicines for diabetes. Our aim was to examine the availability and affordability of metformin, sulfonylureas, and insulin across multiple regions of the world and explore the effect of these on medicine use.

Methods In the Prospective Urban Rural Epidemiology (PURE) study, participants aged 35–70 years (n=156 625) were recruited from 110 803 households, in 604 communities and 22 countries; availability (presence of any dose of medication in the pharmacy on the day of audit) and medicine cost data were collected from pharmacies with the Environmental Profile of a Community's Health audit tool. Our primary analysis was to describe the availability and affordability of metformin and insulin and also commonly used and prescribed combinations of two medicines for diabetes management (two oral drugs, metformin plus a sulphonylurea [either glibenclamide (also known as glyburide) or gliclazide] and one oral drug plus insulin [metformin plus insulin]). Medicines were defined as affordable if the cost of medicines was less than 20% of capacity-to-pay (the household income minus food expenditure). Our analyses included data collected in pharmacies and data from representative samples of households. Data on availability were ascertained during the pharmacy audit, as were data on cost of medications. These cost data were used to estimate the cost of a month's supply of essential medicines for diabetes. We estimated affordability of medicines using income data from household surveys.

Findings Metformin was available in 113 (100%) of 113 pharmacies from high-income countries, 112 (88·2%) of 127 pharmacies in upper-middle-income countries, 179 (86·1%) of 208 pharmacies in lower-middle-income countries, 44 (64·7%) of 68 pharmacies in low-income countries (excluding India), and 88 (100%) of 88 pharmacies in India. Insulin was available in 106 (93·8%) pharmacies in high-income countries, 51 (40·2%) pharmacies in upper-middle-income countries, 61 (29·3%) pharmacies in lower-middle-income countries, seven (10·3%) pharmacies in lower-income countries, and 67 (76·1%) of 88 pharmacies in India. We estimated 0·7% of households in high-income countries and 26·9% of households in low-income countries could not afford metformin and 2·8% of households in high-income countries and 63·0% of households in low-income countries could not afford insulin. Among the 13 569 (8·6% of PURE participants) that reported a diagnosis of diabetes, 1222 (74·0%) participants reported diabetes medicine use in high-income countries compared with 143 (29·6%) participants in low-income countries. In multilevel models, availability and affordability were significantly associated with use of diabetes medicines.

Interpretation Availability and affordability of essential diabetes medicines are poor in low-income and middle-income countries. Awareness of these global differences might importantly drive change in access for patients with diabetes.

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Introduction

The global burden of incident and prevalent diabetes and diabetes-related morbidity and mortality are increasing.[1] Most people with diabetes remain unidentified, untreated, or inadequately treated, particularly in low-income and middle-income countries (LMICs)[2] despite the availability of simple diagnostic tests and cheap medicines. The problem is a large and growing one especially for LMICs where most of the world's patients with diabetes reside.[3] The WHO framework for health systems states that a well functioning health system ensures equitable access to essential medical products, vaccines, and technologies of

Research in context

Evidence before this study

We searched PubMed and reference lists of identified papers for papers on access, availability, and affordability of diabetes medicines from inception to June 25, 2018, with no language restrictions. We were particularly interested in information available from low-income and middle-income countries (LMICs). We identified several papers that reported on availability or affordability, or both, of diabetes medicines from single countries or regions, including a number from LMICs. We identified a few papers that examined this issue across multiple countries, but most of these papers accessed data from secondary data sources, did not involve direct data collection, and did not relate this data to use of diabetes medicines.

Added value of this study

This report provides a global perspective on the availability and affordability of essential medicines for diabetes, including comparative data from LMICs. The data used in this study were collected directly from individuals and communities, unlike other methods that collect data from key informants, secondary data sources, and policy and health system documents. Direct data collection from communities and individuals provides information on the downstream implementation of policies and more comprehensive information about the patient experience. Our analyses use data collected at baseline from 156 625 participants in 604 communities and 22 countries. An estimated 61% of the global total number of people with diabetes reside in these 22 countries. We found that the availability and affordability of essential medicines for diabetes is poor in some low-income countries, both in terms of poor availability on pharmacy shelves and prohibitive costs for people on average incomes. Availability and affordability of insulin was particularly poor and the disparity between oral hypoglycaemics and insulin was several times greater in low-income countries than in high-income countries. For example, metformin was available in 100% and insulin in 94% of pharmacies audited in communities from high-income countries, whereas metformin was available in 65% and insulin in 10% of pharmacies in low-income countries. Also, about 0·7% of households with patients with diabetes could not afford metformin in high-income countries; this proportion was 26·9% of households in low-income countries. For insulin, the divide between high-income and low-income countries was greater, with 2·8% of households not able to afford insulin in high-income countries compared with 63·0% of households in low-income countries.

Implications of all the available evidence

The poor availability and affordability of essential diabetes medicines in many communities, especially those from LMICs, is a substantial driver of lower use of these medicines. Access to medicines is recognised by WHO as part of the right to health. Although several countries have programmes to provide subsidised medicines, the data presented here show universal access is still a distant prospect and that government and industry really are not doing enough to ensure the availability and affordability of these essential medicines to people that need them. These data also underwrite the importance of having strong monitoring systems to track the progress towards universal access to essential medicines.

assured quality, safety, efficacy, and cost-effectiveness, and their scientifically sound and cost-effective use. To achieve such objectives, WHO also state that information is needed on prices, supply, distribution systems, and rational use.[4] Data is scarce on the availability and affordability of diabetes medicines, particularly from LMICs. Data from selected countries hint towards a poor availability of insulin,[5–8] and reviews have called for greater attention to the availability and affordability of essential medicines for diabetes (especially insulin), a discussion of possible barriers, and a need for a global perspective.[9]

Most people (80%) with type 2 diabetes reside in urban environments, but despite the availability of essential medicines in some areas, access to these medicines is not guaranteed in many LMICs. Previous studies have highlighted the very large gaps in the availability and affordability of essential medicines for chronic diseases in LMICs and the need to monitor them.[10–13] In 2007, a survey[14] of availability of 32 medicines to treat cardiovascular disease, diabetes, chronic respiratory disease, and glaucoma in six LMICs found less than 7·5% of these medicines were available in the public sector, and the cost of a 1-month course of intermediate-acting insulin ranged from 2·8 days of wages in Brazil to 19·6 days of wages in Malawi. Availability and affordability of these medicines might affect their use. Several countries have brought in schemes to subsidise the cost of diabetes medicines, but the penetration of these programmes is uncertain. Better data are needed from individuals, communities, and large populations ascertained with uniform methods across populations to better quantify the problems of availability and affordability of diabetes medicines and to inform the development of interventions to tackle this issue.

The aim of our analyses was to examine the availability and affordability of essential medicines for diabetes (metformin, sulfonylureas, insulin) across different countries and regions and to explore the effect of availability and affordability on use of these medicines.

Methods

Study design and sampling

For the current analyses we used data collected in pharmacies as part of a community audit and data collected from representative samples of households and adults aged 35–70 years. Data on availability was therefore ascertained during the pharmacy audit, as were data on

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cost of medications. These cost data were used to estimate the cost of a month's supply of essential medicines for diabetes. We estimated affordability of medicines using income data from household surveys.

The current study was done within the framework of the Prospective Urban Rural Epidemiology (PURE) study,[15] a multicountry prospective cohort study involving 22 countries for which data are currently available: four high-income countries (Canada, Saudi Arabia, Sweden, and United Arab Emirates); eight upper-middle-income countries (Argentina, Brazil, Chile, Malaysia, Poland, South Africa, Turkey, and Russia); five lower-middle-income countries (China, Colombia, Iran, occupied Palestinian territory, and Philippines); and five low-income countries (Bangladesh, India, Pakistan, Tanzania, and Zimbabwe). Economic classification is based on a country's classification at study commencement according to World Bank data from 2006.[16] Ethics committees at each centre approved the protocol and all participants provided written informed consent.[7]

The PURE study has been described previously,[17] but in brief its original objective was to document and follow variations in community and individual determinants of cardiovascular and other chronic diseases with a particular focus on low-income and middle-income regions where few data exist. The sampling was both purposive and representative, with selection of countries with local infrastructure able to implement the study protocols, selection of communities from urban and rural settings within a country, urban sampling to select high, middle, and lower socioeconomic settings, and individual (adults aged 35–70 years) sampling to be representative of the community sampled.[17,18] Household and individual sampling was designed to achieve a representative sample of that community of adults; however, to achieve this goal some customisation of sampling framework by centre was required. For example, in rural India and China, door-to-door visits were the usual way that representative samples were achieved, but in high-income countries census lists, phone book lists, or similar were used to approach households by phone. Among the households initially approached at baseline, 78% of the individuals eligible participated in the main study.[15] Although the community sampling was not nationally representative, previous analyses[18] of the PURE cohort have shown that characteristics and health conditions of participating individuals are similar to available representative data from the countries concerned. Data collection is ongoing in the PURE study, but for our analyses we included data from countries recruited between 2001 and 2017 and communities within the country were recruited during the same time period (appendix).

	Communities	Households	Participants	People with known diabetes*
Total	604	110 803	156 625	13 569 (8·7%)
High-income countries	113	12 900	17 154	1651 (9·6%)
United Arab Emirates	3	1062	1498	390 (26·0%)
Sweden	23	2934	3920	119 (3·0%)
Canada	69	7962	10 242	784 (7·7%)
Saudi Arabia	18	942	1494	358 (24·0%)
Upper-middle-income countries	127	29 695	40 560	4230 (10·4%)
South Africa	6	2432	2860	179 (6·3%)
Brazil	14	4525	6075	533 (8·8%)
Chile	5	2417	3567	377 (10·6%)
Argentina	20	5319	7490	555 (7·4%)
Poland	4	1467	1951	142 (7·3%)
Malaysia	29	9664	12 870	1788 (13·9%)
Turkey	38	2669	4221	505 (12·0%)
Russia	11	1202	1526	151 (9·9%)
Lower-middle-income countries	208	43 459	62 582	4233 (6·8%)
China	93	28 824	43 155	2311 (5·4%)
Columbia	55	5320	6892	447 (6·5%)
Iran	20	4099	6013	615 (10·2%)
Occupied Palestinian territory	35	1541	1548	326 (21·1%)
Philippines	5	3675	4974	534 (10·7%)
Low-income countries	68	5998	7870	483 (6·1%)
Zimbabwe	3	1002	1214	58 (4·8%)
Bangladesh	55	2003	2924	176 (6·0%)
Pakistan	4	1064	1735	165 (9·5%)
Tanzania	6	1929	1997	84 (4·2%)
India	88	18 751	28 459	2972 (10·4%)

Data are n or n (%). *Known diabetes: self-reported or on drugs to lower blood glucose concentration.

Table 1: **Number of communities, households, and participants with diabetes**

Data collection

Baseline data collection included information on participants' health, risk factors, treatments, and clinical measurements and information on their family and households. Participants were asked if they had been diagnosed with diabetes, if they were taking medications regularly for diabetes, and to list all their medications consumed at least once a week for the past month.

Covariates include sociodemographic data collected from individuals and households (age, gender, urban or rural, marital status, education, occupation, total household members, monthly household income, monthly expenditure on food, health insurance), co-morbidities (cardiovascular diseases, smoking status, alcohol use), and BMI.

Data were collected from 604 communities (four high-income, 13 middle-income, and five low-income countries) with the Environmental Profile of a Community's Health (EPOCH) instrument. This instrument was designed specifically for use in the PURE study and its development and validation have been reported previously.[19,20] EPOCH community assessments were only done in communities with at least 30 PURE participants (90% of PURE communities). The EPOCH instrument collected information on the availability and cost of medicines from a local community pharmacy.

Pharmacies were selected as those which were closest to the central point of the community's identified central business district or local shopping area. If no pharmacies were located within a 1 km walking distance, researchers were instructed to search for the nearest pharmacy located up to 20 km from the central starting point. At the pharmacy, data on availability and cost of a prespecified list of medications were collected—these medicines were mainly selected from the WHO Essential Medicines list.[21] Our analyses include the diabetes medications of a daily dose of metformin 1000 mg, gliclazide 80 mg, glibenclamide 5 mg, and insulin 50 IU/mL.

Definitions and outcomes

Our primary analysis was to describe the availability and affordability of metformin and insulin and also of commonly used and prescribed combinations of two medicines for diabetes management: two oral drugs (metformin plus a sulphonylurea [either glibenclamide (also known as glyburide) or gliclazide]) and one oral drug plus insulin (metformin plus insulin).

Our secondary analysis was to examine the association of availability and affordability with use of these medicines by patients with known diabetes. Known diabetes was defined if a participant reported "yes" to the question of a medical diagnosis of diabetes or was on diabetes medications.

We defined availability as the presence of medicines for diabetes at any dose in the pharmacy on the day of the survey. We defined medicines to be affordable when the total monthly costs at standard doses and recommended frequencies were less than 20% of the household capacity-to-pay. This cost is expressed as the total monthly cost of the medicines (eg, cost of 1-month's supply of metformin at 1000 mg daily) as a proportion of the monthly household capacity-to-pay. If a household had two or more people with diabetes, we multiplied the cost of the diabetes medicines by the number of people with diabetes for that household.

Household capacity-to-pay was defined as the household income remaining after basic subsistence needs have been met. Subsistence needs were defined as the household monthly income spent on food. This approach is consistent with the scientific literature on catastrophic health expenditures.[10] We also examined affordability with respect to the combined costs of the medicines (eg, metformin 1000 mg plus insulin 50 IU/mL). We defined these combined costs as affordable if they comprised less than 20% of a household's capacity-to-pay. The arbitrary threshold of 20% was based on previous literature and approaches to assessing catastrophic health expenditure, and was the same approach we have used in previous papers.[22,23,24]

We have provided estimates of the proportion of households containing participants with known diabetes who might not be able to afford medicines for diabetes.

Statistical analysis

In our descriptive analyses we report the countries included, number of communities, and households and participants with diabetes across different income groups and regions. We calculated the mean and median costs of all medicines for lowering blood glucose concentration and present data according to country income group, urban or rural setting, and country. We present results as the median (IQR) of all participants in high-income countries, upper-middle-income countries, lower-middle-income countries, and low-income countries. We present data from India separately from other low-income countries because, in our previous research on availability and affordability of cardiovascular medicines,[10] India was seen to be very different from all of the other low-income countries, and observations might relate to the size of its domestic pharmaceutical industry as well as to particular policies, such as selective process controls.[25]

We analysed the proportion of participants with a diagnosis of diabetes who report medication use by income quintiles and tertiles within country groups.

We converted all data on income and medicine costs from local currency to US dollars adjusted for purchasing power parity (PPP) and standardised to 2015 prices using World Bank inflation rates. PPP is defined as the number of units of a country's currency required to buy the same amounts of goods and services in the domestic market as US$1 would buy in the USA.[24]

We analysed the association between the availability and affordability of medicines for diabetes with the use of these medicines using multilevel mixed-effects logistic regression models, accounting for clustering at the country, community, and household levels. We adjusted models for possible confounders, including age, sex,

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See **Online** for appendix

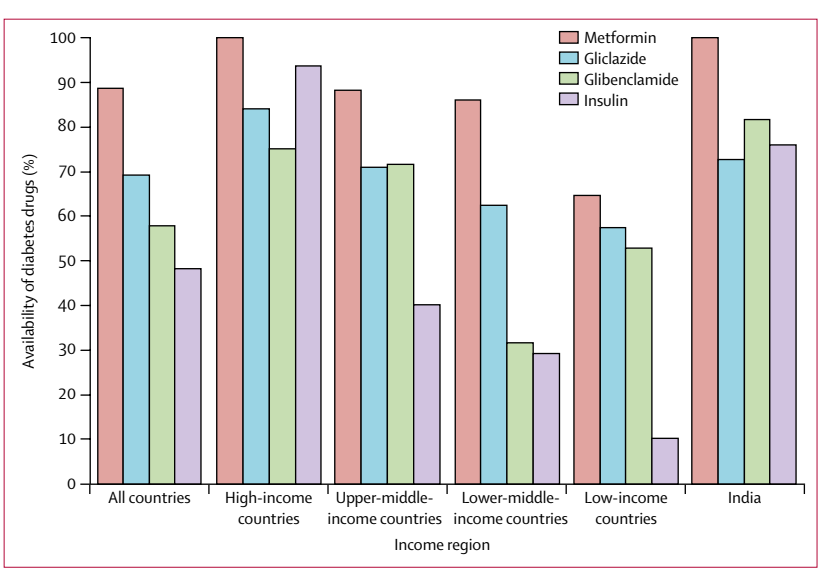

Figure 1: **Availability of metformin, glibenclamide, gliclazide, and insulin in the PURE communities by income region and in India**
PURE=Prospective Urban Rural Epidemiology.

	n	Capacity-to-pay, US$	n	Costs of metformin, US$	n	Costs of gliclazide, US$	n	Costs of glibenclamide, US$	n	Costs of insulin, US$
All	96 864	199·9 (68·4–533·5)	99 983	5·2 (3·5–8·8)	74 214	8·9 (6·4–10·6)	76 573	3·8 (1·3–7·1)	60 888	33·1 (12·7–47·3)
High-income countries	10 865	2456·7 (1613·1–3583·0)	12 900	9·9 (4·8–14·4)	9896	10·6 (8·6–14·5)	11 831	7·1 (5·7–16·2)	12 793	39·1 (23·3–42·9)
Upper-middle-income countries	23 437	288·8 (117·3–681·7)	26 361	6·4 (4·9–11·1)	22 148	10·6 (9·6–15·3)	24 471	6·0 (2·6–11·1)	17 745	83·1 (39·6–111·3)
Lower-middle-income countries	41 006	170·4 (72·1–336·5)	37 966	3·1 (0·5–8·1)	22 881	6·0 (1·7–8·3)	23 741	0·7 (0·2–3·6)	12 313	16·6 (1·0–51·6)
Low-income countries*	4759	41·5 (8·0–92·0)	4005	5·9 (4·3–6·7)	2526	8·2 (7·2–8·9)	3039	0·7 (0·4–4·2)	1732	33·6 (18·5–37·1)
India	16 797	74·0 (20·3–262·0)	18 751	4·3 (4·1–5·2)	16 763	7·9 (7·2–9·2)	13 491	3·8 (1·64–4·1)	16 305	16·3 (12·7–41·0)

Excluding India, costs are median (IQR) adjusted for purchasing power parity. Costs were calculated at household level and were adjusted for inflation and purchasing power parity. Assuming 30 days per month, daily dose of metformin 1000 mg, gliclazide 80 mg, glibenclamide 5 mg, insulin 50 IU/mL. Zimbabwe was not included in this analysis because data for purchasing power parity were unavailable.
Fewer households are in the current analysis as we were unable to calculate the capacity-to-pay for some households due to missing values in either household income, the price for medication, or dose.
*Excluding India.

Table 2: **Monthly household capacity-to-pay and costs of each of the essential medicines for diabetes in different countries**

education, smoking status, number of household members, urban and rural setting, and years since diabetes diagnosis, and odds ratios (OR) and 95% CIs are reported. A p value of <0·05 was considered significant for regression models.

When the medication was available in the community but the costs were missing, we imputed the costs from the neighbouring communities. We c onsidered all other missing values as missing and we did no imputations. We used SAS 9.4 (SAS, Cary, NC, USA) for data analyses.

Role of the funding source

The study's sponsors had no role in study design, data collection, analysis, interpretation, or write-up. Lead and corresponding authors had full access to all study data and were responsible for submitting the manuscript. All authors contributed to the research, commented on drafts, and agreed to submit the final draft for publication.

Results

The PURE study is an ongoing prospective cohort study that started in 2001, with most countries starting recruitment in 2005–06 and, for this paper, we included data up to 2017. The analyses included 604 communities, 110 803 households, and data from 156 625 participants, of which 13 569 (8·7%) reported a diagnosis of diabetes (table 1; appendix). In most of the 22 countries, medications were partially subsidised particularly in hospitals (appendix).

Metformin was the most widely available diabetes medicine, available in 536 (88·7%) of 604 community pharmacies surveyed: 113 (100%) of 113 pharmacies in high-income countries, 112 (88·2%) of 127 pharmacies in upper-middle-income countries, 179 (86·1%) of 208 pharmacies in lower-middle-income countries, and 44 (64·7%) of 68 pharmacies in low-income countries, excluding India where it was available in 88 (100%) of 88 community pharmacies surveyed (figure 1). Glibenclamide and gliclazide had medium availability and insulin was the least available. Glibenclamide was available in 418 (69·3%) of 604 pharmacies overall: 95 (84·1%) in high-income countries, 90 (70·9%) in upper-middle-income countries, 130 (62·5%) in lower-middle-income countries, 39 (57·4%) in low-income countries, and 64 (72·7%) in India. Gliclazide was available in 350 (57·9%) of 604 pharmacies overall: 85 (75·2%) in high-income countries, 91 (71·7%) in upper-middle-income countries, 66 (31·7%) in lower-middle-income countries, 36 (52·9%) in low-income countries, and 72 (81·8%) in India. Insulin was available in 292 (48·3%) of 604 pharmacies overall: 106 (93·8%) in high-income countries, 51 (40·2%) in upper-middle-income countries, 61 (29·3%) in lower-middle-income countries, seven (10·3%) in low-income countries, and 67 (76·1%) in India. As expected, communities in India had greater availability of all diabetes medicines than did otherwise similar countries.

The median monthly cost of metformin was US$5·2 (IQR 3·5–8·8), ranging from $4·3 (4·1–5·2) in India to $9·9 (4·4–14·4) in high-income countries (PPP adjusted; table 2), and differences between urban and rural costs were minimal (appendix). Country comparisons are included in the appendix. The similar costs of medicines across regions indicates that affordability is mainly driven by the relative differences in income and not the differences in actual cost of the medicine. Metformin was the most affordable diabetes medicine, with the monthly cost as a median of 2·3% (IQR 0·6–10·0) of the capacity-to-pay overall, ranging from 0·4% (0·2–0·8) in high-income countries, 2·3% (0·9–7·4) in upper-middle-income countries, 2·1% (0·4–7·9) in lower-middle-income countries, 13·4% (5·4–60·0) in low-income countries, and 8·8% (2·4–43·1) in India (figure 2). Conversely, insulin was less affordable, with the monthly cost as a median of 10·0% (IQR 1·7–50·1) of the capacity-to-pay overall, ranging from 1·2% (0·6–2·0) in high-income countries, 16·8% (4·9–59·1) in upper-middle-income countries, 5·5% (0·8–27·4) in lower-middle-income countries, 65·8% (19·5–244·9) in low-income countries, and 39·7% (11·1–148·7) in India (figure 2).

We estimated that 13·8% of households containing participants with known diabetes might not be able to afford a monthly supply of metformin (defined as >20% of the threshold of their capacity-to-pay). This proportion ranged from 0·7% in high-income countries, 9·6% in upper-middle-income countries, 13·8% in lower-middle-income countries, 26·9% in low-income countries, and 24·6% in India (figure 3). Insulin was less affordable—overall an estimated 36·7% of households with participants with diabetes would be unable to afford insulin ranging from 2·8% in high-income countries, 47·1% in upper-middle-income countries, 34·7% in lower-middle-income countries, 63·0% in low-income countries, and 51·4% in India (figure 3A, B). Unaffordability was greatest in rural low-income countries (eg, 48·4% for metformin) and rural India (52·0% for metformin). An estimated 36·4% of participants from the lowest tertile of income in low-income settings and 52·6% of participants in India were unable to afford metformin.

Among 13 569 participants with known diabetes, 6239 (46·0%) reported using oral hypoglycaemic agents (OHA), 803 (5·9%) insulin, 341 (2·5%) both OHA and insulin, and 6868 (50·6%) reported no medication use (table 3). The proportion of participants with known diabetes who reported taking any diabetes medications was highest in high-income countries (74·0%) and was lower in upper-middle-income countries (50·1%), lower-middle-income countries (56·0%), low-income countries (29·6%), and India (28·5%). The proportion reporting no diabetes medication use was 26·0% in high-income countries, 49·9% in upper-middle-income countries, 44·0% in lower-middle-income countries, 70·4% in low-income countries, and 71·5% in India (table 3), and an urban–rural gradient was observed particularly in lower-middle-income and low-income countries (appendix). Among participants with known diabetes from the poorest tertile of the population in India, 88·7% were not on any medicines for diabetes (table 3). Similar but slightly more pronounced trends in use of medicines were shown when stratified by education (appendix).

After accounting for covariates, including economic region and wealth, availability and affordability were significantly associated with use of OHA, and availability was associated with use of insulin and OHA plus insulin (table 4). The association of availability with use of diabetes medicines was minimally attenuated by adjusting for covariates. The association of affordability was attenuated after adjusting for age, gender, country income level, and location, though it remained a significant predictor of use of OHAs after full adjustments but not for insulin.

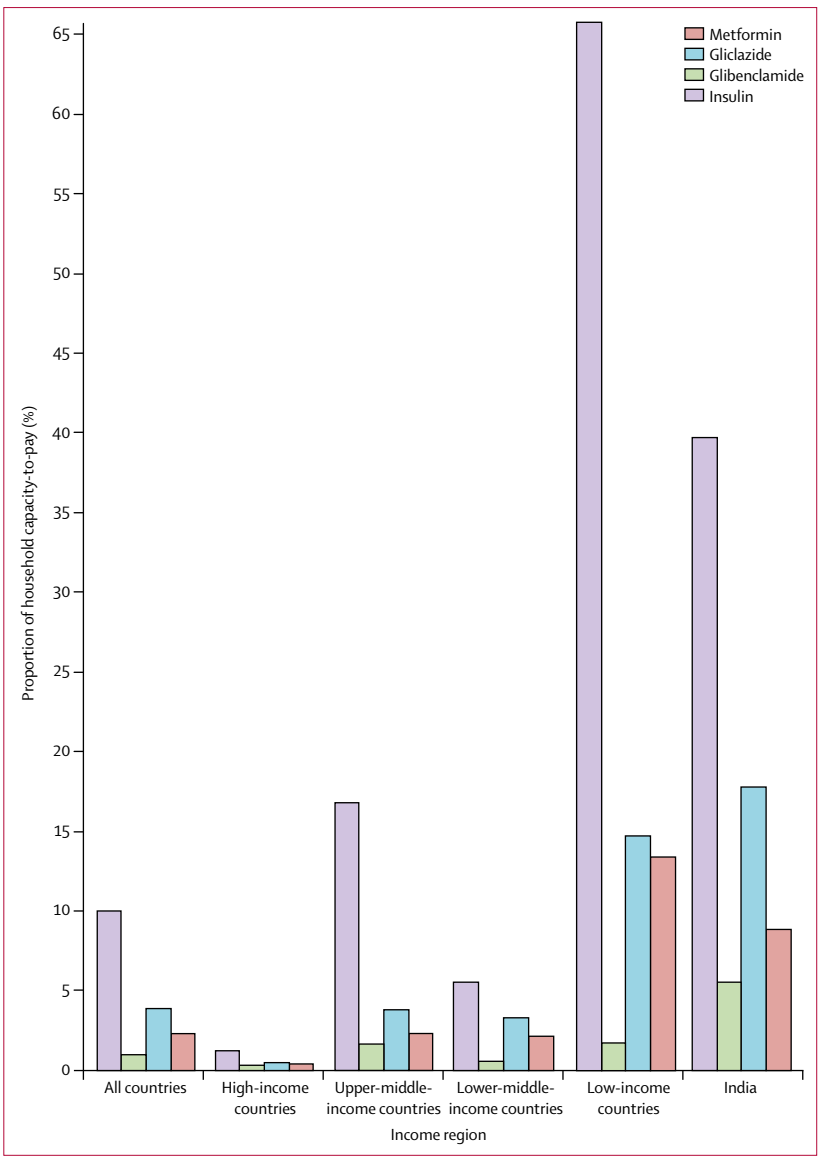

Figure 2: **Median monthly cost of each of the essential medicines for diabetes as a proportion of a household's capacity-to-pay**

Capacity-to-pay is defined as monthly household income minus monthly household food expenditure. If capacity-to-pay is ≤0, then we assumed that each medication costs 100% of household capacity-to-pay. For IQR values see appendix.

Discussion

According to the International Diabetes Federation Diabetes Atlas (8th edition),[26] an estimated 425 million people have diabetes globally; the estimated number of people with diabetes in the 22 countries studied here is 261 million. We found that the availability of diabetes medicines, and particularly the availability of insulin, is poor. Overall insulin was available in about half of the pharmacies that OHAs were available in, and this gap was driven by the larger gap in the difference in availability of insulin versus OHAs in low-income countries versus the minimal gap in high-income countries. Many people with diabetes in this study were also estimated to be unable to afford diabetes medicines, especially insulin. The cost of insulin was multiple times higher than the cost of OHAs, and the difference in cost between insulin and OHAs was much wider in low-income countries, hence the reason why more than half

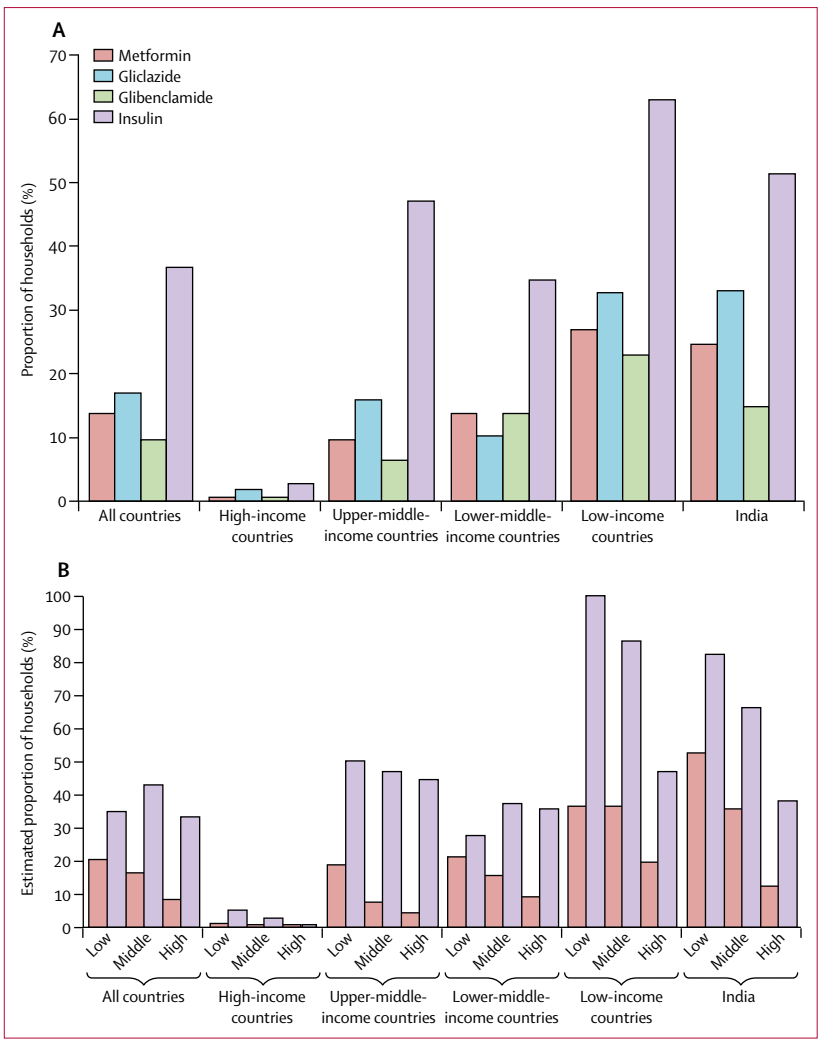

Figure 3: **Proportion of households with participants with known diabetes who might not be able to afford metformin, glibenclamide, gliclazide, and insulin (A) and estimated proportion who might not be able to afford metformin or insulin by tertiles of household income (B)**

Affordability was defined as the cost that will not exceed 20% of monthly capacity-to-pay (monthly expenditure minus cost of food). The capacity-to-pay is adjusted by the number of members of a household. Missing values were not imputed and were mainly due to non-availability of medication and also missing values in household income, monthly food expenditure, medication dose, or medication availability. 18·8% of known patients with diabetes had a component of the information missing for the calculation of metformin affordability, and 48·2% of known patients with diabetes had a component of the data missing for affordability of insulin. The analysis accounted for the number of patients with diabetes in a household. With 2 or more people with diabetes in the household, the cost of the diabetes medicines was multiplied by the number of people with diabetes for that household.

of people with diabetes in low-income countries were probably unable to afford insulin.

Both availability and affordability were significant determinants of use of OHAs and availability was a significant determinant of use of insulin among participants with diabetes, even after accounting for individual characteristics such as education, comorbidities, age, and gender. Hence, availability and affordability are likely to be important in the explanation of why fewer than half of people with diabetes are using essential medicines for diabetes and why the use of OHAs among participants with diabetes ranges from about three quarters in high-income countries to about a quarter in low-income countries.

We extend previous research in 35 LMICs that found a mean availability for the lowest price antidiabetes generics of approximately 49·5% in the public sector compared with 65·2% in the private sector[27] by examining affordability by different households with differing incomes and the association with use. These findings also help to understand why many people with type 1 diabetes in low-income countries do not survive, even though they have a disease that is eminently treatable.[28] Insulin availability and affordability has been highlighted in the medical literature as a global issue affecting low-income populations in high-income countries as well as populations of LMICs. In LMICs, studies have shown that insulin was available in 56% of facilities in the public sector and only 39% of facilities in the private sector[29]—the complexity of the supply chain is likely to be an important contributor to this difference.[30] The role of health coverage in protecting the poor is apparent. In India, with its large pharmaceutical industry, availability of medicines is much better than in similar countries, yet over half of those in the lowest income tertile would be unable to afford metformin, whereas the figure is only 10% for those in the highest income tertile.

Although we have focused on antidiabetic medicines, they represent only part of the problem. Most patients with diabetes will need additional medicines, including those that lower blood pressure and statins to manage the patients' overall cardiovascular risk, and will incur additional costs from diabetes-related comorbidities. Our studies from PURE also show poor availability and affordability of cardiovascular medicines for hypertension and the secondary prevention of cardiovascular disease. Many chronic health conditions coexist, hence the availability and affordability issues would probably be magnified.[10,24] A case-control study[31] of 1182 participants in Bangladesh showed that having diabetes was associated with twice as many days of inpatient treatment, 1·3 times more outpatient visits, and 9·7 times more medications being used, imposing huge financial burdens. Consideration of the costs of blood glucose concentration monitoring, regular assessment of kidney function, and eye examinations is also necessary. Taken together, current recommendations for the management of diabetes are not affordable by a very high proportion of people in LMICs.

WHO and many other bodies have recognised that access to essential medicines is part of the right to health. Access to medicinal products and technologies as part of the right to health is the first country indicator of strategic objective 11 (improved access, quality and use of medical products and technologies) of the WHO Medium Term Strategic Plan for 2008–13.[32] Access to essential medicines globally still has a long way to go because the availability and affordability of medicines in many regions reported here is so poor. This situation requires a multifaceted

response addressing the entire range of health systems building blocks, which create numerous barriers to effective care.[33] For medicines the cost of insulin needs to be addressed, the manufacture of which is dominated by three large multinational companies with intellectual property issues surrounding the newer delivery devices acting as a barrier to lower cost supplies.[9,34,35] A further problem relates to distribution and storage in many countries, although the use of evaporative systems based on clay pots is offering a partial solution in some countries.[36] Equally important, although often overlooked, is the cost of test strips, reflecting a business model in

	Not using any diabetes medicines	Oral hypoglycaemic agents	Insulin	Oral hypoglycaemic agents plus insulin
Overall	6868/13 569 (50·6%)	6239 (46·0%)	803 (5·9%)	341 (2·5%)
Lowest wealth	1725/3361 (51·3%)	1525 (45·4%)	205 (6·1%)	94 (2·8%)
Middle wealth	2203/4252 (51·8%)	1917 (45·1%)	231 (5·4%)	99 (2·3%)
Highest wealth	2741/5644 (48·6%)	2695 (47·7%)	353 (6·3%)	145 (2·6%)
High-income countries	429/1651 (26·0%)	1115 (67·5%)	212 (12·8%)	105 (6·4%)
Lowest wealth	155/592 (26·2%)	401 (67·7%)	78 (13·2%)	42 (7·1%)
Middle wealth	129/476 (27·1%)	317 (66·6%)	58 (12·2%)	28 (5·9%)
Highest wealth	141/577 (24·4%)	396 (68·6%)	75 (13·0%)	35 (6·1%)
Upper-middle-income countries	2112/4230 (49·9%)	1995 (47·2%)	242 (5·7%)	119 (2·8%)
Lowest wealth	640/ 1303 (49·1%)	627 (48·1%)	73 (5·6%)	37 (2·8%)
Middle wealth	738/1453 (50·8%)	672 (46·2%)	85 (5·8%)	42 (2·9%)
Highest wealth	699/1418 (49·3%)	677 (47·7%)	82 (5·8%)	40 (2·8%)
Lower-middle-income countries	1861/4233 (44·0%)	2211 (52·2%)	256 (6·0%)	95 (2·2%)
Lowest wealth	561/1045 (53·7%)	450 (43·1%)	48 (4·6%)	14 (1·3%)
Middle wealth	561/1355 (41·4%)	741 (54·7%)	79 (5·8%)	26 (1·9%)
Highest wealth	701/1776 (39·5%)	1003 (56·5%)	127 (7·2%)	55 (3·1%)
Low-income countries*	340/483 (70·4%)	135 (28·0%)	10 (2·1%)	2 (0·4%)
Lowest wealth	55/67 (82·1%)	12 (17·9%)	NA	NA
Middle wealth	106/156 (67·9%)	48 (30·8%)	3 (1·9%)	1 (0·6%)
Highest wealth	176/254 (69·3%)	73 (28·7%)	6 (2·4%)	1 (0·4%)
India	2126/ 2972 (71·5%)	783 (26·3%)	83 (2·8%)	20 (0·7%)
Lowest wealth	314/354 (88·7%)	35 (9·9%)	6 (1·7%)	1 (0·3%)
Middle wealth	669/812 (82·4%)	139 (17·1%)	6 (0·7%)	2 (0·2%)
Highest wealth	1024/ 1619 (63·2%)	546 (33·7%)	63 (3·9%)	14 (0·9%)

Data are n/N (%) or n (%). Lowest wealth, middle wealth, and highest wealth refer to tertiles of wealth within each category. NA=not available. *Excluding India.

Table 3: **Participants with a self-reported diagnosis of diabetes who reported medicine use across tertiles of income in a range of country incomes**

	Unadjusted	Adjusted for age, gender	Adjusted for age, gender, country income, and location	Additionally adjusted for education	Additionally adjusted for smoking status	Additionally adjusted for number of years since diagnosis of diabetes	Additionally adjusted for household members	Additionally adjusted for availability of the medication
Availability of diabetic medication								
Oral hypoglycaemic agents	1·94 (1·50–2·52)	1·92 (1·48–2·49)	1·97 (1·51–2·59)	1·98 (1·51–2·60)	1·98 (1·51–2·59)	1·95 (1·49–2·56)	1·96 (1·49–2·57)	..
Insulin	1·48 (1·27–1·73)	1·49 (1·28–1·73)	1·49 (1·28–1·73)	1·35 (1·14–1·60)	1·34 (1·13–1·58)	1·35 (1·13–1·62)	1·35 (1·13–1·61)	..
Oral hypoglycaemic agents plus insulin	1·72 (1·36–2·18)	1·73 (1·37–2·20)	1·53 (1·18–1·99)	1·54 (1·19–2·00)	1·51 (1·16–1·96)	1·54 (1·18–2·02)	1·54 (1·18–2·02)	..
Affordability of diabetic medication								
Oral hypoglycaemic agents	1·81 (1·55–2·11)	1·82 (1·56–2·12)	1·26 (1·07–1·48)	1·23 (1·04–1·45)	1·21 (1·02–1·43)	1·24 (1·05–1·46)	1·24 (1·05–1·46)	1·24 (1·05–1·46)
Insulin	1·79 (1·35–2·37)	1·82 (1·37–2·42)	1·30 (0·96–1·78)	1·28 (0·94–1·75)	1·30 (0·97–1·74)	1·27 (0·92–1·76)	1·26 (0·91–1·74)	1·26 (0·91–1·74)
Oral hypoglycaemic agents plus insulin	1·93 (1·11–3·36)	1·95 (1·12–3·40)	1·12 (0·63–2·00)	1·11 (0·62–1·98)	1·13 (0·62–2·06)	1·12 (0·62–2·02)	1·12 (0·62–2·03)	1·12 (0·62–2·03)

Data are odds ratios (95% CIs), all of which were calculated on the same sample of participants, after excluding all the missing values. Known diabetes: self-reported diabetes or on drugs to lower blood glucose concentration. Affordability was defined as the cost that will not exceed 20% of monthly capacity-to-pay, considering that some households have more than one person with diabetes. Cost was multiplied by the number of people with diabetes for that house.

Table 4: **Associations between availability and affordability and use of essential medicines for diabetes in participants aware of their diabetes (ie, known diabetes)**

which manufacturers make profits from sales of strips typically designed for use with only one type of glucometer and the high rates of hyperglycaemia that this business model is likely to be contributing to.[37] Several studies[38,39] have also shown the importance of adequate numbers of trained staff, appropriate patient-centred models of care, evidence-based guidelines, and social support for patients. Ensuring robust systems exist to monitor the situation of availability and affordability to medicines is also an important way of improving access to medicines.[40] Some information is available from selected countries that improving affordability improves use. In Iran, some improvement occurred in diabetes medicine consumption with good affordability of diabetes medicines, but use of diabetes medicines was still suboptimal with authors indicating that this was due to other barriers to medicines use, including under-diagnosis and inappropriate management.[41]

This study has some limitations. We only collected information on essential medicines for diabetes and do not have costs of the newer drugs. The cost of new medications, such as pioglitazone, acarbose, meglitinides, dipeptidyl peptidase 4 inhibitors, and sodium-glucose cotransporter-2 inhibitors, is likely to be prohibitive in many countries. The data collection protocol did not distinguish between type 1 and 2 diabetes, though most of the PURE participants with diabetes are likely to have type 2 diabetes.[15] The self-reported diagnosis of diabetes might depict different groups in high-income versus low-income countries—ie, with more access to the medical system, more people with mild diabetes might be diagnosed in high-income countries, yet in low-income countries the diagnosis might have been made in only people who were highly symptomatic.

We did not examine or account for the cost of other medicines that patients might have been taking, which might have an effect on our estimates of affordability. We collected information from selected community pharmacies; in some countries, public hospital departments or clinics provide medications for free and we could not account for the presence of such clinics in our analyses. Medicines, such as insulin, might only be available from hospitals in some communities. We collected data from one retail pharmacy per community at a single point in time and this study includes data captured in multiple communities over a 7-year period; prices and medication availability might change between pharmacies and across different times and we do not have data to support the pharmacies surveyed being necessarily representative of the general price in that community or country.

We only calculated affordability in communities where the medicines were available and we could thus obtain medicine cost, hence our estimates of affordability are likely to be worse than we have reported because the calculation did not account for additional opportunity costs—ie, if patients had to travel to obtain medicines. We defined affordability on an arbitrary 20% of the household capacity-to-pay. This cutoff is widely used in such studies of income but is somewhat arbitrary and perceived as a high bar by many. Thus, the cutoff might underestimate the level of affordability. Affordability was calculated for a 1-month supply of metformin 1000 mg, but the dose of OHAs or insulin will vary and again might cause our findings to underestimate affordability. The study involves a selected number of countries and communities, and the strengths, limitations, and representativeness of the sampling method of the PURE study have been previously discussed.[42]

An increasing body of evidence supports the fact that the availability and affordability of chronic disease medications is related to the use of these treatments. WHO has set a voluntary target of 80% availability and 50% use of affordable essential medicines to treat non-communicable diseases in the public and private sectors by 2025.[11] The analyses presented here suggest that this target is only being consistently met in high-income countries for OHAs and insulin. These data draw further attention to the need for governments to implement strategies to make essential medications for cardiovascular disease and diabetes more widely available and affordable to achieve the WHO target.

Contributors

All authors participated in designing the study, generating hypotheses, interpreting the data, and critically reviewing the report. CKC wrote the first draft of the paper. SY is the principal investigator of the PURE study. CR and WH analysed the data and had full access to all data. DC and MM contributed to development of the Environmental Profile of a Community's Health instruments and commented on the paper. All other authors contributed through commenting on data interpretation in the manuscript and in being local investigators involved in operations at the study sites.

Declaration of interests

We declare no competing interests.

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