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Persistent low adherence to hypertension treatment in Kyrgyzstan: How can we understand the role of drug affordability?

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It is well known that cardiovascular diseases (CVD) are a growing cause of mortality and morbidity in low-and middle-income countries (LMIC). While hypertension (HTN), a leading risk factor for CVD, can be easily managed with widely available medicines, there is a huge gap in treatment for HTN in many LMIC. One such country is Kyrgyzstan, where HTN is a major public health concern and adherence to medication is low. The reasons for low adherence in Kyrgyzstan are not well understood, but some evidence suggests that HTN medicines may be unaffordable for low-income families, resulting in inequitable access to HTN treatment. With data from the 2010 Kyrgyzstan Integrated Household Survey, we estimate the prevalence and factors associated with adherence to HTN medication in Kyrgyzstan. We then investigate the hypothesis that affordability may be an important factor in adherence to HTN medication. Using the novel coarsened exact matching approach, we estimate the economic burden faced by households with at least one member with elevated blood pressure (EBP) in Kyrgyzstan and their risk of catastrophic spending on health care. We find that EBP households have significantly higher total expenditure on health, as well as on medicines, and are more likely to experience catastrophic health spending, suggesting that out-of-pocket expenditure for EBP may be prohibitively expensive for the poorest in Kyrgyzstan. Our findings also reveal a high prevalence of self-medication (i.e. purchasing and using medication without a doctor's prescription), and increased expenditure due to self-medication, among those with EBP. Our research suggests that affordability of HTN medicines may be an important factor in low adherence to treatment in Kyrgyzstan. Low affordability may be due partly to prescription of medicines that are not

reimbursable under the national drug benefit plan, but more research is needed to identify solutions to the affordability problem.

Introduction

The countries of the former Soviet Union (fSU) have the highest burden of ischemic heart disease (IHD) of any region in the world (1) yet their health systems have struggled to respond. This is especially apparent with hypertension (HTN), a leading risk factor for IHD, which often goes undetected and untreated in this region. (2) In Kyrgyzstan, a low-income former Soviet country, HTN is a particularly pressing public health concern. (3) The estimated prevalence of raised blood pressure (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or on treatment, based on a 2007 household survey), is just over 30%. (3) The most recent Global Burden of Disease Study, although based on modelled data, ranks HTN as the second-leading cause of disability-adjusted life years in the country, after dietary risk factors. (4)

The Kyrgyz government has responded by making HTN one of six priority conditions, which since 1996 have been the focus of a package of reforms that include removing official fees for primary care visits for all Kyrgyz citizens, developing and distributing HTN treatment guidelines, training health professionals in HTN management, and including HTN medicines in the subsidized Additional Drug Benefit plan, a national scheme for central purchasing and distribution of generic medicines to pharmacies. (3)

Despite these efforts, changing how people respond to HTN remains a challenge. The above-mentioned 2007 study revealed that only 27% of those with elevated blood pressure (EBP) were aware of their condition and even fewer (17% of those with EBP) were following a daily regimen of medical treatment. (3) A separate study in 2010 suggested that only 30.7% of individuals who reported having been diagnosed with HTN by a doctor were taking medication daily. (2) The authors of the 2007 study suggested that low awareness of EBP is likely a result of low utilization of primary health care, especially among men, which results in a large share of asymptomatic EBP going undiagnosed, leading them to propose two hypotheses to explain low adherence to medications. (4) First, medical practice in Kyrgyzstan may not be fully in line with guidelines, despite training efforts,

and patient engagement is weak and ineffective. Second, despite wide availability of generic medicines in the country, affordability may be a concern due to a preference among physicians and patients for branded or more costly generic drugs. From a policy perspective, it is important to understand whether inadequate medical practice or affordability drives poor adherence because the two factors require different policy responses. The former calls for further training, stronger monitoring efforts, reform of financial incentives, and effective mechanisms for patient empowerment. In contrast, the latter calls for measures to encourage use of generic drugs, market interventions and greater subsidies.

There is evidence that lends support to the affordability hypothesis as a key driver low adherence. Research from other countries in the region has identified out-of-pocket costs as a significant barrier to accessing medicines for chronic conditions. (5) In Kyrgyzstan specifically, data from repeated cross-sectional surveys between 2001 and 2007 suggest that, while health system financing reforms have succeeded in reducing out-of-pocket (OOP) payments for inpatient care and improving access to outpatient care, the financial burden faced by the poor when seeking care remains significant, especially for drugs. (6) Further research supported by the World Health Organization (WHO) on drugs for hypertension in 2013 found that a month's supply of hydrochlorothiazide (a diuretic) in Kyrgyzstan cost the equivalent of 8.3 days wages for a worker on minimum wage (28 Som or approximately \$0.60 USD per day) and 0.69 days wages for a worker making the average wage. (7) For statins (cholesterol-lowering drugs) the situation is worse, with a month's supply of atorvastatin costing 31 days wages for a minimum-wage worker and 2.58 days wages for a worker on the average wage. In contrast, in the survey on which the above-mentioned 2007 study was based, only 10% of those not taking prescribed medication in the last 24 hours cited affordability as the reason. (3) However, this could be an artefact of the wording and sequencing of the question, with its focus on the last 24 hours only, which may fail to capture the overall financial burden of out-of-pocket drug costs and its impact on adherence. In sum, empirical evidence thus far is conflicting and calls for further exploration of whether hypertension medicines are affordable in Kyrgyzstan and whether affordability is related to adherence.

In our study, we explore the affordability hypothesis in more depth. Specifically, we seek to explore i) the determinants of adherence to hypertension medicines in Kyrgyzstan, in particular household economic status, and ii) what the economic impact of drug expenditure is on households with EBP at different socio-economic levels. Our exploration of the affordability of medicines for hypertension and its role in adherence is important for the current policy discourse in Kyrgyzstan but will also be useful for other low and middle income countries where significant primary care and health financing reforms have been implemented in line with international standards, but where HTN outcomes have been slow to change.

Methods

We used data from the Kyrgyzstan Integrated Household Survey (KIHS) 2010. The KIHS combines a diary method and quarterly face-to-face interviews to record household consumption. Every 3 to 4 years, a health module is added to the first quarter interviews of the KIHS to record health care utilization and related household expenditures. Since 2007, the health module has included a small section on hypertension measurement and cardiovascular disease risk factors. The KIHS is based on a random sample of the population stratified by oblast (region) and urban/rural place of residence. The samples are representative at the national and regional levels. The survey over-samples some remote populations in rural areas to ensure power for poverty estimates so sampling weights are used in all analyses. The KIHS 2010 included 4,681 households consisting of 19,091 individuals. The total population of Kyrgyzstan is estimated at 5.548 million, with a median age of 25, a life expectancy of 69 years and a healthy life expectancy of 61 years. The leading cause of death in Kyrgyzstan is ischemic heart disease (31.7%), followed by stroke (13.8%). (8)

In KIHS 2010, each respondent over 18 years had their blood pressure measured using an electronic sphygmomanometer (Model:A&D UA-767 Plus). Blood pressure was measured once, while the participant was seated. Because the standard criteria for diagnosing HTN in surveys requires repeated blood pressure measurements over the course of several days, here we use the term EBP. (9) For the purpose of this analysis, EBP was defined as systolic blood pressure greater than or equal to 140 mmHg, or diastolic blood pressure greater than or equal to 90 mmHg, or having taken medicine for

hypertension in the last 24 hours. Blood pressure measurements were recorded for roughly 89% of eligible participants (i.e. 18 years of age or older), resulting in an 11% non-response rate for this measure. As in the 2007 survey, non-response was non-random; missing values differed by age and gender with a greater than average share of missing values among younger people and among men. Consequently, imputation was used, following the approach taken in the 2007 study (3), with values estimated from means of region (n=8), age category (18-29, 30-39, 40-49, 50-59, 60-69, 70+) and gender specific strata. This imputation technique ensured that there were values for systolic and diastolic blood pressure for everyone aged 18 years or older.

Adherence was defined as reporting having taken anti-hypertensives in the last 24 hours (among those who were aware of their condition due to doctor diagnosis). Logistic regression was used to estimate the impact of socioeconomic status on adherence, controlling for age, gender, oblast, urban/rural place of residence, marital status and insurance status (i.e. whether or not the individual was enrolled in the mandatory insurance program; 97% of survey respondents were enrolled). Socioeconomic status was defined by each household's monthly per capita consumption, divided into terciles.

Investigating the economic burden of anti-hypertensives on households in Kyrgyzstan empirically is challenging. While the KIHS provides information about blood pressure and general out-of-pocket medicine expenses, it is not possible to separate out-of-pocket payments for anti-hypertension medicines from other medicines. To overcome this challenge, we use coarsened exact matching (CEM) to match households with at least one member with EBP with households with no EBP that are similar in other characteristics that might affect drug expenditure. This matching allows us to suggest that differences in out-of-pocket health expenditure and risk of catastrophic health spending ($\geq 40\%$ of effective income (income after food spending) spent on health (10) are attributable to having a household member with EBP. The CEM method has been described in detail elsewhere, (11, 12) and used in recent research to investigate the impact of angina on household health expenditure. (5) Briefly, CEM attempts to control for the potential confounding of 'pre-treatment' covariates on the outcome of interest, by matching 'treatment' cases with 'non-treatment' cases that are approximately similar with regard to those covariates. In our case, 'treatment' cases are households containing at

least one member with elevated blood pressure (EBP) and 'non-treatment' controls are households where no-one has EBP. Relative to beginning analysis with a parametric regression model, 'pre-processing' the data using matching reduces model dependence and statistical bias. (11) Matching methods enable us to make the treatment group as similar as possible to the control group making the treatment variable closer to being independent of the background covariates.(13) CEM has an advantage over other methods of matching observational data such as propensity-score matching (PSM) and exact matching (EM) in that it doesn't require that the matched observations are balanced in terms of pre-treatment covariates as does PSM, nor does it require matched observations to be precisely similar in terms of these covariates as in EM.(5, 11, 14)

We used CEM to account for potential confounding by the following pre-treatment household characteristics: i) household size ii) socio-economic status of the household) iii) proportion of females in the household (to account for the possibility of higher health expenditure associated with older men) iv) proportion of people over the age of 60 in the household and v) proportion of children under the age of 2 in the household. After matching, we used linear regression to analyse the difference in mean total health care expenditure, mean total expenditure on medicines and mean total expenditure on self-medication associated with having at least one member with EBP in the household. We then used logistic regression to analyse the odds of catastrophic spending among EBP households, compared with non-EBP households.

Results

Descriptive results: sample characteristics, hypertension prevalence, awareness and adherence

The characteristics of our sample are described in Table 1. The sample was almost equally divided by gender, urban/rural place of residence and oblast. Those aged less than 18 years were not included in subsequent analyses of EBP.

Table 2 shows the estimated prevalence of EBP, the percentage of individuals who are aware of their condition, and the percentage of those who are aware that are adhering to hypertension medication. The crude prevalence of EBP for the whole population is 23.7%. EBP prevalence is slightly higher

among women compared to men, and as expected, in older age groups. Less than half (48.5%) of the total population of individuals who are aware of having hypertension are adhering to medical treatment, and adherence is lowest in younger age groups, especially among young men. The percentage of individuals with EBP who are aware their condition was higher in the richest income tercile (40.2%, 95% CI: 32.7,47.5) compared to the middle (31.1%, 95% CI: 25.2, 37.0) and poorest (21.4, 95%CI: 16.7, 26.0) groups.

Determinants of adherence

The results of our logistic model of adherence (among those who are aware of their HTN status) are shown in Table 3. Adjusting for possible confounders, odds of adherence to medical treatment increased significantly as socio-economic status increased. Those in the richest income tercile were 2.28 times more likely to adhere to medical treatment compared to those in the poorest tercile. There was no significant association with age, gender, or urban/rural dwelling. However, those who were divorced were 60% as likely to adhere to medication and there were significantly lower odds of adherence in four oblasts: Naryn (OR=0.30), Batken (OR=0.18), Talas (OR=0.16) and Chui (OR=0.27).

Economic burden of hypertension treatment

Our weighted, unmatched analysis of expenditure among households (who reported expenditure >0) with and without a member with EBP suggests that households with at least one member with EBP experience greater out of pocket expenditures for prescribed outpatient medicines than households without EBP. (Table 4) Expenditure on anti-hypertensives, our primary interest in this study, would be counted in the prescribed outpatient drug category. (Table 4, Column 1) The difference in mean per capita spending on outpatient medicines between these groups is 585.14 KGS (12.7 US\$).

Spending varies significantly by socio-economic status. Among the poorest third of the population, mean per capita spending on outpatient medicines among households with EBP amounts to 1376.65 KGS (29.9 US\$) or 31 % of annual per capita effective income in that group. As expected the middle and richest thirds spend more, 1549.86 KGS (33.7 US\$) and 4024.75 KGS (87.5 US\$) respectively,

but this amounts to a lower percentage of their annual per capita effective income (17% and 19% respectively).

Because expenditure on self-medication was higher than expected, we examined its prevalence among those with EBP and found that, on average 19% of males with EBP (9% in the youngest age category and 45% in the oldest) reported self-medicating. For females this figure was 36% (10% in the youngest category and 46% in the oldest). The data do not allow us to know for what conditions individuals are self-medicating.

After matching on the proportions of people in the household over the age of 60, under the age of 2, male, household size, urban vs. rural residence and consumption tercile, EBP households were found to be spending 335.57 KGS more in total on health expenditure, almost 400 KGS more per capita on drugs and 208.69 KGS more on self-medication. The 400 KGS difference in per capita spending on drugs is equivalent to roughly 3% of annual per capita household non-food consumption among all households (12 022.45, S.E. = 338.06 KGS). The odds of catastrophic health spending among EBP households are 1.48 times higher than that of non-EBP households. (Table 5)

Discussion

To the best of our knowledge, this is the first study that analyses the role of various socio-demographic and socio-economic factors, in explaining low levels of adherence to anti-hypertensive drug regimens in Kyrgyzstan. The crude prevalence of EBP we found using 2010 KIHS data is slightly lower than that of the 2007 study, despite using the same definition. This difference may be due to an artefact of the data arising from the collection process (e.g. more highly skilled data collectors or less mis-reporting of taking drugs for EBP). Alternatively, it may represent some improvements in treating HTN in Kyrgyzstan since 2007 due to the development of initiatives such as quality improvement training for physicians with respect to identification and treatment of HTN, and HTN clubs for patients that provide education and support of lifestyle improvements. (15)

Our findings confirm the low rate of adherence reported in 2007, as less than half of the total population of individuals in our study who are aware of having hypertension are adhering to medical

treatment. This may be due to inaccurate prescription advice given by physicians, a poor understanding of the importance of daily adherence on the part of patients or a preference for brand-name drugs that are unaffordable for daily use by poorer patients. These are issues that should be further explored in qualitative studies. Our results provide new evidence that poorer individuals are indeed less likely to adhere to HTN medication regimens. Using a novel approach to match on potential confounders, we further found that households with at least one member with EBP had significantly higher total expenditure on health, as well as on medicines, and were more likely to experience catastrophic health spending, suggesting that out-of-pocket expenditure for EBP may be prohibitively expensive for those in the poorest income groups in Kyrgyzstan.

Our findings also showed a high prevalence of self-medication (i.e. purchasing and using medication without a doctor's prescription) among individuals with EBP. Self-medication is a common practice in countries of the former Soviet Union (16) and can include treating one's illnesses with herbs, alcohol and traditional medicines. (17) In a recent study in 8 FSU countries, the most frequent reason cited for not seeking health care when doing so would be justified was the cost of treatment (including drugs), followed by the choice to self-medicate. (16) In a study using the same survey, 25% of Kyrgyz respondents reported that they would use a folk healer if they had one of ten common conditions, by far the highest frequency in the 8 countries. (18) While self-medication may be a cultural phenomenon, in cases where it involves the use of cheaper drugs or other remedies, it may also imply unaffordability of doctor-prescribed medical treatment, suggesting that the influence of drug costs on adherence may be even greater than is apparent from individuals' reports of reasons for non-adherence. However, it is also possible that some cases involve attempts to manage real or perceived side effects of anti-hypertensive medication. While our findings suggest an increase in expenditure among EBP households due to self-medication, this difference was not large enough to conclude that self-medication is a major driver of expenditure or adherence to prescribed treatment.

The Kyrgyz government has acknowledged the importance of ensuring access to outpatient pharmaceuticals in order to strengthen primary care. As part of a programme of health care reform, mandatory health insurance was introduced in 1996 and included among its benefits the Additional

Drug Package (ADP) that subsidized the cost of essential outpatient medicines. (19) This includes four classes of cardiovascular medicines: ACE inhibitors (enalapril and lisinopril); diuretics (hydrochlorothiazide, frusemide); calcium channel blockers (amlodipine, verapamil and nifedipine); and beta blockers (bisoprolol and atenolol). These medicines are sold at prices comparable to international guide prices. Subsequent assessments of the ADP have found that it has been crucial in ensuring popular support for the reform programme and for increasing demand for primary care services and access to essential medicines in remote areas. (20) It has been shown to have improved access to medicines, increased generic and rational prescribing practices and led to a partial introduction of prescription-based sales of medicines. (19) However, some other important cardiovascular medicines are not included in the ADP and, as noted above, statins are much more expensive, typically twelve fold higher or more, than the international guide price.(21)

Nevertheless, affordability of medicines remains a problem and may be partly due to irrational prescribing practices as well as high levels of self-medication. (22) There is a lack of popular understanding of rational drug use in Kyrgyzstan, which is problematic where almost all medicines can be purchased over-the-counter without prescription, and there is a low adherence to clinical protocols among medical professionals. (22) Both doctors and patients have been reluctant to embrace generic substitution as almost 60% of doctors believe that the effectiveness of cheaper generics under International Nonproprietary Name (INN) is much lower in comparison with much more expensive branded drugs (23). (Research in 2008 by the WHO into the quality of public-sector drugs in Kyrgyzstan suggests that this belief is not wholly unfounded, as the quality of 62% of anti-hypertensives in the country could not be proven. (24)) Only 30% of funds allocated for the reimbursement of patients through the ADP are for generic unbranded medicines while 70% goes to more expensive generics from certain popular manufacturers. (22) Moreover, a recent assessment by the WHO in 2013 reported that funds allocated to the ADP are underused, which suggests that doctors are prescribing medicines that are not included on the reimbursement list. (7) In addition, internal migration, which has been considerable but extremely complex,(25) affects uptake of the ADP because people often do not enroll with a new primary care facility at their new place of

residence and without registration, they do not have access to ADP benefits. (20) It should also be noted that the ADP does not necessarily cover the full cost of the prescribed medicine but rather pays according to a reference price, which may be less than the price for which the pharmacist sells it. (19) Our findings highlight the fact that despite the positive steps taken in Kyrgyzstan to ensure free primary health care and to subsidize medicines for HTN, inequity in health care access for HTN may still exist, as demonstrated by lower adherence to medicines and greater financial burden suffered by poorer income groups. The most recent health reform in Kyrgyzstan - Den sooluk (2012-16) - is a continuation of the previous Manas Taalimi reform programme (2006-2011) with continued aims of improving the quality and accessibility of care and the health of the population. (26) The Den Sooluk focuses especially on selected priority diseases including CVD, as the main cause of mortality. Given the continued focus on CVD through the Den Sooluk, levels of awareness and adherence to medication for CVD conditions (including HTN) could be different now than they were in 2010, but the impact of this programme has yet to be evaluated. Updated KIHS data are scheduled to become available next year - analyses of these data that can follow up on this paper, identifying any changes in awareness and adherence, would provide valuable insights into the effectiveness of these reforms.

Limitations

As indicated in our Methods section, we relied on a single measurement of blood pressure while seated in order to define EBP. Using only one measurement may result in either under- or over-estimate HTN; however, in our case more than one measurement was not feasible and the definition of EBP used in our study is consistent with that used in international literature on HTN prevalence. (9) Our definition of adherence may also introduce some limitations, as it is possible that individuals who report taking medication in the preceding 24 hours are not necessarily taking medication every day. In this case we would be over-estimating prevalence of adherence in this population. Our analysis is also limited by the fact that we could not estimate the effect of education on adherence, as the KIHS 2010 did not include information on education. Education is likely associated with awareness of HTN and adherence to treatment, and also likely to be correlated with income. However,

the KIHS 2010 was primarily focused on level of health care utilization rather than determinants, and only a small number of demographic variables was included.

As also discussed above, it is not possible in the KIHS to separate out expenditure specifically related to HTN. Reported spending on outpatient medicines could also include medicines for other non-HTN-related conditions (e.g. common cold remedies, allergy medicines, etc). While it is likely that expenses for non-HTN-related conditions are evenly distributed between households with and without EBP, our matching analysis allowed us to more accurately attribute any differences in expenditure to HTN-related treatment. However, there are a number of health conditions that are more likely in persons with hypertension, such as cardiovascular disease and stroke. Thus, our approach may overestimate the burden specifically attributable to hypertension. The greater financial burden of EBP households in fact is likely to be due to a range of cardiovascular conditions. Nevertheless, our approach shows that having hypertension is a good and easily observable marker to identify households more likely to experience catastrophic health expenditures. This can perhaps be used for targeting of health benefits, for example subsidies for medicines.

Conclusion

Ensuring the affordability of medicines in Kyrgyzstan is an important policy priority, but a broad and complex set of measures is required to address it. The reimbursement of HTN treatments through the ADP is important, but measures to support rational prescribing and consumption patterns are also necessary, and until the mistrust of cheap generics, and the lack of strict regulation of the quality of these medicines, is overcome, the affordability of medicines for long-term conditions will remain a key concern for households.

This paper contributes to our understanding of how self-medicating is an important aspect of affordability and needs to be routinely taken into account in countries where most drugs can be purchased over the counter. It also points to a need for more research on trust, health beliefs and the role of advertising in how patients make decisions about the consumption of medicines.

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