TITLE: Prevalence and factors associated with out-of-pocket pharmaceutical expenditure among primary health care patients: evidence from the Prover Project

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ABSTRACT

Objectives: To determine the prevalence and associated factors of out-of-pocket pharmaceutical expenditure (OOPPE) among primary health care (PHC) patients.

Methods: The study is part of the Prover Project, an exit survey carried out in 2017 in a large city (population 234,937) in Minas Gerais State, Brazil. A representative sample of patients (n=1219) from pharmaceutical services based on PHC was selected. Three components of OOPPE were assessed: the general prevalence, the types of medicines purchased (medicines for the treatment of chronic diseases, medicines for the treatment of acute diseases or herbal medicines) and coverage by the National Health System (SUS). The factors associated with OOPPE were examined applying a modified Andersen's behavioral model of health services use. Data were analyzed using descriptive statistics and logistic regression.

Results: The overall prevalence of OOPPE was 77%. Most patients who had OOPPE purchased medicines to treat chronic diseases (94%). In addition, these patients purchased medicines covered by public insurance but were out-of-stock (85%). OOPPE was associated with enabling factors, such as higher personal income (OR=1.92; 95%CI:1.02-3.62), holding health insurance (OR=1.40; 95%CI:1.01-1.95) and higher neighborhood trust (OR=1.34; 95%CI:1.01-1.79), and with need factors, that is, poorer perception of health (OR=1.63; 95%CI:1.20-2.21), multiple comorbidities (OR=1.70; 95%CI:1.18-2.46), and higher number of prescribed medicines (OR=2.84; 95%CI:1.90-4.26).

Conclusion: We found a high prevalence of OOPPE, identifying individuals more likely to incur these expenses. These findings are useful to inform policymakers from the healthcare system to plan and implement the needed interventions to protect primary care patients from this financial burden.

HIGHLIGHTS

I – Out-of-pocket pharmaceutical expenditure (OOPPE) has a large impact on global health expenditure. Low-income patients with multiple comorbidities are the most financially burdened especially in middle-income countries. Even though Brazil has one of the world's largest public health systems, which includes free access to medicines, patients still spend a significant amount on medical treatment.

II –This study offers an insight into the prevalence and the factors associated with OOPPE among primary health care (PHC) patients of the National Health System (SUS) in a large municipality in Minas Gerais, Brazil. The overall prevalence of OOPPE was almost 80%. We found evidence that patients with better socioeconomic conditions, higher social capital levels and worse health status were more likely to have OOPPE.

III – Our results suggest that public policies should focus on interventions to protect from OOPPE patients with worse health status, improving the supply of medicines among this group.

1. INTRODUCTION

Out-of-pocket pharmaceutical expenditure (OOPPE) is one of the main drivers of spending on health, especially in middle-income countries [1]. Brazil is no exception, even though the National Health System (SUS) was designed to offer free access to medicines within its pharmaceutical programs [2]. Research carried out in the country has found widespread shortages of medicines at the public community pharmacies. Consequently, access to medicines by patients is substandard [3-6] leading them to purchase their treatments from the private sector [7].

As a result, Brazilians spend a significant amount on medicines. It was estimated, for instance, that OOPPE reached almost 30% of the household health expenses, corresponding to more than R$100 billion reais (USD 19.1 billion, approximately), with an increase of 7.1% between 2010 and 2017 [8,9]. In 2017, specifically, 92% of medicines expenditures were borne by Brazilian households [8-9].

OOPPE may trigger social and health problems by creating financial barriers to access medicines and encouraging inefficient use patterns, especially for those that can least afford it, such as poorer individuals and patients regularly receiving health care [7]. In Brazil, the income committed to OOPPE is almost three times higher among the poorest, that spend, on average, 7.3% of their total income purchasing medicines [10]. Empirical evidence has also shown that OOPPE is particularly problematic in people with multiple comorbid disorders [11-13] and lower

incomes [7,10]. Other characteristics associated with OOPPE are gender [14], age [11,15], education level [15], health insurance [14] and health status [11,14].

Nevertheless, little is known about the prevalence and the associated factors of OOPPE in Primary Health Care (PHC). PHC in Brazil is the core of SUS [16], addressing the most prevalent problems in the community, such as hypertension, diabetes and depression, offering services as patient treatments, health promotion and disease prevention [17]. There is also a lack of studies exploring the role of social context for OOPPE. One of the key elements of social context is the social capital (SC) [18]. There is no consensus on the definition of SC, but there is an agreement that it encompasses 'social networks, the reciprocities that arise from them and the value of these for achieving mutual goals' [19,20]. Luz et al (2011 and 2013) [21,22] found that low levels of SC were associated with cost-related medication non-adherence, suggesting that high stocks of SC can act as a buffer against health inequities, helping people access services and resources, such as medicines [21]. Thus, it is coherent to assume that SC can also play a role in the occurrence of OOPPE, but this has not been assessed to date.

Therefore, our study estimated the prevalence and assesses the impact of individual factors and SC on OOPPE at PHC.

2. METHODS

2.1. Study area and participants

This study is part of the Prover Project, an exit-survey in the public community pharmacies conducted between August and November of 2017 in a large municipality (population greater than 200,000 inhabitants) in the state of Minas Gerais, Brazil [23]. The municipal Human Development Index (HDI) is 0.764 [8], slightly better than Brazil as a whole (0.755) [8]. The top 3 causes of death in the municipality between 2008 to 2017 were the diseases

of the circulatory system, cancer and external causes, following the same pattern of the rest of the country [8].

In terms of the SUS organization, the city is considered a health pole, meaning that it is a reference for healthcare provision to other municipalities in the same region [24]. The city is divided into health districts, five of which have public community pharmacies responsible for dispensing medicines, offered by the public system, to the population covered by the adjoined area.

The sample size was estimated considering 50% of prevalence of the event of interest, 95% confidence level and 3% of tolerated margin of error, resulting in 1067 individuals. To compensate for possible losses, a percentage of 15% was added, totaling a sample of 1228 people. The frame population was stratified into subpopulations. The sample was divided proportionally to the number of patients registered in each of the five public community pharmacies of the PHC, based on information from the Municipal Health Secretary. The eligible population for the survey consisted of PHC patients aged 18 years or older, using the public community pharmacies for six or more months and in possession of a medical prescription at the time of the interview.

The interviews were conducted after dispensing by a trained team through a multidimensional, structured and pre-tested questionnaire. The instrument was developed based on questionnaires applied in large surveys [25-27]. During the data collection, the interviewers approached all patients in the public community pharmacies and provided information about the project and its purposes. After the medicine delivery process, patients were approached again and invited to participate in the survey. Individuals who did not accept were invited to complete a refusal questionnaire, a short version of the main instrument, containing questions about sex, age, and self-reported skin color.

2.2.Data analyses

OOPPE

OOPPE was measured according to (1) the occurrence of any expenditure on medicines in the last three months (yes/no question); (2) expenses incurred to purchase medicines covered by SUS but out-of-stock in the public pharmacy (yes/no question); (3) type of medicines purchased (medicines for the treatment of chronic diseases/ medicines for the treatment of acute diseases/ herbal medicines. This question was multi-valued, that is, the patient could choose one or more response options). Herbal medicines were evaluated as a separated category because they are included in the Municipal List of Essential Medicines (REMUME).

Factors associated with OOPPE

Dependent variable

The outcome, OOPPE, was defined by the occurrence of any expenditure on medicines in the last three months, categorized as yes/no, the former being the category of reference.

Independent variables

The independent variables were organized based on the healthcare utilization model of Andersen [28] combined with the neighborhood model by Mohnen et al (2019) [29]. We considered three sets of factors: (1) Predisposing, (2) Enabling and (3) Need.

1. **Predisposing factors:** sex (male; female), age (18-59; 60 or more), self-reported skin color (white; nonwhite), marital status (Divorced/widowed/single; Married/live Together) and education (0-4; 5 or more years of study).

2. **Enabling factors:** personal income (less than 1; 1-2; 3 or more Brazilian minimum wage, equivalent to BRL 937 or USD 283), individual health insurance (not insured;

insured) and perceptions of SC based on the model of Loch et al (2015) [26]. The variables of perceptions of SC were 1) number of close friends (four or more; less than four); 2) number of people who would be willing to lend the respondent money, if necessary (at least one person; no person); 3) trustworthiness of the neighborhood's inhabitants, according to the opinion given about the following statement "most of the people who live in the neighborhood/location can be trusted" (positive = completely agree; partly agree; and negative = do not agree nor disagree; disagree in part or totally disagree with the statement); 4) perception of the frequency with which people help each other in the neighborhood (positive = always or almost always; and negative = sometimes, hardly ever or never); 5) perception of security in the neighborhood (positive = consider the neighborhood to be very or moderately safe; negative = consider the neighborhood to be neither peaceful nor violent; moderately violent; or very violent); 6) participation in community or civic activities (having participated in or performed at least one kind of the following activities in the previous 12 months: council meeting, open meeting or group discussion; intentional contact with some politician; protest or demonstration, electoral or informational campaign, reported some local issue to the newspaper, radio or television, notified the police about some local problem; not having participated in any of the mentioned activities) [27].

3. **Need factors**: self-reported health (Very good/ good; Fair/ poor/ very poor), number of chronic diseases (assessed based on the report of previous medical diagnosis of hypertension, cardiovascular disease, diabetes, lung disease, peptic ulcer, anxiety/depression and hypercholesterolemia) and number of prescribed medicines used in previous two weeks (0-2; 3-4; 5 or more).

2.3.Statistical analyses

Bivariate and multivariate analysis were based on Pearson's chi-square test and logistic regression analyses to evaluate how the variates were associated with the likelihood of OOPPE. Covariates that had a p-value of 0.2 or less in the bivariate analysis were initially included in the multivariate models. A backward elimination process eliminated nonsignificant variables at the p-value<0.05 level. Multicollinearity was analyzed using bivariate correlation tests between the explanatory variables. After the logistic regression model has been fit, a global test of goodness of fit of the resulting model was performed. Statistical analyses were performed using Stata version 14.0.

2.4. Ethics Review

Ethics approval (1.395.369) was received from the Ethics Research Committee of the Oswaldo Cruz Foundation, Brazil. Informed consent was obtained from each respondent prior to survey administration.

3. RESULTS

A total of 1,219 individuals met the inclusion criteria and participated in the study (Figure 1). The comparison between respondents (n = 1,219) and non-responders (n = 387) did not reveal any statistically significant differences for sex (p = 0.193), skin color (p = 0.982) and age (p = 0.294).

The description of the survey participants' characteristics is shown in **Table 1**. The following characteristics predominated: female sex (65.2%), monthly personal income between one and two Brazilian minimum wage (65.3%) and not having health insurance (71.7%). A large number of participants reported three or more chronic diseases (39.7%), five or more prescribed medicines used in the two weeks prior to the survey (42.7%) and fair or poor or very poor self-reported health status (57.4%). Moreover, the study population reported low levels of

SC, ranged from 38.9%, for those who did not have anyone able to lend money, and 66.1% for those who did not participate in community activities.

Among the participants, 77% had some OOPPE in the three months prior to the interview and the majority had to use the private pharmacy to buy medicines that were covered by SUS that were unavailable in the public community pharmacy (**Figure 1**). In relation to the characteristics of OOPPE, **figure 1** shows that among the participants who had some spending on medicines, the majority bought medicines for the treatment of chronic diseases (94%).

The significant results (p<0.05) of the multivariate analysis of factors associated with OOPPE are shown in **Table 2**. Among the enabling factors, individuals who had a monthly personal income of more than two Brazilian minimum wage were almost twice as likely to spend money on medicines compared to individuals with lower income. The chance of OOPPE was also greater among those who had health insurance and who reported high neighborhood trust. Considering need factors, a fair/poor/very poor self-reported health status and the presence of three or more chronic diseases were significantly associated with OOPPE. Moreover, the number of prescribed medicines used showed a dose-response relationship with OOPPE. The higher the number of prescribed medicines used, the greater the reporting of OOPPE.

4. DISCUSSION

Out-of-pocket payments for medicines can create a financial barrier to access, resulting in unmet needs, or lead to financial hardship for people using health services [7]. Our study assessed the prevalence and associated factors of OOPPE among PHC patients. We found that OOPPE was very common (77%), and were often made for medicines that were covered by the public system yet unavailable in public pharmacies. In addition, OOPPE was associated with

monthly personal income, health insurance, neighborhood trust, self-reported health status, the number of chronic diseases, and the number of prescribed medicines.

Prior studies carried out in countries with free distribution of medicines, such as Ukraine and Austria, have shown great divergence in their results. For example, in Ukraine the prevalence of OOPPE was 96% [30]. In contrast, Austria, a high-income country, found a prevalence of just 12% [15]. It is important to note, however, that direct comparisons between the prevalence estimates from different studies should be carried out with caution, as there are methodological differences, such as the place of study [15,30-33] the age range of the participants [31,32] the types of medicines included for evaluation [32] and also differences intrinsic to the health systems of each country [15,30].

Although advances have been occurring in the provision of medicines around the world, large inequities remain in middle-income countries and progress is particularly slow in improving access to essential medicines [7]. In this study, the prevalence of OOPPE was 77%. This result is in agreement with prior studies conducted in Brazil, where the prevalence of OOPPE has ranged between 65% and 83% [31-33]. On the other hand, considering that we included only patients regularly receiving health care in SUS, a lower rate of OOPPE would be expected. The health system operates under the premise of free and universal distribution of medicines, thus it should protect patients, especially the poor ones, from this expenditure [34].

The majority of patients had OOPPE on medicines that were covered by SUS but that were out-of-stock in the public community pharmacies. This result confirms previous findings in the same municipality showing that the unavailability of medicines in SUS was a recurring issue in the perception of pharmacists and patients [35]. Recently, another study assessed the availability of medicines in the public system and found that only 39.4% of patients had access to all prescribed medicines [3]. The adequate provision of free medicines would reduce OOPPE

and increase access to medicines. The unavailability of medicines in the system, however, makes patients spend more on prescription medicines or stop taking some medications [36], worsening the quality of life and increasing morbidity and mortality [37].

Finally, we found that purchased medicines for chronic diseases were the reason for the occurrence of OOPPE. It is likely that individuals with chronic diseases require more health care and are more likely to receive a medical prescription, as well as make greater use of medications, especially those for continuous use. In this situation, the high level of OOPPE is worrisome since one of the SUS priorities is to provide free access to medicines for diabetes, hypertension, and other prevalent chronic diseases [36]. As these medicines are not always available at SUS, patients make direct payments to obtain their treatments which, in turn, may drive them into further impoverishment, as long-term treatments can indicate a constant economic burden [7]. Considering the population using PHC is mainly composed of individuals with chronic diseases [38] and these health conditions are responsible for 70% of the mortality rate in the country [39], the importance of an adequate supply of medicines for continuous use for the population using SUS is reinforced.

Another aspect investigated in this study was the factors associated with OOPPE. Three enabling factors (higher monthly personal income, presence of health insurance and a high level of neighborhood trust) and three need factors (self-reported health, number of chronic diseases and number of prescribed medicines) contributed to explain OOPPE. Our results regarding personal income are consistent with that observed in other studies showing a positive association between higher income and OOPPE [11,15]. It is possible to assume that the population with the highest income has the easiest access to medicines through the private sector while the population with the lowest income seeks more the public sector and depends on a free provision of medicines for do not compromise their family budget and their treatment [6,40].

The results found about health insurance are also in agreement with other studies, which point to the link of health insurance as an important factor explaining the higher OOPPE [14]. It can reflect the fact that patients with health insurance usually are financially better able to cover the costs of prescription medicines and consequently have more OOPPE [41].

In this study the higher level of neighborhood trust, operationalized as a generalized toward other people [27], was associated with the occurrence of OOPPE. The level of neighborhood trust is an indicator of SC. Although there is no consensus in the literature around the concept and operationalization of SC [42], several studies have shown its association with health outcomes, such as better self-perceived health [27], reduction of under-utilization of medication for financial reasons [34] and reduction in overall mortality [43]. Nevertheless, we did not find other studies that investigated the role of SC for OOPPE to allow direct comparisons. On the other hand, previous studies showed that social capital might be associated with better adherence to medical treatment despite cost pressures [34]. The relationship between OOPPE and adherence is complex, since many patients continue use their medications even when facing high medication costs, low incomes, and lack of prescription medication coverage [44,45]. Our results reinforce the idea that even populations that share similar vulnerabilities, such as high health needs and low socioeconomic conditions, can behave very differently regarding their prescribed medication depending on the social and cultural context to which they belong.

In relation to the need factors considered in this study, all of them were associated with the occurrence of OOPPE. Patients who have worse health conditions were more likely to have OOPPE, it would be expected given the expenditure profile revealed in the descriptive analysis. Patients with three or more chronic conditions, for instance, were almost twice as likely to have OOPPE when compared to those who related have up to two chronic diseases in the same period. Another need factor for determining OOPPE was the number of prescribed medicines

used in the previous two weeks. This finding is consistent with that observed by other authors who showed that individuals with greater prescribed medicines had significantly fewer chances of obtaining all pharmacotherapy in the public system [46,47].

Finally, patients with negative self-reported health were more likely to have OOPPE, similar result was found by Costa-Font (2007) [14]. It was predicted to some extent, as previous authors postulate that the worst the self-reported health, the greater the number of chronic diseases and the use of medicines [48,49]. These findings are in agreement with previous studies [12,13,14] and evidence that SUS is failing to attend precisely the patients with greater health needs, such as the those in worse health.

Some study limitations deserve consideration. Firstly, surveys are inherently prone to information bias, which could affect their results. To avoid this bias, several methodological precautions were taken, such as recruiting, training, and supervising the field team to assure the compliance with the study protocol, pre-testing and piloting the instruments and monitoring the entire process of data collection.

Secondly, evaluating OOPPE is particularly challenging considering the absence of consensus in the literature on how to measure this variable, the recall period, and where and how to collect data. We used a 10-item questionnaire addressing different aspects of OOPPE and covering various recall periods and specific details of the last purchase to minimize memory bias. Patients reported whether the prescribed medicines were covered by SUS. Therefore, to minimize the information bias, we only included participants who had been users of the public community pharmacies, and, consequently, of the health care system, for at least six months. The greater experience with the system allowed them to provide more accurate information on expenditure on medicines out-of-stock in the public pharmacies.

Thirdly, due to logistical and cost factors, we adopted a non-random sampling technique, and this option could have, theoretically, generated voluntary response bias and undermined the conclusions of our study [50]. However, we strove to control for this potential source of bias. We stratified the frame population into subpopulations and adopted standardized operational procedures for participants enrollment, avoiding selection bias.

Our study was conducted in a health pole municipality, thus strategic for the health care system organization, and with social and health profile comparable to Brazil as a whole. It is expected to find similar prevalence rates and associated factors of OOPPE among primary care patients in other parts in Brazil, especially large municipalities, between 100 and 900 thousand inhabitants, considering the primary care in the country is subjected to the same policies, regulations of the execution and financing [51-53]. Additionally, the analysis of the profile of the study participants and non-participants did not reveal statistically significant differences, and the study population is similar to the population served in PHC in Brazil [54]. Together, these points reinforce the external validity of our results [55,56].

5. CONCLUSION

We found a high prevalence of OOPPE among primary care patients, threatening an already vulnerable population. Patients with better socioeconomic status and with higher levels of SC are more able to access their treatment through the private system. Additionally, patients in poor health are being particularly financially burdened. These results highlight weaknesses in pharmaceutical management practices, thus policies aimed at reducing OOPPE should focus on interventions directed to decline the shortages of medicines in SUS.

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Table 1 – Characteristics of primary health care patients (n=1,219). Prover Project, 2017.

| Variables (n = 1,219)	Frequency (n)	Percent (%)
Predisposing characteristics		
Sex		
Male	424	34.8
Female	795	65.2
Age		
18-59	549	45.0
60 or more	670	55.0
Skin color		
White	547	46.7
Nonwhite	624	53.3
Marital Status		
Divorced/Widowed/ Single	516	42.4
Married/Live Together	700	57.6
Education[a]		
0-4	590	48.7
5 or more	621	51.3
Enabling characteristics		
Monthly personal income [b]		
< 1	335	27.7
1-2	791	65.3
> 2	85	7.0
Health insurance		
No	874	71.7
Yes	345	28.3
Number of close friends		
0-3	711	58.3
4 or more	508	41.7
Number of people able to lend money		
0	464	39.0
1 or more	727	61.0
Neighborhood trust		
Low	524	43.4
High	682	56.6
Willingness to help		
Low	597	50.1
High	595	49.9
Neighborhood safety		
Low	788	65.1
High	422	34.9
Participation in community activities		
No	806	66.1
Yes	413	33.9
Need characteristics		
Self-reported health		
Very good/ good	512	42.6
Fair/ poor/ very poor	690	57.4
Number of chronic diseases		
0-2	735	60.3
3 or more	484	39.7
Number of prescribed medicines used in previous two weeks		
0-2	330	27.1
3-4	367	30.1

| 5 or more | 522 | 42.8 |

[a] in years of study; [b] 1= monthly Brazilian minimum wage (BRL 937.00 or USD 282.80 during the study period)

Table 2 – Factors associated with out-of-pocket pharmaceutical expenditure (OOPPE) among primary health care patients (n=1,219). Prover Project, 2017.

Variables	OOPPE		COR (95%CI)	AOR (95%CI)
	Yes	No		
Predisposing factors				
Sex				
Male	323	101	1[a]	-
Female	611	184	1.04 (0.79-1.37)	-
Age				
18-59	405	144	1[a]	-
60 or more	529	141	1.33 (1.02-1.74)*	-
Skin color				
White	430	117	1[a]	-
Nonwhite	465	159	0.79 (0.61-1.04)**	-
Marital Status				
Divorced/Widowed/ Single	407	109	1[a]	-
Married/Live Together	524	176	0.80 (0.61-1.05)**	-
Education[b]				
0-4	465	125	1[a]	-
5 or more	463	158	0.79 (0.60-1.03)**	-
Enabling factors				
Monthly personal income [c]				
< 1	240	95	1[a]	1[a]
1-2	364	93	1.44 (1.08-1.93)*	1.30 (0.95-1.78)
> 2	257	77	1.58 (0.88-2.83)**	1.92 (1.02-3.62)*
Health insurance				
No	652	222	1[a]	1[a]
Yes	282	63	1.52 (1.11-2.08)*	1.40 (1.01-1.95)*
Number of close friends				
0-3	539	172	1[a]	-
4 or more	395	113	1.11 (0.85-1.46)	-
Number of people able to lend money				
0	346	118	1[a]	-
1 or more	565	162	1.19 (0.90-1.56)	-
Neighborhood trust				
Low	383	141	1[a]	1[a]
High	539	143	1.39 (1.06-1.81)*	1.34 (1.01-1.79)*
Willingness to help				
Low	445	152	1[a]	-
High	469	126	1.27 (0.97-1.66)**	-
Neighborhood safety				
Low	590	198	1[a]	-
High	338	84	1.35 (1.01-1.80)*	-
Participation in community activities				
No	621	185	1[a]	-
Yes	313	100	0.93 (0.71-1.23)	-
Need factors				
Self-reported health				
Very good/ good	351	161	1[a]	1[a]
Fair/ poor/ very poor	571	119	1.90 (1.65-2.19)*	1.63 (1.20-2.21)*
Number of chronic diseases				
0-2	514	221	1[a]	1[a]
3 or more	420	64	2.82 (2.07-3.83)*	1.70 (1.18-2.46)*
Number of prescribed				

medicines used in previous two weeks	199	131	1[a]	1[a]
0-2	280	87	2.11 (1.53-2.94)*	1.81(1.29-2.55)*
3-4	481	41	4.47 (3.19-6.27)*	2.84 (1.90-4.26)*
5 or more				

[a] Indicates reference category; [b] in years of study; [c] 1= monthly Brazilian minimum wage (BRL 937.00 or USD 282.80 during the study period). *$p<0.05$; **$p<0.20$. CI: confidence interval; COR = crude odds ratio; AOR = adjusted odds ratio; Goodness-of-fit teste 0.5810.
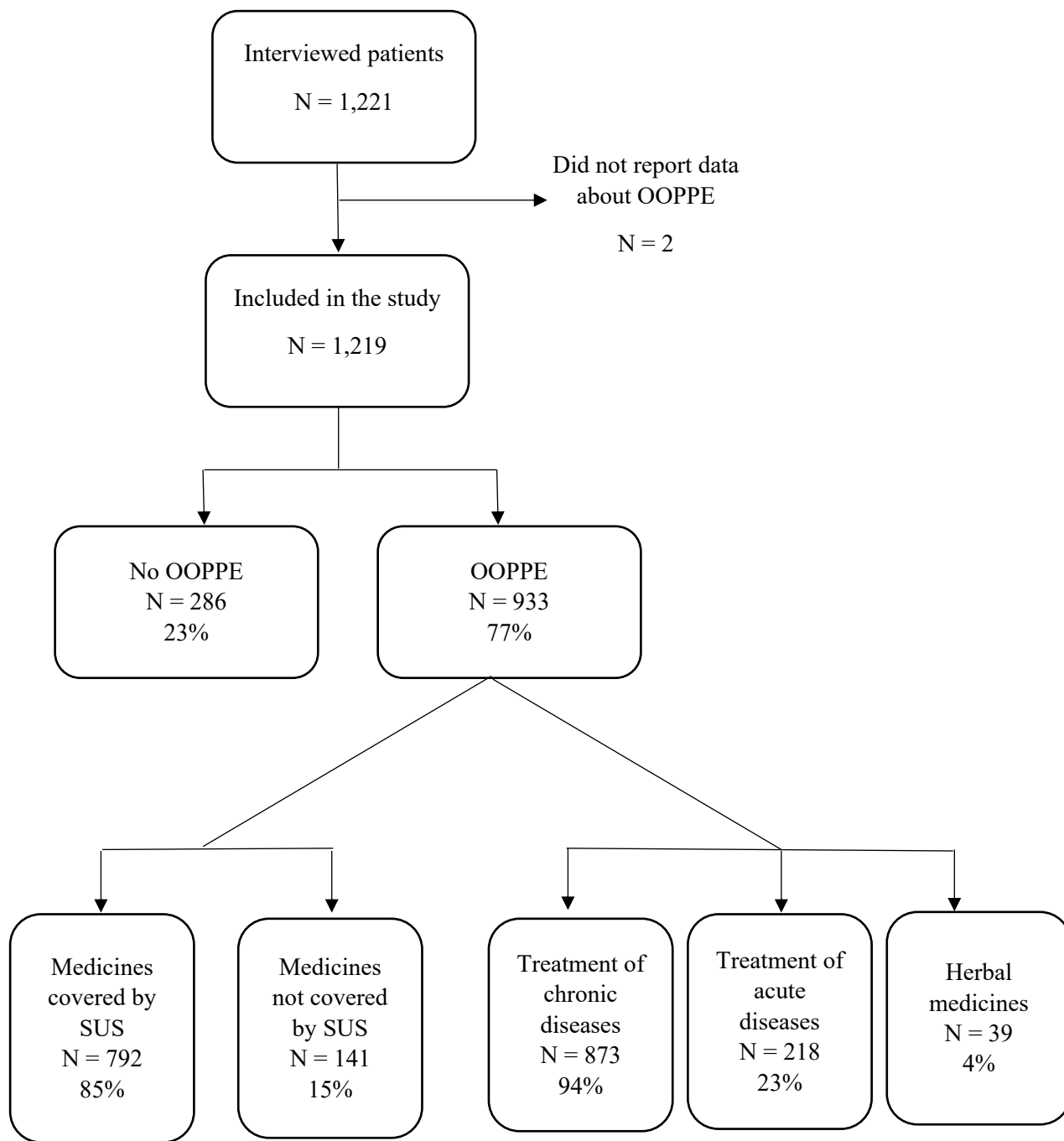
OOPPE: Out-of-pocket Pharmaceutical Expenditure; SUS: National Health System

Figure 1 - Flowchart of the interviewed patients regarding their evaluation of OOPPE. Prover Project, 2017.