Availability and affordability of blood pressure-lowering medicines and the effect on blood pressure control in high-income, middle-income, and low-income countries: an analysis of the PURE study data

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Summary

Background Hypertension is considered the most important risk factor for cardiovascular diseases, but its control is poor worldwide. We aimed to assess the availability and affordability of blood pressure-lowering medicines, and the association with use of these medicines and blood pressure control in countries at varying levels of economic development.

Methods We analysed the availability, costs, and affordability of blood pressure-lowering medicines with data recorded from 626 communities in 20 countries participating in the Prospective Urban Rural Epidemiological (PURE) study. Medicines were considered available if they were present in the local pharmacy when surveyed, and affordable if their combined cost was less than 20% of the households' capacity to pay. We related information about availability and affordability to use of these medicines and blood pressure control with multilevel mixed-effects logistic regression models, and compared results for high-income, upper-middle-income, lower-middle-income, and low-income countries. Data for India are presented separately because it has a large generic pharmaceutical industry and a higher availability of medicines than other countries at the same economic level.

Findings The availability of two or more classes of blood pressure-lowering drugs was lower in low-income and middle-income countries (except for India) than in high-income countries. The proportion of communities with four drug classes available was 94% in high-income countries (108 of 115 communities), 76% in India (68 of 90), 71% in upper-middle-income countries (90 of 126), 47% in lower-middle-income countries (107 of 227), and 13% in low-income countries (nine of 68). The proportion of households unable to afford two blood pressure-lowering medicines was 31% in low-income countries (1069 of 3479 households), 9% in middle-income countries (5602 of 65 471), and less than 1% in high-income countries (44 of 10 880). Participants with known hypertension in communities that had all four drug classes available were more likely to use at least one blood pressure-lowering medicine (adjusted odds ratio [OR] 2·23, 95% CI 1·59–3·12); p<0·0001), combination therapy (1·53, 1·13–2·07; p=0·054), and have their blood pressure controlled (2·06, 1·69–2·50; p<0·0001) than were those in communities where blood pressure-lowering medicines were not available. Participants with known hypertension from households able to afford four blood pressure-lowering drug classes were more likely to use at least one blood pressure-lowering medicine (adjusted OR 1·42, 95% CI 1·25–1·62; p<0·0001), combination therapy (1·26, 1·08–1·47; p=0·0038), and have their blood pressure controlled (1·13, 1·00–1·28; p=0·0562) than were those unable to afford the medicines.

Interpretation A large proportion of communities in low-income and middle-income countries do not have access to more than one blood pressure-lowering medicine and, when available, they are often not affordable. These factors are associated with poor blood pressure control. Ensuring access to affordable blood pressure-lowering medicines is essential for control of hypertension in low-income and middle-income countries.

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See Online for appendix

Research in context

Evidence before this study

We searched PubMed on March 1, 2017, with no language or date restrictions, for articles on the availability and affordability of blood pressure-lowering medicines in countries at various stages of economic development. Our search terms included "availability", "affordability", "blood pressure lowering drugs or medicines", and "antihypertensive". We excluded studies that did not include a measure of affordability.

We identified four studies that assessed the availability and affordability of different medicines, including blood pressure-lowering medicines. Only two studies provided a description of the availability of blood pressure-lowering medicines; one for six low-income and middle-income countries and the other in 36 countries of high, middle, and low income. Both studies estimated affordability using the number of days' wages needed to pay the lowest paid, unskilled government worker to purchase a 1 month supply of the medicines. This approach to estimation of affordability does not allow for interhousehold comparisons. Neither study assessed the association between availability and affordability and use of blood pressure-lowering medicines or blood pressure control.

Added value of this study

Our study describes the availability and affordability of commonly used blood pressure-lowering medicines, as well as combination therapy using multiple therapies (eg, antidiabetic drug and a statin), in countries of high, upper-middle, lower-middle, and low income. Furthermore, to our knowledge, our study is the first to examine the association between availability and affordability of blood pressure-lowering medicines and use of these medicines and blood pressure control.

Our findings show that a large proportion of communities in low-income and middle-income countries do not have access to more than one blood pressure-lowering medicine and, when available, they are often not affordable. Our results indicate that multiple blood pressure-lowering drug classes need to be available and affordable to improve hypertension control.

Implications of all the available evidence

Improvement of the availability and affordability of blood pressure-lowering medicines is essential to improve control of hypertension, particularly in low-income and middle-income countries, where 80% of the cardiovascular disease (CVD) burden exists. Our results are therefore directly relevant to public policies targeted at reducing the global burden of CVD, particularly the goal of a 25% reduction in premature CVD deaths by 2025, and the even more ambitious targets in the Sustainable Development Goals.

However, improvement of hypertension control at the population level will also require strategies beyond improvement of access to low-cost blood pressure-lowering medicines. Further research is warranted into contextual and cultural barriers, factors associated with the health-care system, and personal preferences.

Introduction

Hypertension affects 1 billion people worldwide and is a major risk factor for cardiovascular disease (CVD).[1] Although blood pressure-lowering medicines reduce CVD events, renal failure, and mortality,[2] their use is suboptimal and blood pressure control is poor.[3]

Most individuals with hypertension require at least two blood pressure-lowering medicines to adequately control their blood pressure.[4] Diuretics, angiotensin-converting enzyme (ACE) inhibitors, calcium-channel blockers, and β blockers all reduce CVD[5] and are the most commonly used blood pressure-lowering medicines. However, use of combination therapy is low, particularly in low-income and middle-income countries.[3] Moreover, although blood pressure-lowering medicines are listed in the WHO Model list of Essential Medicines,[6] little is known about their availability and affordability and the relation to hypertension control. About one in four people with hypertension also have diabetes,[7,8] and trials indicate that statins double the benefit of blood pressure-lowering drug therapy by further reducing CVD events.[9,10] Therefore, optimal management would include a combination of at least two blood pressure-lowering medicines, a statin, and added antidiabetic drug (when needed).

Here we describe the availability and affordability of the four common classes of blood pressure-lowering medicines, statins, and metformin in 20 countries at varying levels of economic development, and examine the association with use of these medicines and blood pressure control.

Methods

Study design and participants

The Prospective Urban Rural Epidemiological (PURE) study recruited 181 162 individuals aged 35–70 years. We analysed the first phase of the study, which included 158 247 individuals from 110 677 households living in 626 communities in 20 countries, for whom a full set of data required for this analysis are available.[11–14] Participant enrolment began in January, 2003; most communities were recruited between January, 2005, and December, 2009 and the process is continuing as new countries join. The countries and communities were selected purposively, with the aim of obtaining a socioeconomically and culturally diverse study sample. Within participating communities, the goal was to enrol a representative sample of households while also ensuring feasibility of long-term follow-up.[11] Although not designed to be nationally representative, we have previously shown that the characteristics and death rates of the enrolled participants were similar to their national populations.[12] A comprehensive description of study design, sampling, recruitment practices, and

participant characteristics has been previously published and is available in the appendix.[11–14]

We categorised countries into four groups on the basis of the World Bank classification at the time the PURE study started (2006). The countries include four high-income countries (Sweden, United Arab Emirates, Canada, and Saudi Arabia), seven upper-middle-income countries (Poland, Turkey, Chile, Malaysia, South Africa, Argentina, and Brazil), four lower-middle-income countries (Colombia, Iran, China, and the occupied Palestinian territory), and five low-income countries (Pakistan, Bangladesh, Zimbabwe, Tanzania, and India). Data for India are presented separately because it has a large generic pharmaceutical industry and previous work has shown that availability of medicines is higher in India than in other countries at the same economic level.[15]

Ethics committees at each participating centre approved the protocol[11,12,14] and all participants provided written informed consent.[11]

Data collection

Availability and prices of blood pressure-lowering medicines were collected by research staff from one pharmacy in each community with the Environmental Profile of a Community's Health (EPOCH) instrument—a reliable and validated tool developed for measuring aspects of the environment that influence cardiovascular risk factors.[15–17] Briefly, communities with at least 30 PURE participants were included in EPOCH, which has two parts: direct observation of the physical and commercial environment and a survey of perceptions of the environment by those living in it.

In the direct observation component, the pharmacy closest to the prespecified central location was visited by research staff to obtain information about the availability of medicines and their prices between Jan 1, 2009, and April 19, 2016. We collected information about the availability and price of three widely used ACE inhibitors (captopril, enalapril, and ramipril), two β blockers (esatenolol [atenolol] and metoprolol), one calcium-channel blocker (amlodipine), and one diuretic (hydrochlorothiazide). Many patients with hypertension also have cardiovascular disease, diabetes, or other indications for statins.[18] We therefore present the availability and price of two widely used statins (atorvastatin and simvastatin) and metformin (commonly used for diabetes).

In the community survey component, trained interviewers collected data from all households and individuals participating in the PURE study using standardised questionnaires. Information about monthly household income and food expenditure was obtained from a knowledgeable member in each household. Names of all medicines taken at least once per week in the past month by all PURE participants were recorded by direct inspection of medicines or prescriptions. Medicines were then coded in the central project office and categorised by drug classes.

Trained research assistants measured sitting blood pressure twice after a 5 min rest period for all PURE participants by use of a standardised procedure with a digital blood pressure measuring device (Omron HEM-757; Omron, Tokyo, Japan). Individuals were deemed hypertensive if they reported having a hypertension diagnosis and receiving blood pressure-lowering treatments, or if the average of two systolic blood pressures was at least 140 mm Hg or the average of two diastolic blood pressures was at least 90 mm Hg. Individuals with known hypertension were the proportion of patients aware of their hypertension diagnosis. Of these individuals, those whose systolic and diastolic blood pressures were less than 140/90 mm Hg were considered to have controlled hypertension.

Definition of availability and affordability

Blood pressure-lowering medicines were considered available if they were physically present in the local pharmacy surveyed on the day of data collection.[15] Total monthly costs of the medicines were estimated with standard doses and recommended frequencies (appendix). The medicines were deemed affordable if the total monthly cost of the lowest cost medicines was less than 20% of households' monthly capacity to pay, consistent with the literature on catastrophic health expenditure[19] and our previous work.[15] We estimated capacity to pay by subtracting basic subsistence needs, which we defined as household expenditure on food, from monthly household income. In a sensitivity analysis, we also subtracted household expenditure on housing (defined as expenditures on rent, mortgage, and utilities), transportation (defined as expenditures on public transit fares and personal vehicle), and food from monthly household income in a subset of PURE participants for whom such data were currently available.

We present equivalised capacity to pay, for which capacity-to-pay estimates were divided by the square root of the household size to allow for interhousehold comparisons. Household incomes, expenditures, and medicine costs were converted from their local currencies into 2010 US$, (after adjustment for inflation[20]), by use of purchasing power parities from the World Bank.[21] We also did sensitivity analyses for thresholds ranging from 10% to 40% of households' capacity to pay (appendix). In our 2016 study,[15] we showed that household capacity to pay is strongly correlated with a household wealth index as well as capacity-to-pay values from the WHO World Health Survey, which confirms the robustness of our measure of capacity to pay (appendix). As discussed in that study, we assumed that participants purchased their medicines from pharmacies rather than non-pharmacy retailers.[15] Furthermore, we assumed that households pay the full cost of the medicines—ie, the costs of the medicines are not partly or fully subsidised by governments or other third parties (eg, health insurance).

Statistical analysis

We estimated the association between availability and affordability and use of blood pressure-lowering medicines and blood pressure control in separate models for participants with known hypertension. Our analysis used multilevel, mixed-effects logistic regression models, accounting for clustering at the community level (appendix). All statistical models were adjusted for the potential confounders of age, sex, education level, years since hypertension diagnosis, and urban versus rural geographical location. For the affordability analysis, we excluded households that did not report information about income or food expenditure, because the absence of this information precluded us from estimating capacity to pay. We report adjusted and unadjusted associations as odds ratios (ORs) with 95% CIs. All statistical analyses were done with Stata (version 14).

Role of the funding source

The funders and sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

564 (90%) of 626 communities had at least one blood pressure-lowering medicine available in the local pharmacy surveyed (figure 1). The 62 (10%) communities with no available blood pressure-lowering medicines were mainly located in low-income and lower-middle-income countries (figure 1). Most communities in high-income countries (108 [94%] of 115) and India (68 [76%] of 90) had all four drug classes available (figure 1). Availability of all four drug classes was lowest in low-income countries (nine [13%] of 68), excluding India (figure 1). We also noted urban and rural differences in the availability of blood pressure-lowering drugs; these differences were most marked in lower-middle-income and low-income countries. For example, 64 (57%) of 112 urban communities in lower-middle-income countries had at least four drug classes compared with 43 (37%) of 115 rural communities (appendix).

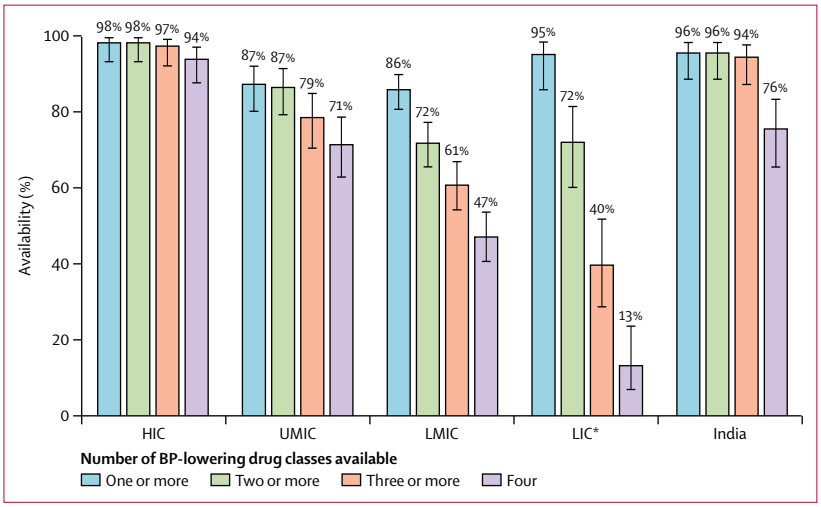


Figure 1: **Availability of BP-lowering medicines in 626 PURE communities**
Error bars represent 95% CIs. BP=blood pressure. HIC=high-income countries. UMIC=upper-middle-income countries. LMIC=lower-middle-income countries. LIC=low-income countries. *Excluding India.

The most common drug class varied across regions; β blockers and calcium-channel blockers were the most commonly available drug classes in countries of upper-middle income (110 [87%] and 104 [83%] of 126 communities, respectively) and low income (57 [84%] and 47 [69%] of 68 communities, respectively), whereas ACE inhibitors and β blockers were the most commonly available drugs in countries of lower-middle income (182 [80%] and 156 [69%] of 227 communities, respectively; appendix). In each group of countries, diuretics were the least expensive drug class, followed by β blockers (data not shown).

We excluded 13 589 households from the affordability analysis that did not report information about income or food expenditure. Individuals in households that reported household income and food expenditure were similar to those in households that did not (appendix). Moreover, imputing the mean value within each community for individuals with missing information about household income and food expenditure did not alter the associations.

Median monthly capacity to pay was highest in high-income countries and lowest in low-income countries (table 1). Household capacity to pay was lower in rural communities across all country groups, with substantial differences in upper-middle-income (urban US$416 *vs* rural $183) and low-income countries ($78 *vs* $32), including India ($167 *vs* $26; appendix).

The monthly costs of the lowest, lowest two, and lowest three cost blood pressure-lowering medicines were highest in absolute terms in high-income countries but, in view of the much higher incomes in high-income countries, this constituted a lower proportion of household capacity to pay than in low-income countries (<1% in high-income countries compared with 1–11% in low-income countries for one to three blood pressure-lowering medicines; table 1). The monthly costs of the lowest cost drugs in upper-middle-income countries were similar to high-income countries; however, they accounted for a larger fraction of household capacity to pay in upper-middle-income countries (table 1). This observation is largely driven by differences in household capacity to pay between high-income and upper-middle-income countries; median capacity to pay in high-income communities was roughly nine times that in upper-middle-income countries (table 1). The difference in capacity to pay between high-income and upper-middle-income communities was further exacerbated once we took into account household expenditure on housing and transportation in the sensitivity analysis (a roughly

12 times difference). Communities in lower-middle-income countries had some of the lowest monthly costs for blood pressure-lowering medicines (table 1). However, when the monthly cost of metformin or the lowest cost statin was added to the cost of the two lowest cost drugs, the median monthly costs increased considerably in lower-middle-income and low-income countries (table 1).

Few households (44 [<1%] of 10 880) in high-income countries were unable to afford the two lowest cost blood pressure-lowering medicines (figure 2), even after taking into account the costs of housing and transportation. The proportion of households unable to afford the two lowest cost drugs was highest in low-income countries (1069 [31%] of 3479), including India (6139 [36%] of 16 955), which had the highest proportion of households unable to afford hypertension medicines (figure 2). Adding the cost of metformin or the lowest cost statin to the monthly cost of the two lowest cost blood pressure-lowering medicines increased the proportion of households unable to afford the medicines, but the increase was most marked in lower-middle-income and low-income countries (figure 2). For example, in low-income countries, 1069 (31%) of 3479 households were unable to afford the monthly cost of the two lowest cost blood pressure-lowering medicines; adding metformin increased the proportion to 39% (n=1366), adding the lowest cost statin increased the proportion to 75% (n=2277), and including both metformin and the lowest cost statin increased the proportion to 80% (n=2441). By contrast, almost all households in high-income countries were able to afford the cost of the two lowest cost drugs and metformin (10 809 [99%] of 10 880), the two lowest cost drugs and the lowest cost statin (10 638 [98%]), or all drugs (10 579 [97%]; figure 2).

In our sensitivity analysis, in which we revised our estimates of household capacity to pay by excluding monthly household expenditure on housing, transportation, and food, from monthly household income in a subset of participants (n=23 888), the proportion of households unable to afford the lowest cost blood pressure-lowering medicines increased in all countries, categorised according to economic development; however, the pattern was similar to that in the main analysis (appendix).

Our subsequent analysis was restricted to the subset of participants with known hypertension (n=33 045; table 2), of whom 19 481 (59%) used at least one blood pressure-lowering medicine, 8697 (26%) used ACE inhibitors or angiotensin II receptor blockers, 6221 (19%) used diuretics, 5028 (15%) used β blockers, and 5146 (16%) used calcium-channel blockers. Use of combination therapy was relatively low, with only 7879 (24%) participants taking more than one blood pressure-lowering medicine (6160 [19%] of 33 045 were taking two drugs, 1489 [5%] were taking three drugs, and 212 [<1%] were taking four drugs). Table 2 shows the baseline characteristics of the population with hypertension.

	Number of communities	Number of Households	Capacity-to-pay (US$)	Capacity-to-pay (housing and transportation costs incorporated; US$)*	Monthly cost of the lowest cost antihypertensive drug (US$)	Monthly cost of the two lowest cost antihypertensive drugs (US$)	Monthly cost of the two lowest cost antihypertensive drugs plus metformin (US$)	Monthly cost of the two lowest cost antihypertensive drugs plus lowest cost statin (US$)†	Monthly cost of the two lowest cost antihypertensive drugs plus metformin and lowest cost statin (US$)†	Monthly cost of the three lowest cost antihypertensive drugs (US$)†
High-income countries	90	10 880	2545 (1617–3585)	2056 (1195–2976)	4 (2–9)	17 (3–25)	26 (7–35)	44 (5–70)	52 (9–84)	33 (6–49)
Upper-middle-income countries	125	25 235	290 (115–671)	171 (49–365)	4 (2–6)	12 (8–14)	18 (11–20)	21 (18–35)	27 (23–43)	22 (20–24)
Lower-middle-income countries	225	40 236	173 (75–338)	137 (45–277)	0·09 (0·09–0·9)	0·33 (0·2–3)	4 (0·5–10)	8 (3–18)	8 (5–24)	1 (0·4–8)
Low-income countries‡	68	3782	52 (21–104)	22 (0·2–63)	0·7 (0·7–1)	2 (2–2)	6 (4–7)	24 (20–24)	24 (24–28)	6 (5–6)
India	89	16 955	61 (18–218)	41 (0–155)	3 (2–4)	9 (6–10)	12 (10–13)	30 (24–38)	33 (27–42)	15 (12–16)
Overall	597	97 088	204 (70–535)	169 (42–462)	2 (0·4–4)	5 (2–11)	10 (4–18)	21 (8–33)	26 (9–39)	11 (4–22)

Data are median (IQR), unless otherwise stated. Monthly capacity to pay and costs are in 2010 US$. Categorisation of economic level for each country is based on the 2006 World Bank classification. Drugs include angiotensin-converting enzyme inhibitors, β blockers, calcium-channel blockers, and diuretics. *Capacity-to-pay estimates based on a subset of PURE participants (n=23 888) with data available for housing and transportation costs, which were incorporated into the capacity-to-pay calculation. †Tanzania excluded because only two classes of blood pressure-lowering medicines were available and statins were unavailable in the communities studied, resulting in 588 communities. ‡Capacity-to-pay and medicine costs exclude India, medicine costs also exclude Zimbabwe because purchasing power parity values were unavailable.

Table 1: **Monthly household capacity to pay and costs of blood pressure-lowering medicines**

Participants with known hypertension living in communities that had all four blood pressure-lowering drug classes available were more likely to use at least one blood pressure-lowering medicine, combination therapy, or have their blood pressure controlled, than were those living in a community where blood pressure-lowering medicines were not available (figure 3). Similarly, participants with known hypertension who were able to afford up to four blood pressure-lowering medicines were more likely to use at least one blood pressure-lowering medicine, combination therapy, or have their blood pressure controlled than were the group not able to afford these medicines (figure 3).

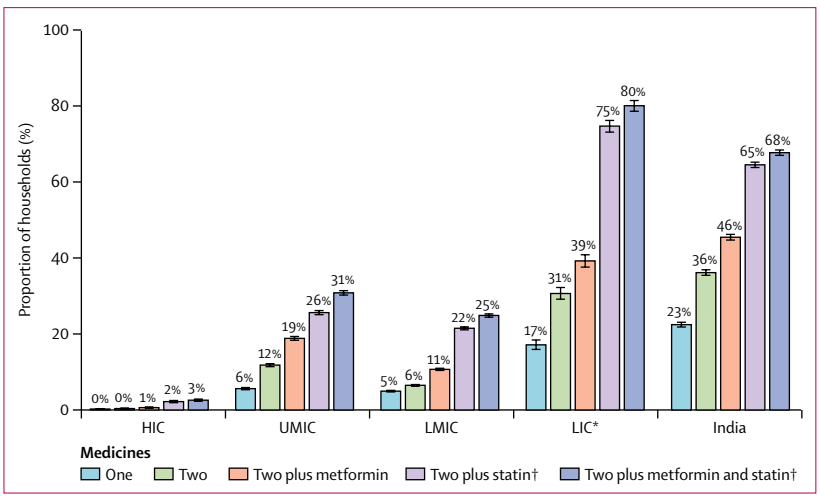


Figure 2: **Proportion of households that could not afford blood pressure-lowering medicines and combination therapy (n=98 785)**
With a 20% capacity-to-pay threshold. Error bars represent 95% CIs. HIC=high-income countries. UMIC=upper-middle-income countries. LMIC=lower-middle-income countries. LIC=low-income countries. *Excluding India and Zimbabwe. †Tanzania excluded because statins were unavailable.

Discussion

Blood pressure-lowering medicines are listed as WHO essential medicines, but their access remains a global concern. Although at least one blood pressure-lowering medicine was available in 90% of the pharmacies surveyed, the availability of two or more classes of drug therapy was lower in low-income and lower-middle-income countries than in high-income countries (and India). Our findings with respect to affordability parallel the patterns observed for availability, with one important exception: even though blood pressure-lowering medicines were widely available in India, they were potentially unaffordable to many households because of low capacity to pay and higher medicine prices than in other low-income countries.

Among participants aware of their hypertension diagnosis, we recorded strong positive associations between availability and affordability of blood pressure-lowering medicines and use of these medicines (including combination therapy) and blood pressure control. Our results indicate that multiple blood pressure-lowering drug classes need to be available and affordable to improve hypertension control. This finding could reflect the needs of different patients or the preferences of different physicians for prescribing specific blood pressure-lowering drugs. Physicians might prefer to prescribe different classes of blood pressure-lowering drugs to patients under the assumption that patients differ in their

	High-income countries		Upper-middle-income countries		Lower-middle-income countries		Low-income countries	
	Men	Women	Men	Women	Men	Women	Men	Women
N	1809	1828	4297	7567	4691	7143	2175	3535
Age (years)	58 (8·3)	57 (8·1)	57 (8·8)	56 (8·9)	56 (9·3)	56 (8·6)	55 (9·7)	53 (9·9)
Education level								
Low*	277 (15%)	448 (25%)	2273 (53%)	4801 (63%)	1558 (33%)	3864 (54%)	481 (22%)	1839 (52%)
Secondary	537 (30%)	591 (32%)	1252 (29%)	1983 (26%)	2084 (44%)	2525 (35%)	1008 (46%)	1339 (38%)
University	991 (55%)	789 (43%)	767 (18%)	776 (10%)	1040 (22%)	741 (10%)	681 (31%)	342 (10%)
Time since hypertension diagnosis (years)								
1–5	665 (37%)	602 (33%)	1726 (40%)	2920 (39%)	1784 (38%)	2690 (38%)	935 (43%)	1470 (42%)
>5	905 (50%)	956 (52%)	1937 (45%)	3689 (49%)	2191 (47%)	3451 (48%)	764 (35%)	1307 (37%)
Living in a rural community	514 (28%)	539 (29%)	1922 (45%)	3397 (45%)	2064 (44%)	3040 (43%)	718 (33%)	1444 (41%)
Blood pressure controlled†	633 (35%)	697 (38%)	829 (19%)	2017 (27%)	886 (19%)	1562 (22%)	548 (25%)	766 (22%)
Diagnosis of cardiovascular disease‡	341 (19%)	182 (10%)	568 (13%)	657 (9%)	1031 (22%)	1196 (17%)	259 (12%)	258 (7%)
Diagnosis of diabetes§	512 (28%)	448 (25%)	1170 (27%)	1927 (25%)	974 (21%)	1384 (19%)	736 (34%)	986 (28%)

Data are mean (SD) or n (%), unless otherwise stated. *Defined as no education, primary education only, or unknown educational level. †Defined as systolic and diastolic blood pressures of less than 140/90 mm Hg. ‡Defined as an individual with previous stroke or coronary artery disease (eg, myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary angioplasty, or angina). §Defined as self-reported or fasting blood glucose concentrations of 7 mmol/L or more.

Table 2: **Baseline characteristics of participants aware of their hypertension diagnosis (n=33 045)**

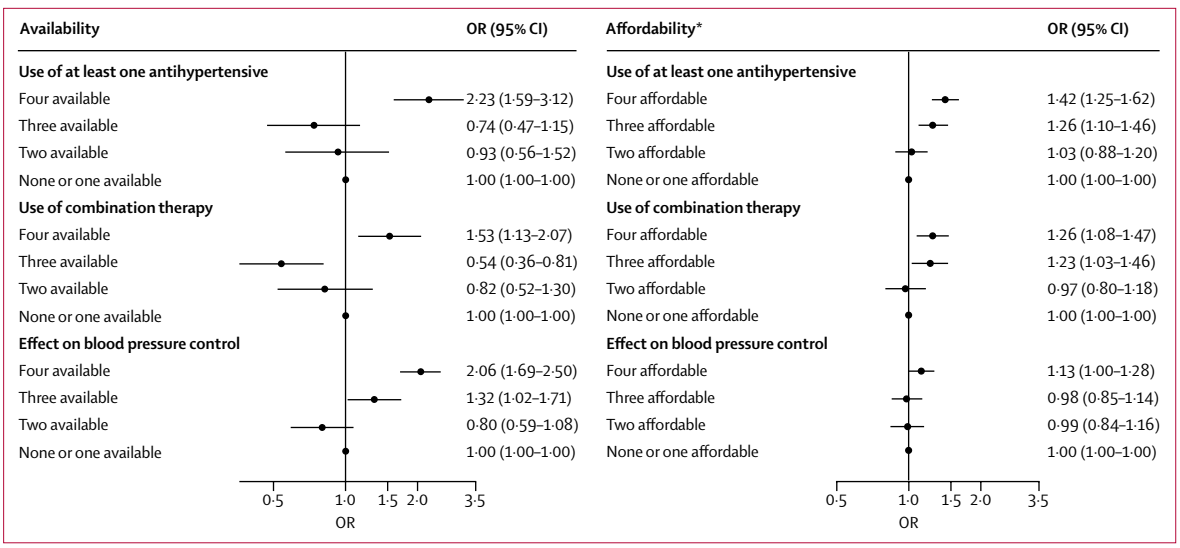


***Figure 3*: Associations between availability and affordability and use of at least one blood pressure-lowering medicine, combination therapy, and blood pressure control in participants with known hypertension (n=33 045)**

Adjusted for age, sex, education, years since hypertension diagnosis, urban versus rural location; clustered at the community level. OR=odds ratio. *Affordability analysis restricted to participants living in communities where at least one blood pressure-lowering medicine was available. In calculating affordability, we used the cost of the lowest cost medicine.

response and tolerance to different medicines. Previous studies have shown that hypertension treatment practices (eg, blood pressure threshold for initiation of drug therapy, or use of specific drugs) vary by patient characteristics, their risk, and by region, and these factors can change over time.[22] Our estimates for affordability and use of blood pressure-lowering medicines and blood pressure control are consistent with findings from studies showing that adherence to medicines declines as out-of-pocket expenditure increases, whereas improvements in insurance coverage for medicine costs and low out-of-pocket expenditure improves adherence.[23,24] These results show the importance of development of policies that seek to make multiple drug classes available and affordable, particularly in low-income and middle-income countries.

We estimate that the median monthly retail cost of the two lowest cost blood pressure-lowering medicines is roughly $4·95. This cost varies from $0·33 in lower-middle-income countries (where the medicines are subsidised by governments—eg, in the occupied Palestinian territory and Iran[25]) to $16·68 in high-income countries. Previous studies have reported costs for a multidrug regimen targeting hypertension and cardiovascular disease,[26] and costs for delivery of a hypertension management programme that includes at least one blood pressure-lowering medicine.[27] However, we obtained our medicine prices directly from the community retail pharmacies in which the PURE participants lived, and therefore represent prices members of that community would actually face, which include mark-ups along the supply chain. By contrast, medicine prices used in the costing exercises done for the multidrug regimen[26] and hypertension management programme[27] use median procurement prices obtained from the International Reference Price Index created by Management Sciences for Health for a select number of developing countries. Previous studies have shown marked differences between prices charged to patients and procurement prices.[28] Furthermore, although organisations such as Health Action International have done extensive studies into the availability and pricing of medicines in many countries,[28–30] our study is, to our knowledge, the first attempt to link such data to use of blood pressure-lowering drugs in countries of different economic levels.

Improvement of hypertension control at a population level will require strategies beyond improvement of access to low-cost blood pressure-lowering medicines.[31] For example, although costs attributed to health-care access are important barriers in low-income and lower-middle-income countries, additional barriers imposed by providers, the broader health systems in which they work (eg, access to a qualified health provider) and patient characteristics (eg, health literacy) are important factors for achievement of blood pressure control.[31] In high-income countries, the effect of availability and affordability was minimal, indicating that other factors are important for blood pressure control in these countries. Further research into contextual and cultural barriers, factors associated with the health-care system, and personal preferences have been done, with additional studies underway in PURE.[32,33] These studies will help develop a comprehensive approach to improve hypertension control globally from the current levels whereby only 13% of individuals with hypertension have controlled blood pressure. However, on the basis of our data, improvement of access to affordable blood pressure-lowering medicines in low-income and

lower-middle-income countries is likely to substantially improve rates of hypertension control in these countries.

Our study has some limitations. In the estimation of affordability, we assumed that households paid the full retail price; therefore, our findings do not take into account the role of insurance or any other form of reimbursement individuals or households might receive. However, previous studies have indicated that most pharmaceutical expenditure in low-income and lower-middle-income countries occurs in the private sector, often in the form of out-of-pocket expenditure.[34] Some patients might prioritise other expenses over the treatment of their hypertension; our measure of affordability does not take into account participant prioritisation or preferences. If medicines are more readily available from non-pharmacy vendors or in pharmacies not surveyed in our study, our estimates of availability are underestimates of true availability.

The methods we used to define hypertension and blood pressure control are standard in large epidemiological studies. Although multiple blood pressure measurements on three to five occasions would provide greater precision, this approach is not feasible in large multicountry studies involving more than 100 000 participants, and is rarely done in routine clinical practice in most settings, especially in lower-middle-income countries.

Of the new drug classes for blood pressure lowering, angiotensin II receptor blockers are used with some frequency, especially when ACE inhibitors are not tolerated. However, drugs in this class are more expensive than ACE inhibitors, as such, our estimates for affordability are unlikely to change. Furthermore, because we used cross-sectional observational data, we cannot show that the associations between availability and affordability, and medicine use and blood pressure control, are causal.

Our results are directly relevant to public policies that are targeted at reducing the global burden of CVD by improving access to essential medicines, particularly the stated goals of a 25% reduction in premature CVD deaths by 2025, and the even more ambitious targets in the Sustainable Development Goals.[35] Until key lifesaving medicines are available and affordable to most populations, hypertension control is likely to be suboptimal, especially in low-income and lower-middle-income countries. Similar conclusions can be drawn from Khatib and colleagues' 2016 report[15] with regards to improving use of proven medicines for secondary prevention. In the context of hypertension control, many patients also have diabetes, CVD, or other indications for statins. Such patients are at high risk and will benefit from combination therapy, which could include two blood pressure-lowering drugs, a statin, or metformin.[10,36] However, these drug therapy combinations are unaffordable for most people in low-income and lower-middle-income countries. For example, a combination therapy that includes the two lowest cost blood pressure-lowering medicines, the lowest cost statin, and metformin is unaffordable for 80% of households in low-income countries. Therefore, improving the outcomes of individuals with hypertension and reducing CVD requires a broader strategy that includes making other essential medicines, such as statins or glucose-lowering medicines, widely accessible and affordable.

Contributors

MWA had the primary responsibility of writing the paper and did the statistical analyses. SY conceived and initiated the PURE study, supervised its conduct and data analysis, reviewed and revised all drafts of this manuscript, and oversaw the work of MWA. MM reviewed and commented on the drafts. SR coordinated the worldwide study and reviewed and commented on manuscript drafts. All other authors coordinated the worldwide study, and reviewed and commented on drafts. All authors approved the final draft.

Declaration of interests

We declare no competing interests.

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