The reach and limitations of medication treatment adherence for hypertension control among patients of the Family Health Strategy: a case study for a midsize city in Brazil*

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Abstract

Although the Family Health Strategy (FHS) has increased the access to public health services in Brazil, some health outcomes among its users are still below the desired standards. One advocated cause for this mismatch is treatment adherence. Many studies suggest that increased levels of medication treatment adherence promote better health outcomes. Some scholars, however, argue that the ability of adherence to correctly improve health depends on a more subtle set of variables, such as absence of drug interaction and a comprehensive system of pharmaceutical care that facilities access and compliance. Based on novel data for patients with hypertension, users of the public primary care system in a mid-size city in Brazil, we analyze: (1) the extent to which medication treatment adherence can improve blood pressure (BP) control (**reach**), and (2) the likely causes for why a large group of highly adhered patients find themselves with high levels of BP (**limitation**). Our data come from a probabilistic, stratified sample of 641 FHS users, 40 years and older, under drug treatment for hypertension for at least 6 months, interviewed in 2014 and followed up in 2016. To provide insights on the reach of treatment adherence we make use of a combination of descriptive statistics and structural equation modeling applied to the 2014 data. The limitations of treatment adherence and their likely causes were addressed using the longitudinal data for those highly adhered in the baseline survey, both within and out of the BP goal. Our results suggest

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that adherence is important for BP control, even after accounting for mediation effects of motivational drivers, such as depression, physical activities, and smoking habits. However, adherence itself has a limited effect since a large proportion of the highly adhered patients are out of the BP goal. The longitudinal data allowed us to investigate two potential indicators of limitations of drug treatment adherence: drug interactions (polypharmacy) and the limited ability of the MGLS to measure the quality of the drug treatment. Altogether, our findings support the importance of the public provision of health services, but highlight the need for the inclusion of persistent pharmaceutical care practices for treatment adherence to reach its full potential.

Keywords: hypertension, drug treatment adherence, public primary care system, Brazil

1 Introduction

Hypertension is a risk factor for coronary heart disease and the single most important risk factor for stroke. In addition to being responsible for about 50% of ischaemic strokes, it increases the risk of hemorrhagic stroke and relates to other chronic conditions, such as diabetes. The World Health Organization data show a global prevalence of hypertension at around 40% among adults 25 years and over in 2008, with estimated 7.5 million deaths (12.8%), and 57 million disability adjusted life years (DALYS) or 3.7% of total DALYS. Africa is the leading region for hypertension prevalence, with 46% of its adult population diagnosed with raised blood pressure (WHO, 2016).

Studies in Brazil estimate that between 14% and 34% of adults are diagnosed with hypertension (Lessa et al., 2006; Nunes Filho et al., 2007). The Longitudinal Study on Adults Health (ELSA, in Portuguese) identified an even higher prevalence. Duncan et al. (2012) estimate that about 18 million Brazilians have hypertension, but only 30% of those have the blood pressure within the prescribed goal. Data from the Brazilian Ministry of Health reveal that in 2012 alone 154,919 hospitalizations related to hypertension were registered, leading to non-negligible costs to the Public Health System (SUS, in Portuguese). The high prevalence and low rates of blood pressure control make hypertension one of the main risk factors for kidney, cardiovascular, and cerebrovascular diseases (Miranzi et al., 2008; James et al., 2014).

Current anti-hypertensive drugs are cost-effective, although blood pressure control therapy may be costly for patients (Heisler et al., 2008; Bernard et al., 2014). In Brazil, the provision of anti-hypertensive medication for free or at a very low cost by the Public Health System through the Popular Pharmacy Program eliminates most financial barriers to medication. Thus, why so many individuals with hypertension have persistent high blood pressure (BP) despite the large and relatively cheap availability of effective anti-hypertensive medication? Three main explanations are given in the literature: clinical inertia (Heisler et al., 2008), drug interactions due to the pharmacological regimen complexity (MacDonell et al., 2013; Rajpura and Nayak, 2014), and poor medication treatment adherence (Krousel-Wood et al., 2004). Clinical inertia refers to the failure from providers to properly increase medication dose or the number of drugs in response to persistently high BP (Giugliano and Esposito, 2011; Gil-Guillén et al., 2010). Studies suggest that clinical inertia is mainly driven by a safeguard in clinical pratice (Giugliano

and Esposito, 2011) and by limited information available for the providers on the history of patients' treatment adherence (Heisler et al., 2008). Treatment adherence is so important that studies estimate that poor medication adherence is the cause of up to 50% of treatment failures and is associated with disease progression, avoidable hospitalizations, disability, and death (Stephenson, 1999; Sokol et al., 2005).

Due to its importance for blood pressure control, ways to leverage medication treatment adherence has been subject of research since the 1960's (DiMatteo et al., 2002). Scholars, however, have been increasingly recognizing the limitations of adherence to pharmacological therapy alone to fight raised blood pressure. The main limitations *intrinsically related to adherence* are: (a) failure in treatment intensification by health providers for patients taking multiple drugs (Heisler et al., 2008); (b) patients' difficulty to follow prescribed medication and tendency to reduce dose intake due to beliefs on necessity and adverse effects (Riegel and Dickson, 2016; Molloy et al., 2014; Rajpura and Nayak, 2014; Clifford et al., 2008; Horne and Weinman, 1999) or cultural differences on beliefs regarding how to manage disease (Horne et al., 2004); and (c) finally, the limitations and lack of comparability of instruments used to measure nonadherence rates (Wu et al., 2008; Hamilton, 2003).

Clinical inertia among highly adhered patients have been seen as a safeguard in clinical practice. That is, in the absence of readily available information for health professionals on accurate measures of patients' adherence dynamics, lack of medication intensification is seen as a precautionary way to avoid unnecessary medication or increase in drug regimen complexity (Heisler et al., 2008). Beliefs on the necessity of treatment and its perceived side effects are particularly high for symptomless diseases, like hypertension. This explains a higher tendency of intentional nonadhered patients to overestimate side effects and underestimate necessity towards the pharmaceutical therapy (Clifford et al., 2008; Rajpura and Nayak, 2014). It also seems that point checks of adherence may hide important volatility of unintended nonadherence. This is a sensitive situation where the patient might have become adhered right before the visit to the doctor's clinic, incorrectly being classified as holder of persistent high blood pressure (Molloy et al., 2014; Vrijens et al., 2008). Even among highly adhered patients the way adherence is defined makes it difficult for the health provider to understand refractory hypertension. This may be explained by patients simply not taking their medications as prescribed, including the right dose and the right time (Krousel-Wood et al., 2004).

Subjective representation of the disease and the understanding of how to follow prescribed treatment and store drugs are still important barriers for adherence to promote blood pressure control (Riegel and Dickson, 2016; Menckeberg et al., 2008). Polypharmacy is also likely to result in low levels of adherence efficacy to control blood pressure, especially when drug interactions request undetected drug intensification (Heisler et al., 2008). Certain adherence measures themselves are also limited in covering all the important dimensions of adherence: understanding, perception of necessity and consequences, frequency of use, and appropriateness of drug dose (Beyhaghi et al., 2016; Hamilton, 2003). The large number of adherence scales proposed lead to great variability of estimates, since they may measure only partial dimensions. Wu et al. (2008), for instance, identify 13 studies using self-reported adherence (same class of measurement) with nonadherence rates varying from 4% to 54%. Despite studies validating certain self-reported scales (Morisky et al., 1986, 2008; Strelec et al., 2003; Prado et al., 2007; Bloch et al., 2008; Santa Helena et al., 2008; Ben et al., 2012; Lavsa et al., 2011; Okello et al., 2016), there is no consensus in the literature on the best way to identify adherence rates (Wu

et al., 2008).

Besides the intrinsically limitations mentioned above, studies have found that the relation between adherence and health outcomes is stronger for non-medication treatments, such as change in life style and health habits (Dosse et al., 2009). This limitation is *extrinsically related to adherence*, but may be an important explanation for why loosely adhered patients to pharmacological therapy may experience better outcomes when adhered to healthier diets and more frequent physical exercises (Appel et al., 2003). Finally, patients' involvement with their care, and the ability of the health care system to provide comprehensive pharmaceutical care seem to play a critical role for medication treatment to reach its full potential (Lee et al., 2006).

Based on novel longitudinal data for patients with hypertension, users of the public primary care system in a mid-size city in Brazil, this paper analyzes (1) the extent to which medication treatment adherence can improve blood pressure (BP) control (**reach**), and (2) the likely causes for why a large group of highly adhered patients find themselves with high levels of BP (**limitation**). To provide insights on the reach of treatment adherence we make use of a combination of descriptive statistics and structural equation modeling applied to the 2014 data (baseline). The limitations of treatment adherence and their likely causes were addressed using the 2016 longitudinal data for those highly adhered in the baseline survey, both within and out of the BP goal. We discuss the importance of promoting patients' adherence to treatment, highlighting the importance of including persistent pharmaceutical care practices within the Family Health Strategy for a successful hypertension drug therapy.

2 Data and Methods

2.1 Data

This study is based on novel survey data from a probabilistic sample of 641 users of the Family Health Strategy in the urban areas of Governador Valadares, Brazil (see Figure 1). The selection of respondents was based on the following criteria: (1) diagnosed with hypertension by a health professional, (2) under pharmacological treatment for at least 6 months, (3) 40 years and older. In order to make the sample representative of the public health care users in the municipality, we first accessed patients' records in all 39 Basic Health Units (BHU) and 3 units pertained to the Community Health Agents Program (CHAP). Based on this information, we calculated the proportion of selected patients by BHU and CHAP units in the city. The minimum sample size for a population with known size and unknown variance was then estimated, based on the following set of parameters: 3% error, 5% significance, and variance for proportions of 0.25. The calculated sample size (641) was distributed by BHU and CHAP units based on their observed population proportions. Figure (1) shows the spatial distribution of PHU and CHAP users compared to the overall population in the city.

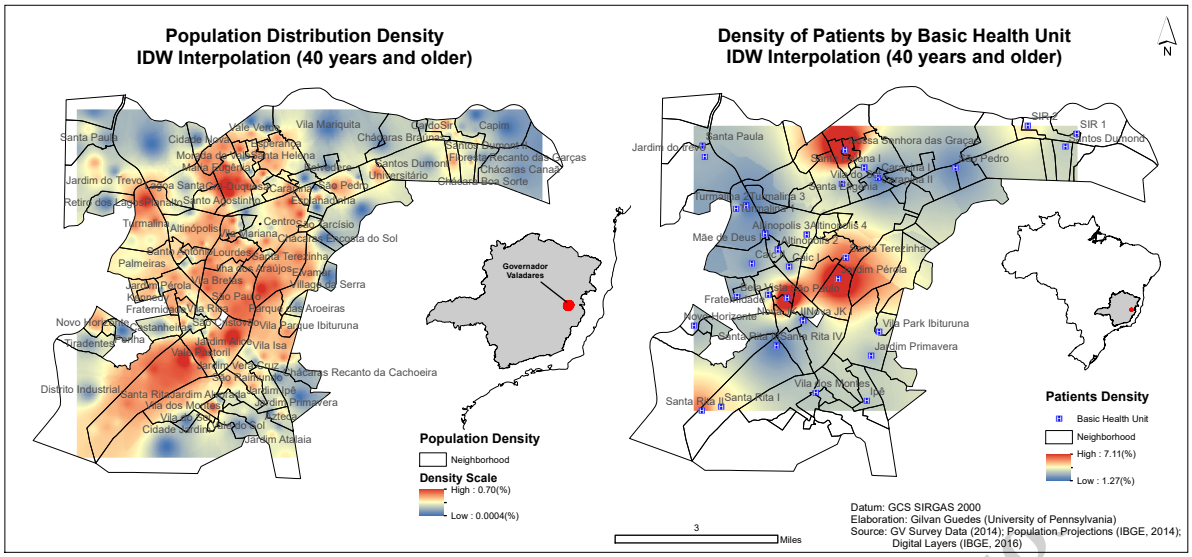

Figure 1: Spatial Distribution of the Primary Health Care System and Actual Population Distribution in Governador Valadares, Minas Gerais, Brazil

Users received home visits by our research team for face-to-face interviews from March to December 2014. The interviews were based on a structured questionnaire containing questions on sociodemographic characteristics, health outcomes, health behavior, quality of life, and depression. The study development meets all ethical requirements involving research with humans established by the 196/96 Resolution of the Brazilian Ministry of Health. The project, entitled "Hypertension: behavioral practices, quality of life, and patients' social representations of the disease and its treatment" and funded by the Brazilian Research Council (CNPq grant 401288/2013-7), was submitted and approved by the Research Ethics Committee at the Universidade Vale do Rio Doce (Process CEP 441.059). The Informed Consent form was read and signed by all interviewed individuals, and a copy was properly filed.

In 2016 all 331 respondents identified as highly adhered to the drug treatment in our 2014 data were followed up. The new data collection aimed at better understanding the likely causes for the limited ability of treatment adherence to reduce hypertension levels. In association with the Pharmaceutical Care Center (College of Pharmacy - Universidade Federal de Minas Gerais), a new questionnaire was designed with detailed information on patients drug use. The drug use screening was divided into two blocks: (1) drugs based on patient's self report (prescribed or not by a health professional), and (2) prescribed drugs. The first drug use screening included the following information: name, purpose, dosage (amount, frequency, intake schedule), time of continuous use, and additional information (taken before food, with milk or water, etc.). The second drug use screening included the same information, in addition to data of prescription. All prescribed drugs were verified by the trained interviewer after the interviewee's consent. Besides drug use history, we repeated blood pressure measurement with the same procedure used for the baseline survey and reapplied the instrument for self-reported medication adherence.

2.2 Data Measurement

In this study we aim at explaining determinants of both medication treatment adherence and being within the blood pressure goal. Since these are instrument-based variables, this section provides detailed information of procedures used to measure them.

Medication Treatment Adherence

The literature on measurement of treatment adherence is vast, suggesting different approaches. The four most accepted methods are the electronic devices to monitor medication adherence (Moore, 2003; Hamilton, 2003; Vrijens et al., 2008), electronic records on pharmacy refill rates (Heisler et al., 2008), pill counts (Hamilton, 2003), and self-reported adherence compound scales (Morisky et al., 1986, 2008; Beyhaghi et al., 2016). Although many authors advocate towards the preciseness and objectiveness of the electronic records on pharmacy refill rates (Heisler et al., 2008; Menckeberg et al., 2008), they depend on a highly integrated record system currently unavailable in Brazil. Electronic devices, on the other hand, are very expensive and therefore not very common, even in developed countries. Pill counts are considered invasive since patients are asked to bring pills currently being undertaken during the interview or visit (Krousel-Wood et al., 2004). In addition, problems such as pill dumping and sharing may overestimate adherence (Hamilton, 2003).

In this study we make use of the 4 items self-reported scale originally proposed by Morisky et al. (1986), applied to our baseline survey. The Morisky Green Levine Medication Adherence Scale (MGLS) consists of 4 questions measuring medication-taking behavior in outpatients being treated for hypertension. The items intend to capture drug errors of omission in four dimensions: forgetting, carelessness, stopping the drugs either when feeling better or worse. Responses are based on *yes* and *no* questions, with the value 1 given to affirmative answers related to non-adherence and 0 to negative answers, related to adherence. The scale is obtained by summing the four items. The final scale varies from 0, indicating maximum adherence, to 1-2, indicating moderate adherence, to 3-4, indicating minimum adherence.

As in Morisky et al. (1986), the scale reliability measured by the Cronbach's alpha is 0.60 in our sample (moderately low). However, different from the original authors' study, item-test correlation for each of the four items differ substantially: forgetting (0.77) and carelessness (0.80) are much higher than stopping drugs when feeling better (0.62) or worse (0.45). This result suggests that the first two dimensions are more meaningful in explaining patients' adherence levels. In the followup survey we applied the revised MGLS proposed by Morisky et al. (2008), which includes 7 yes/no items and one 5-categories item related to frequency of action.

For the longitudinal analysis performed in this study we use a subset of three variables from the revised scale, which are comparable to the baseline MGLS, in order to capture any likely change in adherence rates for the highly adhered patients identified in the baseline survey. The three variables are: forgetting, stopping taking the drugs either when feeling better or worse. This exercise was performed to reduce change in the adherence rate associated with difference in the scale measurement. The MGLS is widely used by the scientific community (Morisky et al., 1986, 2008; Nokes et al., 2000; Hamilton, 2003; Lavsa et al., 2011; Okello et al., 2016) as a reliable, simple, and quick way to assess patients adherence to drug treatment. The Brazilian Portuguese version of the MGLS has been applied by other studies in the Brazilian context (Strelec et al., 2003; Prado et al., 2007; Bloch et al., 2008; Santa Helena et al., 2008; Ben et al., 2012).

Blood Pressure

In both survey waves, 2014 and 2016, our blood pressure measurement was based on the use of a calibrated aneroid sphygmomanometer. We took blood pressure measurements after the face-to-face interview in order to increase rapport and attenuate potential "white coat effect". To avoid noise in the measurement of the blood pressure, the process was repeated three times with 5 minutes intervals between measurements. The final value for each parameter (diastolic and systolic pressure) was based on the simple average of the 3 measurements taken. To classify respondents as patients within the blood pressure goal we followed the criteria described in the Eight Joint National Committee - JNC 8:

- 60 years or older: within the blood pressure goal if parameters are lower than 150 x 90 mmHg
- 60 years or older, and diagnosed with diabetes or chronic kidney disease: within the blood pressure goal if parameters are lower than 140 x 90 mmHg
- 59 years or younger: within the blood pressure goal if parameters are lower than 140 x 90 mmHg

In this study we use a dummy variable equal to 1 if the patient is within the blood pressure goal, as measured by the JNC 8 criterion.

Additional Patients' Attributes

We use the main attributes referenced in the literature as determinants of treatment adherence and blood pressure control (Krousel-Wood et al., 2004; DiMatteo et al., 2002). Since this study uses both cross-section and longitudinal analysis, and since not all variables were measured in both waves, we separately explain the baseline variables (used for regression purposes) and the additional measures (used for the longitudinal descriptive analysis).

We start describing the variables from the baseline survey. For descriptive purposes, we used age groups (continuous for the regression analysis), sex (1 = male), presence of a partner (1 = yes), occupational status (categorical), color (1 = black), and educational attainment level (count for the regression analysis) as sociodemographic charateristics of patients. Behavioral health indicators used were engagement in non-drug treatment (1 = yes), presence of related (1 = yes) and non-related (1 = yes) comorbidities, family helping with treatment (1 = yes), regular practice of physical activities (count for the regression analysis) and smoking habits (1 = yes). Related comorbidites used are: cerebrovascular stroke, diabetes, heart attack, congestive heart failure, kidney failure, high cholesterol, and respiratory diseases. Non-related comorbities used are: cancer, spine conditions, osteoporosis, arthrosis, and arthritis . Time since diagnoses (continuous for the regression analysis) was used to control for exposure. Finally, we used two motivational measures: difficulty to follow treatment orientations as prescribed by the health professionals (1 = yes) and depression level (continuous for the regression analysis).

Depression level was measured by the psychometric test known as the Beck Depression Inventory (BDI) in its version translated and validated for the Brazilian Portuguese (Gorenstein and Andrade, 1996, 1998). The instrument consists of 21 items, including symptoms and attitudes, with Likert-type scales from 0 to 3. The resulting score based on the summation of all items varies from 0 to 63. Higher score values correlate to higher

probability of depressive symptoms. For descriptive purposes we categorized the continuous score into moderate or high (17 to 63), light (10 to 16), and minimum or no depression (0 to 9).

In addition to the previous attributes, we used the following variables in the longitudinal descriptive analysis. From the 2014 baseline survey we used 4 indicators of *life style and health behavior*: consumption of fruits and vegetables (1 = no), fatty foods (1 = yes), junk food (1 = yes), and salt-rich food (1 = yes). We also included 2 indicators of *utilization of health services*: treatment interruption at least once (1 = yes) and doctor's visit in the last 12 months (1 = yes). From the 2016 followup survey we used 4 indicators of *life style and health behavior*: obesity (1 = yes if Body Mass Index - BMI > 29), consumption of high-sodium spices (1 = yes), reading of food labels (1 = yes), engagement in non-medication treatment (diet or physical exercise). Three indicators of *access and utilization of health services* were also available in the followup survey: visit to a cardiologist (1 = yes) or a nutritionist (1 = yes) for blood pressure control, and private health insurance coverage (1 = yes). Finally, we analyzed 4 indicators of *medication for other morbidities*: intake of 2 or more medications (1 = yes), insulin regularly (1 = yes), and at least one oral diabetes medicine (1 = yes). All indicators are self reported, except for the BMI. The BMI was measured using a balanced scale and a measuring tape as recommended by the literature on anthropometric measures (Group et al., 1986).

2.3 Methods

2.3.1 Reach of medication treatment adherence

Based on the baseline survey (2014), we use the Recursive Linear Regression System (RLRS) model to account for the effect of treatment adherence on the probability of being within the blood pressure goal, taking into account mediating effects of sociodemographic and behavioral measures on both health indicators. The use of RLRS allows for more accurate estimates of effects and more efficient coefficients when non-observed explanatory variables correlate with current explanatory variables in the system. This is very likely to occur in the case of our analysis, since past history of treatment and motivational and behavioral dynamics are not included in the questionnaire, likely affecting both dependent variables. Since the model is recursive, it is always identified (Greene, 2012) and can be solved using maximum likelihood methods (both Full Information and Limited Information Maximum Likelihood) or asymptotically distribution free procedures under strong departure from multivariate normality in the linear projection form of errors.

Although modern programs allow for the generalized systems of equations estimation, solving the likelihood of the equation systems under different probability distributions, they do not provide most measures of model goodness-of-fit. The RLRS, however, allows for the estimation of fit measures as post-estimation results, resulting in better control of statistical reliability of estimates. Thus, we transformed our MGLS ordinal scale into the continuous variable based on simulation. We simulate the continuous MGLS based on the Probability Integral Transform Theorem proposed in Angus (1994). The simulation here used assures that the cumulative distribution of the simulated variable mimics the cumulative distribution of the original ordinal variable. Thus, both basic univariate and bivariate distribution moments are virtually identical. These results, as discussed by Guedes et al. (2015), are insensitive to the interpolation method applied (linear, square, or cubic). The simulated scale was used in the regression analysis in its logged form. To assess model fit, we used the traditional variables from the Structural Equation Modeling

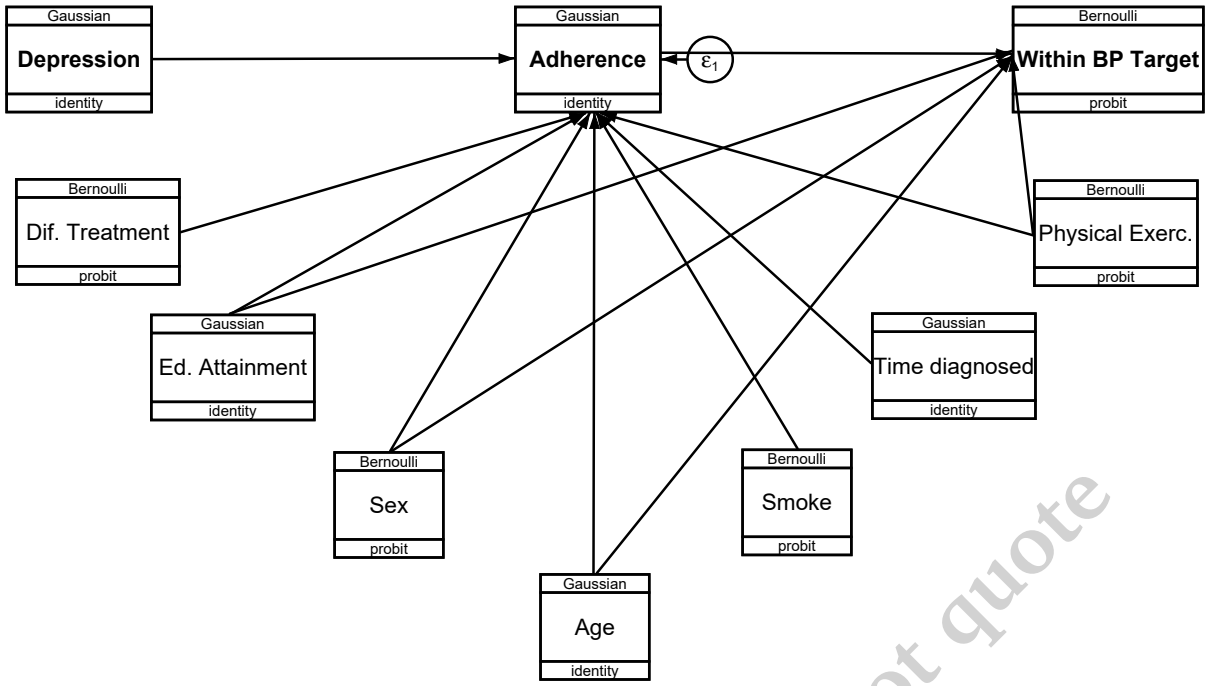

Figure 2: Conceptual Structure of the Generalized Path Model for Treatment Adherence and Hypertension

literature: Coefficient of Fit Index (CFI) larger than 0.85, Root Mean Square Error (RMSE) ≤ 0.05, and Root Mean Square Error of Approximation (RMSEA) ≤ 0.05 (Bollen and Long, 1993). All estimations were performed in Stata MP 14.0 software® with the `sem` command.

Our RLRS, schematically pictured in Figure 2, is represented by the following system of equations:

$$\begin{aligned} y_1 &= \beta_0 + \beta_1 y_2 + \boldsymbol{\beta_k Z_k} + \epsilon_1 \\ y_2 &= \theta_0 + \boldsymbol{\theta_k Z_k^*} + \epsilon_2 \end{aligned} \tag{1}$$

where y_1 is the logit of being within the blood pressure goal, y_2 is the natural log of the MGLS. $\boldsymbol{Z_k}$ is a vector of control variables, as described in Section 2.2. $\boldsymbol{Z_k^*}$ is a subset of control variables used as covariates for blood pressure control (Figure 2).

2.3.2 Likely limitations of treatment adherence

To provide some insights on how medication treatment adherence may render important, but limited information on blood pressure control we followed up 331 patients identified as highly adherent in the 2014 survey. Among these patients, 48.3% had raised blood pressure despite their highly adhered status. The main question we seek to address in this study is: why there are some many highly adhered patients to the medication treatment with persistent high blood pressure? This apparent paradox suggests a potential limitation for the medication treatment adherence. This limitation may arise from at least three sources: 1) How exactly do patients adhere? Are they taking the right dose, at the right time? Is there any potential drug interaction? 2) How adherence is measured? How sensitive are the instruments used to measure adherence? Are they covering all relevant dimensions of medication adherence? 3) Are there other factors affecting blood pressure

that can exacerbate or mitigate the effects of a fully operational medication treatment? Are life style, eating habits, stress, and sleeping patterns good candidates?

We followed up only the highly adhered patients in 2014 based on the MGLS instrument in order to minimize the influence of adherence on blood pressure control. We used the following strategy. We started looking at how adherence and blood pressure statuses changed from 2014 to 2016 as possible evidence of positive association. We then analyzed how health behavior, life style, utilization of health services, and use of other medications as a proxy for drug interactions would help explain the transition in the blood pressure status over time, regardless of change in adherence. Finally, we compare change in adherence rate by the change in blood pressure status using different scales of medication treatment adherence, shedding light on how sensitive results would be to different instruments used.

Our strategy to understand potential limitations for drug treatment adherence is based on a preliminary descriptive analysis of 106 patients already interviewed. A more in-depth study of adherence limitation requests the full sample, in addition to detailed analysis of history of drug use, dose and interactions, patients' experience with drugs, their perception of necessity and side effects. Some of these information are available in our followup instruments, but are still being collected and will be included in the final version of this study.

3 Results

Table (1) presents descriptive results for the Governador Valadares (GV) survey comprising 641 adult individuals with hypertension. It is worth noting that these are in-network patients of the Public Primary Care System. In order to qualify and capture potential sample selectivity in the baseline survey we compare it with two other official databases: the 2010 Demographic Census and the 2013 Brazilian Health Survey. We restrict the compared population in the official databases to those 40 years and older. However, some differences remain. For the Census, data refer to the urban seat of Governador Valadares, but do not restrict to the individuals with hypertension. The Brazilian Health Survey, on the other hand, allows for the identification of the population with this chronic condition, although it does not disaggregate to the municipality level, thus referring to the population over 39 years old and resident of Minas Gerais. In general, the GV sample is slightly older, less educated, with a higher proportion of women, married, blacks, and unemployed individuals than in the overall city population at the same age range. The population with hypertension, at the state level, seats in the middle in terms of sociodemographic characteristics.

Table 1. Sociodemographic Characteristics of the Sample, Governador Valadares, Brazil, 2014

Variables	Observations	%	% in the population (2010 Demographic Census)	% in the population 40+, under drug treatment for hypertension in the State of MG (2013 NHS)
Age Group				
40 to 59	246	38.38	67.04	45.42
60 to 69	179	27.93	17.74	26.94
70 +	216	33.69	15.21	27.64
Sex				
Female	489	76.29	51.12	64.58
Has a partner				
Yes	383	59.75	67.53	50.28
Occupational status				
Working	123	19.19	50.57	37.50
Unemployed	188	29.33	2.66	0.83
Retired / housekeeper / student	330	51.48	46.77	61.67 (1)
Black				
Yes	473	74.02	58.33	56.53
Educational attainment				
Illiterate	147	22.97		22.2
Elementary school	427	66.72	72.45 (2)	50.56
High school	50	7.81	18.11	18.47
College +	16	2.5	9.44	8.75

Source: Primary survey data - N = 641 interviews (Governador Valadares, 2014)

(1) Not in the economically active population

(2) Illiterate individuals or those with elementary school (complete or incomplete)

Table 2. Descriptive characteristics of health behavior and outcome variables among users of the primary public health system diagnosed with hypertension, Governador Valadares, Brazil, 2014.

Variables	Observations	%	% in the population 40+, under drug treatment for hypertension in the State of MG (2013 NHS)
Within the blood pressure goal			
Yes	362	56.47	61.54
Depression level (Beck Depression Inventory)			
No depression	297	46.33	
Light	198	30.89	
Moderate + Severe	146	22.78	
Adherence to drug treatment			
Minimum	65	10.14	
Intermediate	245	38.22	
Maximum	331	51.64	
Engage in a non-drug treatment for hypertension			
Yes	375	58.69	
Time since first diagnosed with hypertension (years)			
0 to 2	54	8.45	12.50
3 to 5	102	15.96	13.33
6 to 10	150	23.47	18.33
11 +	333	52.11	55.83
Hypertension related commorbidities			
Yes	285	44.43	52.99
Hypertension non-related commorbidities			
Yes	489	76.29	34.86
Smoke			
Yes	67	10.45	15.56
Practice physical exercise regularly (< 3 times/week)			
No	524	81.75	79.31
Do you have any difficulty to follow treatment			
Yes	144	22.54	
Does family help with treatment			
Yes	325	50.94	

Source: Primary survey data - N = 641 interviews (Governador Valadares, 2014)

Table (2) describes the variables related to health outcome and behavior. We compare our survey population with the one for the state of Minas Gerais, derived from the 2013 National Health Survey. According to the table, for most patients hypertension was

diagnosed for more than five years. This time span is very similar to the observed for the state population. A large proportion of the sample is out of the blood pressure goal (43.5%), despite being under pharmacological treatment for at least 6 months, as described in Section (2.3). This proportion is even higher than the one found for the State of Minas Gerais (around 38.5%). Treatment adherence is low, with almost half of the patients showing non desired levels of adherence (48.4%), along with a considerably high prevalence of patients adopting non-pharmaceutical therapy for blood pressure control (58.7%). The finding for treatment adherence is surprising, since only 22.5% of patients reported any difficulty to follow treatment orientations. Despite sample selectivity on age and sex, the prevalence of those smoking and doing physical activities are very close to the observed in the state. Comorbidities, however, differ significantly. While the prevalence of hypertension related comorbidities are lower for the study sample, non-associated comorbidities are way higher than in the state. The large difference for the latter comparison may be explained by lack of questions on osteoporosis in the population survey. Depression level is very high in GV sample, with 23% of the sample showing moderate or severe symptoms. Comparison of depression levels with the National Health Survey was not possible because the survey does not contain the BDI scale.

3.1 Reach of medication treatment adherence

Table (3) shows bivariate descriptive statistics for the two outcomes analyzed in this study. Results suggest that patients within the blood pressure goal are more likely to be adhered to the drug treatment. However, a non-trivial proportion of highly adhered patients showed persistent hypertension (40.2%). At the same time, among the weakly adhered, 46.2% have their blood pressure within the prescribed goal. Among the explanatory variables used, lack of physical activity and difficulty to follow treatment orientation appear as statistically negatively associated with the two health outcomes. Adherence to treatment was found to be positively associated with time since diagnosis and non-smoking habits. Table (4) suggests that sociodemographic characteristics seem to play a small role in explaining the two outcome variables, especially for the blood pressure goal. Among these variables, only age is significantly associated with treatment adherence.

Table (5) displays the estimated coefficients for the structural equation path model for treatment adherence and its influence on the probability to be within the blood pressure goal. We first focus on the main drivers of treatment adherence. Our model suggests that lower levels of depression, healthy behavior (regular practice of physical activities and not smoking), lack of difficulty to follow treatment, and longer time since first diagnosed increase the levels of adherence. Some of those effects are important in magnitude. For instance, a decline in the depression score from 17 (moderate depression) to 7 (no depression) would increase the level of adherence by 6% on average. By the same token, an increase in the level of physical activities by one day per week would raise adherence by 2%. By contrast, patients with difficulty to follow treatment and those with smoking habits have a 22.5% and 17.9% lower levels of treatment adherence, respectively. We found no evidence for the influence of sociodemographic attributes.

If we look at the model for blood pressure we found that highly adhered patients (average score of the Morisky-Green scale as 4.52) are approximately 43.2% more likely to be within the blood pressure goal than those loosely adhered (average score of the Morisky-Green scale as 1.75). In addition to drug treatment, regular practice of physical activities and higher educational attainment significantly contribute to the control of

Table 3. Bivariate descriptive statistics between health outcome variables, health characteristics and health behavior among hypertensive users of the primary health care services - Governador Valadares, Brazil, 2014 (row %)

Variables	Endogenous Outcome Variables						
	Within the blood pressure goal			Adherence to drug treatment			
	Yes	No	P-value (χ^2)	Low	Moderate	High	P-value (χ^2)
Within blood pressure goal							
No	-	-	-	8,29	37,02	54,7	0,098
Yes	-	-	-	12,54	39,78	47,67	
Adherence to drug treatment							
Low	46,15	53,85	0,098	-	-	-	-
Moderate	54,69	45,31		-	-	-	-
High	59,82	40,18		-	-	-	-
Beck Depression Inventory scale							
No depression	55,56	44,44	0,771	6,40	35,02	58,59	0,003
Light	58,59	41,41		13,64	37,88	48,48	
Moderate + Severe	55,48	44,52		13,01	45,21	41,78	
Health characteristics							
Time since diagnosed with hypertension							
0 to 2 years	66,67	33,33	0,355	20,37	42,59	37,04	0,000
3 to 5 years	52,94	47,06		21,57	35,29	43,14	
6 to 10 years	58,00	42,00		7,33	42,67	50,00	
11 years and over	54,95	45,05		6,31	36,64	57,06	
Presence of hypertension-related comorbidities							
No	55,06	44,94	0,418	11,52	36,24	52,25	0,304
Yes	58,25	41,75		8,42	40,70	50,88	
Presence of hypertension non-related comorbidities							
No	52,63	47,37	0,274	8,55	40,13	51,32	0,708
Yes	57,67	42,33		10,63	37,63	51,74	
Health behavior and family support							
Do you smoke?							
No	56,79	43,21	0,632	8,71	38,50	52,79	0,002
Yes	53,73	46,27		22,39	35,82	41,79	
Physical activity status							
Active	64,10	35,90	0,066	4,27	33,33	62,39	0,011
Non-active	54,77	45,23		11,45	39,31	49,24	
Do you receive family support for hypertension treatment?							
No	53,99	46,01	0,224	11,18	39,30	49,52	0,386
Yes	58,77	41,23		8,62	37,23	54,15	
Do you find it difficult to follow treatment orientations?							
No	58,79	41,21	0,030	7,88	36,57	55,56	0,000
Yes	48,61	51,39		16,67	44,44	38,89	

Source: Primary survey data - N = 641 interviews (Governador Valadares, 2014)

Table 4. Bivariate descriptive statistics between health outcome variables and sociodemographic characteristics among hypertensive users of the primary health care services - Governador Valadares, Brazil, 2014 (row %)

Variables	Endogenous Outcome Variables						
	Within the blood pressure goal			Adherence to drug treatment			
	Yes	No	P-value (χ^2)	Low	Moderate	High	P-value (χ^2)
Sociodemographic characteristics							
Age group							
40 to 59	53,25	46,75	0,342	14,63	39,43	45,93	0,006
60 to 69	60,34	39,66		10,61	35,20	54,19	
70 and older	56,94	43,06		4,63	39,35	56,02	
Sex							
Female	57,06	42,94	0,595	10,84	37,63	51,53	0,553
Male	54,61	45,39		7,89	40,13	51,97	
Marital status							
Not partnered/married	54,65	45,35	0,445	8,91	37,21	53,88	0,556
Partnered/Married	57,70	42,30		10,97	38,90	50,13	
Race / ethnicity							
Non-black	56,02	43,98	0,887	8,43	33,73	57,83	0,174
Black	56,66	43,34		10,78	39,75	49,47	
Schooling							
Illiterate	53,06	46,94	0,342	5,44	35,37	59,18	0,454
Elementary	55,05	44,95		11,07	39,41	49,51	
Middle school	58,33	41,67		11,67	39,17	49,17	
High school	64,00	36,00		12,00	38,00	50,00	
College and higher	75,00	25,00		18,75	31,25	50,00	

Source: Primary survey data - N = 641 interviews (Governador Valadares, 2014)

Table 5. Coefficient Estimates of the Generalized Structural Equation Path Model for Drug Treatment Adhrence and Blood Pressure Goal - Governador Valadares, Brazil, 2014

Variables	Within the blood pressure goal	Adherence to drug treatment
Adherence to drug treatment (log scale)	**0.352****	
	(0.115)	
Score of the Beck Depression Inventory		**-0.006***
		(0.002)
Time since first diagnosed (years)		**0.004****
		(0.001)
Do you smoke		**-0.165+**
		(0.091)
Practice of physical exercise (days/week)	**0.050+**	**0.019***
	(0.027)	(0.007)
Do you have any difficulty to follow treatment?		**-0.203****
		(0.057)
Educational attainment (years)	**0.038***	-0.009
	(0.016)	(0.007)
Sex	-0.136	0.001
	(0.120)	(0.036)
Age	0.007	0.001
	(0.005)	(0.002)
Constant	**-0.898***	**1.289****
	(0.355)	(0.136)
Observations	640	640

Robust standard errors in parentheses
** p<0.01, * p<0.05, + p<0.1
Source: Primary survey data - N = 641 interviews (Governador Valadares, 2014)

hypertension by 5.1% for each additional day per week and 3.9% for each additional year completed, respectively. Sex and age were not significant.

3.2 Limitations of treatment adherence

Table (6) presents the sociodemographic and health attributes of the highly adhered individuals, as measured in 2014, according to their blood pressure status in 2014. We found no relevant differences for most variables, except for practice of physical exercise, consumption of salt, related comorbidities, and treatment interruption. Curiously, patients within the blood pressure goal are more likely to eat salt (24.8% against 17.3%), to have related comorbidities (50.5% against 41.4%), and to have interrupted the medication treatment at least once (14.4% against 7.6%) compared to those with raised blood pressure. Just for sedentary status they score better (74.8% against 82.7%).

Table (6) also shows the same characteristics according to blood pressure transitional states from 2014 to 2016 (three last columns). It is worth noting that this is a preliminary analysis, showing results for the 106 patients already interviewed in the followup. Although the longitudinal sample is limited for inference at this stage, it gives a taste of

the potential for analyzing patient's evolution when the fieldwork is completed. A selectivity analysis was performed comparing the 106 followed patients with the 225 still to be interviewed, among the 331 highly adhered patients as measured in 2014. We found no statistically significant differences regarding time since first diagnosed, time under treatment, age, sex, race, and educational attainment. The only variable that differs between groups is the 2014 blood pressure status. The prevalence of already interviewed patients within the blood pressure goal is lower (48.6%) than those to be interviewed (65%). The absence of selectivity for the partial followup sample gives us some confidence to provide initial results for the highly adhered patients (results upon authors' request)[1].

We observe a very strong transition to controlled levels of blood pressure: 88.9% (48) of those out of blood pressure goal in 2014 found themselves within the goal in 2016. Only 1.92% (1) of those with controlled blood pressure in 2014 got worse in 2016. This is a remarkable improvement, despite an overall decline in the medication treatment adherence during the period (Table 7). This preliminary result highlights a potential limitation of medication treatment adherence alone for blood pressure control. Further analysis on other patients' attributes may help elucidate this apparent paradox. Tables (6) and (7) show a very consistent pattern when patients who remained out of the blood pressure goal are compared with those who controlled the pressure or remained within the goal over time. The former are more likely to be male, illiterate, and black. They are also more likely to have worse health behavior indicators (sedentary, worse diet habits, less visits to health professionals), health outcomes (higher prevalence of comorbidities, especially diabetes, and obesity), and drug use patterns (more likely to use insuline and drugs for diabetes, and two or more medications other than anti-hypertensives).

Another limitation refers to the ability of the instruments used to measure and discriminate the quality of adherence. When we compare adherence from 2014 to 2016 using the more readily comparable subset of items from the MGLS we find that 100% of those who stayed uncontrolled over time (7 patients) are classified as highly adhered, as in 2014. By contrast, patients who have their blood pressure controlled in 2016 are precisely the ones reporting a declining level of adherence. When we use the revised MGLS (Morisky et al., 2008), the non-adherence rate by transitional state seems to be more consistent, with those who stayed uncontrolled showing the lowest level of medication treatment adherence. Health professionals then should pay attention to what kind of information a particular adherence instrument can provide when deciding upon the patient's treatment.

4 Discussion and Conclusion

This paper analyzed the reach and potential limitations of the medication treatment adherence for blood pressure control. Treatment adherence is so important that studies estimate that poor medication adherence is the cause of up to 50% of treatment failures and is associated with disease progression, avoidable hospitalizations, disability, and death (Stephenson, 1999; Sokol et al., 2005; Lee et al., 2006). Our analysis was performed in a Brazilian mid-size city, including users of the Primary Health Care, 40 years and over, diagnosed with hypertension, and under medication treatment for at least 6 months. The study includes all Basic Health Units and Community Health Agents Programs in the Governador Valadares urban area, making our sample representative of the patients

[1]Our team is currently interviewing the remaining patients, with fieldwork scheduled to be completed by November 2016. The final version of this study will include the full followup sample.

Table 6: Descriptive analysis of patients highly adhered to the medication treatment in 2014 by blood pressure status in 2014 and transition in blood pressure status from 2014 to 2016 according to characteristics measured in 2014 - Governador Valadares, Brazil

Variables	Blood pressure 2014			Transition in blood pressure status 2014 to 2016		
	Within	Out	P-value (χ^2)	Stayed within goal	Moved to within	Stayed or moved to out
Sociodemographic Attributes						
Female	78.8	72.2	0.167	84.0	77.1	71.4
Age group						
40 to 59	32.8	36.1	0.807	28.0	37.5	28.6
60 to 69	30.3	27.8		24.0	35.4	28.6
70+	36.9	36.1		48.0	27.1	42.9
Educational Attainment						
Illiterate	23.7	30.1	0.150	26.0	22.9	42.9
Elementary school	63.6	63.9		66.0	70.8	57.1
High school	9.1	5.3		8.0	6.3	0.0
College +	3.5	0.8		0.0	0.0	0.0
Black	71.1	70.7	0.939	76.0	60.4	100.0
Life Style and Health Behavior						
Do not practice physical actitivy	74.8	82.7	0.087	82.0	81.3	100.0
Smoke	9.1	7.5	0.614	4.0	2.1	28.6
Do not eat fruit and vegetables	40.4	48.9	0.128	44.0	50.0	71.4
Eat fatty food	50.5	52.6	0.704	48.0	60.4	71.4
Eat junk food	56.6	60.9	0.433	64.0	68.8	65.7
Eat salt	24.8	17.3	0.107	24.0	18.8	0.0
Health Indicator						
Have diabetes	27.8	30.1	0.651	28.0	27.1	42.9
Presence of related commorbidities	50.5	41.4	0.102	50.0	41.7	42.9
Presence of non-related commorbiditie	71.2	70.7	0.916	74.0	72.9	85.7
Utilization of health services						
Interrupted treatment (at least once)	14.4	7.6	0.058	14.3	0.0	14.3
Doctor's visit (last 12 months)	90.4	93.2	0.365	90.0	100.0	100.0
Engaged in health group actitvites	49.0	53.0	0.433	58.0	58.3	85.7
Happy with the health service	78.5	80.5	0.313	84.0	79.2	71.4
Observations (2014)	198	133		50	48	7

Source: Primary survey data - N = 331 (105) interviews (Governador Valadares, 2014 and 2016)

Table 7: Descriptive analysis of patients highly adhered to the medication treatment in 2014 according to the blood pressure status in 2016 and transition in blood pressure status from 2014 to 2016 according to characteristics measured in 2016 - Governador Valadares, Brazil

Variables	Blood pressure		Transition in blood pressure status 2014 to 2016		
	Within	Out	Stayed within goal	Moved to within	Stayed or moved to out
Self-reported Adherence					
Highly adhered to medication treatment*	80.6	100.0	72.0	89.6	100.0
Highly adhered to medication treatment**	61.2	57.0	56.0	66.7	57.1
Perceived Necessity and Drug Experience					
Medication is not necessary	12.1	14.3	18.0	6.3	14.3
Any medication makes you feel sick	9.1	28.6	2.0	16.7	28.6
Life Style and Health Behavior					
Obese (Body Mass Index > 29)	34.3	57.1	32.0	37.5	57.1
Do not practice physical actitivy	88.9	85.7	86.0	91.7	85.7
Smoke	3.0	28.6	4.0	2.1	28.6
Eat fatty food	45.5	57.1	44.0	47.9	57.1
Use high sodium spices	61.6	71.4	64.0	60.4	71.4
Read food labels	33.3	14.3	42.0	22.9	14.3
Engaged in non-medication treatment (diet and physical exercise)?	51.0	28.6	46.0	55.3	28.6
Access and Utilization of Health Services					
Doctor's visit (last 12 months)	93.9	85.7	94.0	93.8	85.7
Go to cardiologist for BP control	50.5	28.6	52.0	50.0	28.6
Go to nutritionist for BP control	15.2	0.0	18.0	12.5	0.0
Do you have private health insurance?	53.5	14.3	56.0	52.1	14.3
Medications for other morbidities					
Take 2 or more medications	66.7	85.7	60.0	75.0	85.7
Take insulin reguarly	11.1	28.6	8.0	14.6	28.6
Take at least 1 medication for diabetes	28.3	42.9	24.0	33.3	42.9
Observations (2016)	99	7	50	48	7

Source: Primary survey data - N = 106 interviews (Governador Valadares, 2016)

* Measure based on 3 items: forgetting, stopping drugs when feeling better or worse.

** Measure based on the 8 items proposed by Morisky et al. (2008)

from the local public health care. The Brazilian Health Care System encompasses a large and comprehensive public sector (SUS, in Portuguese) and a private health sector. Private health insurance and out-of-pocket expenses finance services in the private sector, hedging 25% of the Brazilian population (insurance coverage). Individuals covered by private health insurance have better socioeconomic status, including higher rates of formal employment and educational attainment than the overall population (**?**Andrade et al., 2013). We find high degree of socioeconomic and demographic homogeneity among our sampled patients since they are users of the public system.

We estimate that 56.5% of the sample patients have blood pressure within the goal and 51.6% are highly adhered to anti-hypertensive treatment as measured by the Morisky-Green-Levine scale. Adherence is within the typical compliance rate of medication treatment, estimated at 50% (**?**Oigman, 2006; Mousinho and Moura, 2008). As expected, our findings show that patients with healthier behavior (regular practice of physical activities and not smoking) and those with longer time since first diagnosed are more likely to be adhered. Individuals engaged in healthy behavior are probably those who care more about their own health, therefore being more likely to follow doctors prescription. Time since first diagnosed is a proxy for exposure to both the disease and the treatment. In this regard, individuals would be more exposed to the consequences of uncontrolled blood pressure, increasing their awareness about the importance of treatment compliance. Exposure, in this case, would also allow them to learn about how to better follow doctors prescription, how to adjust their own behavior, and how to deal with idiosyncratic drugs efficacy and side effects.

Similar to other studies (DiMatteo et al., 2000; Jonas et al., 1996; Scalco et al., 2005), we found a highly significant effect of depression on levels of adherence. Hopelessness, social isolation, fatigue, and impairments in cognitive focus accompanying depression are the underlying reasons for decline in adherence among these patients. As highlighted by (Jonas et al., 1996; DiMatteo et al., 2000), depression symptoms lead patients to abandon treatment or become a partial complier. In this case, lack of treatment efficacy due to lower adherence increases the chance of related comorbidities, leading to further increase in depression. Thus, beating depression in its early stages is key to improve adherence and achieve blood pressure control.

As supported by international and national studies (Strelec et al., 2003; Prado et al., 2007; Bloch et al., 2008; Santa Helena et al., 2008; Ben et al., 2012; Krousel-Wood et al., 2004), we find that medication treatment adherence is key for blood pressure control. According to our results, highly adhered patients are 43% more likely than those loosely adhered to be within the blood pressure goal. The importance of treatment compliance has called attention of many scholars, leading to a large pool of evidence about its effect on blood pressure control (**?**DiMatteo et al., 2002; Oigman, 2006; Mousinho and Moura, 2008; **?**). Scholars, however, have been increasingly recognizing the limitations of adherence to pharmacological therapy alone to fight raised blood pressure. Indeed, we found a high proportion of highly adhered patients out of the blood pressure goal (40.2%), even being under medication treatment for at least 6 months and assisted by a multi-professional health care team. The literature raises three main limitations for medication compliance. Firstly, it is argued that health providers fail to adjust treatment for patients taking multiple drugs (Heisler et al., 2008). As comorbidities are common among patients with hypertension, they are more prone to take more than one type of medication, increasing the potential for drug interaction and reduction in dose effectiveness. Because other morbidities may follow a different treatment protocol and a different response, one protocol

for blood pressure control can lose effectiveness anytime. Therefore, doctors should be aware of this situation in order to adjust the type, number, and dose of anti-hypertensive drugs accordingly as frequently as possible. A dynamic approach to clinical treatment protocol requires a collective effort from health professionals and a comprehensive health care system.

Secondly, patients sometimes have difficulty to follow prescribed medication. In addition, studies suggest that beliefs on necessity and side effects (Riegel and Dickson, 2016; Molloy et al., 2014; Rajpura and Nayak, 2014; **?**; Horne and Weinman, 1999) and cultural differences on beliefs regarding how to manage disease (Horne et al., 2004) lead to decrease in dose intake. Self-reported measures of adherence, such as the MGLS and the revised MGLS (Morisky et al., 1986, 2008), capture some of these subjective dimensions of adherence, such as forgetting, carelessness, beliefs on adverse effects and necessity. However, the ability of instruments to capture quality information on each dimension vary (Wu et al., 2008; Hamilton, 2003). This is particularly relevant in the case of self-reported adherence measures, because they are unable to capture objective dose, time schedule, and drugs storage and profile. On the other hand, these scales are easy to apply in a clinical setting to help health professionals decide upon patients treatment adjustments. For this very reason, (Heisler et al., 2008) suggest that an effective way to improve the quality of medication treatment protocol is empower providers with readily available information on different instruments measuring adherence with appropriate measurement intervals.

Finally, pharmacological adherence must be seen along with non-medication treatment, since medication and some health behaviors may reinforce each other. Diet, life style, and preventive health habits are likely to improve effects of certain drugs in fighting raised blood pressure (Grimm et al., 1997). In certain instances, patients may achieve blood pressure control with healthy diet and physical exercise alone (Appel et al., 2003). This is a very important aspect of adherence, since it may help reduce potential for drug interactions and resistance to certain class of drugs. By the same token, lack of involvement in healthy behavior may render poor results for blood pressure control, even among highly adhered patients. DiMatteo et al. (2002), for instance, found that adherence to non-medication treatments have a stronger effect on lowering blood pressure than medication. This is not to advocate against medication use, but to emphasize that change in life style brings positive externality beyond decreasing the risk of a specific disease.

This paper addresses some of the limitations to treatment adherence raised by the literature. At this stage, we have preliminary findings that suggest that life style, diet and healthy behavior wit large are likely causes for a group of highly adherent patients with raised blood pressure to have achieved control after one year. We also found that patients taking more than two drugs and insulin and oral drugs for diabetes are more likely to have uncontrolled blood pressure. Drug interactions and medication sub-dose and underprescribing might be the likely cause. To come to a final conclude this paper still needs to address the following issues: finalize the complete sample and complete the analysis of drug use and interaction looking at each patients drug pool. With this in hand we will provide a more solid storyline on limitations of medication treatment and its implications for FHS to monitoring and counseling of patients for the management of the medication treatment. FHS is part of the Primary Care System composed by multidisciplinary teams and involves household visits by the Community Health Agents (CHA).Our findings will detect the possible limitations of treatment adherence. This analysis will be relevant to physicians and especially for the CHA who closely monitors patients during the household visits.

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