

Title Page

Title: The prevalence of depressive symptoms among older patients with hypertension in rural China

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ABSTRACT

Objective: The comorbidity of depression and hypertension (HTN) is common and complicates the management of both conditions. This study investigated the prevalence of depressive symptoms among older patients with HTN in rural China, and explored the relationship between the two conditions.

Methods: The baseline data of older patients diagnosed with HTN included in the Depression/HTN in Chinese Older Adults – Collaborations for Health (COACH) study were used for the analysis. The COACH study was conducted in rural villages of Tonglu County, Zhejiang Province, China. In all, 10,389 older village residents had HTN (57.2% female, mean age 71.5±8.1 years). Blood pressure (BP) was measured using a calibrated manual sphygmomanometer and stethoscope. Depressive symptom was measured using the Chinese version of the nine-item Patient Health Questionnaire (PHQ-9).

Results: Among 10,389 patients with HTN, 12.8% had significant depressive symptoms (PHQ-9≥10). Rates of significant depressive symptoms were 5.3% and 32.8% among patients with controlled and uncontrolled HTN (systolic blood pressure≥140 and/or diastolic blood pressure≥90), respectively ($X^2=8.701$, $p<0.001$). Logistic regression analysis indicated that those in older age group (≥70 years) and with uncontrolled HTN have higher rates of significant depressive symptoms than those who are younger (age 60 to <70) and with controlled HTN.

Conclusion: Our findings show high rates of depressive symptoms among patients with HTN in rural China, and higher rates of depressive symptoms among patients with uncontrolled HTN. These support the development and dissemination of integrative care approaches for older adults with HTN and depression in rural China.

Keywords: Prevalence, Depressive symptoms, Hypertension, Older adults, Rural China

INTRODUCTION

China is the most populous country in the world, and over half of Chinese live in rural regions (Yearbook, 2014). While the pace of development is rapid in urban areas, rural regions lag behind (Xuechun, 2010). With more and more younger and middle-age adults moving to the cities for work, there is an increasing need for mental health care for older adults remaining in rural regions. Although it is well recognized that psychiatric comorbidity, especially depression, has a negative long-term impact on health outcomes for older adults with hypertension (HTN) (Musselman et al., 1998, Sandstrom et al., 2016, Smith et al., 2013, Adamenko, 1967), to date, few studies have explored the relationship between depression and HTN in rural China.

HTN is a major risk factor for cardiovascular morbidity and mortality, representing two thirds of all strokes and one half of all ischemic heart disease (Jonas et al., 1997). Approximately one fourth of adults have been diagnosed with HTN around the world, and the proportion will reach about one third by 2025 (Mittal and Singh, 2010). Many adults with HTN live in China, where the prevalence is up to 41.9%, and the prevalence is even higher in rural areas compared to urban areas (Li et al., 2016, He, 2016).

HTN is often accompanied by somatic symptoms, a lower quality of life, and role impairment (Ong et al., 2007, Lewington et al., 2016, He, 2016). In addition, HTN is associated with psychological distress, as well as depression (Liao et al., 2004, Kretchy et al., 2014, Tevie and Shaya, 2015, Baldissera and Bueno, 2012). Depression is a treatable illness that disproportionately places older adults at risk for

functional and cognitive decline. Depression is the leading cause of disability among patients with chronic diseases such as HTN, with an estimated 350 million people worldwide affected (Mittal and Singh, 2010), and a lifetime risk of 7% (Davidson et al., 2000). Individuals suffering from depression experience functional impairment, poor clinical outcomes, and increased health care expenditures. At its worst, depression can lead to suicide and all-cause mortality (Markovitz et al., 1993).

Many studies have addressed the interplay between HTN and depression. Epidemiologic studies have found that patients with HTN are more likely to develop depression, and clinical depression has also been found to be an independent risk factor for hypertension (Davidson et al., 2000, Markovitz et al., 1993, Jonas et al., 1997, Ong et al., 2007, Meurs et al., 2015). Furthermore, depression is associated with poor adherence to antihypertensive medications (Krousel-Wood and Frohlich, 2010), which results in up to 50% of treatment failures (Stephenson, 1999). Accordingly, patients with both HTN and depression have a higher risk of mortality compared to patients with a single condition (Hajjar et al., 2006, Kayano et al., 2015).

In general, HTN is a risk factor for depression, and depression complicates HTN management. However, the prevalence of depression in hypertensive patients in rural China is unknown. This study investigated the prevalence of depressive symptoms in older patients with HTN using baseline data from the Depression/HTN in Chinese Older Adults – Collaborations for Health (COACH) study. We took the opportunity afforded by the COACH study to evaluate the co-occurrence of HTN and depressive symptoms in rural China and the public health significance of addressing patients' mental health needs with coexisting HTN.

METHODS

Setting and Participants

Data for this study were taken from screening and baseline assessments conducted for the COACH study, an ongoing project funded by the National Institutes of Mental Health USA designed to compare collaborative depression care management to care as usual (CAU) for the treatment of comorbid depression and HTN in Chinese older rural village residents (Conwell, 2016). COACH study subjects reside in rural villages of Tonglu County, one of 55 counties in Zhejiang Province. We selected Tonglu County as the study site because both its population size and average household income are at the mean of all counties in the province. In Zhejiang province, each village clinic has a standardized electronic medical record system (EMR) supported by the Zhejiang Provincial Center for Disease Control and Prevention in which each patient is registered. Each patient registered in the EMR of selected villages was a potential participant. Village doctors used the EMR to identify all patients over age 60 in their village who had a diagnosis of HTN. The village doctors then visited each potential participant, either in their homes or the village clinic, checked their blood pressure according to specified standards, and administered the Chinese version of nine-item Patient Health Questionnaire

(PHQ-9). Those who screened positive for clinically significant depressive symptoms (PHQ-9 \geq 10) were invited to meet with the research team, and provided written informed consent. The study protocol was approved by the Institutional Review Board of Zhejiang University. Data used in our analysis included the baseline data (including demographic characteristics) of the COACH study collected in years 2013 and 2014.

The inclusion criteria of the screening were: (1) community-dwelling residents registered to the selected village; (2) age \geq 60 years, the typical retirement age in rural China; (3) a chart diagnosis of HTN; (4) capable of independent communication with interviewers; (5) capable of giving informed consent. The study was approved by the human subject protections board of Zhejiang University.

Among the 12,914 patients with HTN diagnoses registered in their EMR (see Figure 1 for participant flow chart), 2525 were excluded because: 1) 798 no longer lived in the village, 2) 210 were unavailable for interview, 3) 926 refused to participant, and 4) 591 were excluded for other reasons. The total number of the participants available for analyses, therefore, was 10,389.

Measurements

Participants' BP measurements were obtained by their village doctors in their home or village clinics using a calibrated manual sphygmomanometer and stethoscope (the quality of the devices were monitored every 6 months). All participants were tested three times for BP with a 2 minute interval between each measurement. The average of the three blood pressure readings was included in the data analysis. BP readings distinguished two HTN conditions: those with controlled HTN (coded 0)

and those with uncontrolled HTN (coded 1). The latter was defined as systolic blood pressure (SBP) ≥ 140 and/or diastolic blood pressure (DBP) ≥ 90 .

The Chinese version of the PHQ-9, which has been shown to have good reliability and validity in community Chinese elderly persons, was used to measure depressive symptoms (Chen et al., 2010). The original PHQ-9 was designed for the primary care settings (Kroenke et al., 2001). As a screening tool, a score of ≥ 10 on the PHQ-9 has been suggested to indicate clinically significant depressive symptoms (used interchangeably with significant depressive symptoms here). We created a dichotomous variable to indicate severity of depressive symptom of the respondents (1=clinically significant symptoms vs. 0=not clinically significant symptoms).

Data Analysis

We performed a descriptive analysis using the demographic data to examine the basic characteristics of our sample and the prevalence of clinically significant depressive symptoms. The correlation between BP and the PHQ-9 scores was examined using Pearson (Spearman) Correlation, and a chi-square test was used to explore the interplay between uncontrolled HTN and significant depressive symptoms. Meanwhile, receiver operating characteristic curve (ROC) analyses were performed to explore the predictive relationship between HTN and significant depressive symptoms. As what the results of ROC analyses indicated, we chose the reading of SBP and HTN conditions (controlled vs. uncontrolled HTN) as well as demographic characteristics as predictors in a logistic regression model with significant depressive symptoms as the outcome. In addition, logistic regression was used to test the interaction effects of age groups (≥ 70 vs. 60-70) and HTN conditions on significant depressive symptoms. Seventy was used to divide the sample because it was the median age. All analyses were performed using the Statistical Analysis System, version 9.4.

RESULTS

Prevalence of significant depressive symptoms among patients with HTN

The number of older adults aged ≥ 60 in studied villages was 40,974, 18.1% of the total population. Among these older village residents, 31.5% (12,914) had a diagnosis of HTN, and 80.4% (10,389) of these hypertensive individuals were included in this study (Table 1). Of the 0,389 study participants

(57.2% female, mean age 71.5 ± 8.1 years), 12.8% had clinically significant depressive symptoms (PHQ-9 \geq 10). Also, 27.2% of the 10,389 patients had uncontrolled HTN. The rate of significant depressive symptoms in patients with uncontrolled HTN (32.8%) was significantly greater than for those whose HTN was controlled (5.3%) ($X^2 = 8.701, p < 0.001$).

Bivariate correlation between BP values and PHQ-9 score

Table 2 shows Pearson correlation coefficients for diastolic blood pressure (DBP), systolic blood pressure (SBP), and PHQ-9 scores. All three variables were used as continuous variables. All coefficients were significant--patients with higher blood pressure readings (both SBP and DBP) had higher PHQ-9 scores. This indicates positive correlations between blood pressure and depressive symptoms.

ROC analysis between significant depressive symptoms and HTN

A ROC analysis using SBP as a test for significant depressive symptoms has an area under curve (AUC) of 0.76 with 95% confidence interval (0.74, 0.78). In statistics, a ROC analysis provides tools to select possibly optimal models and to discard suboptimal ones independently from (and prior to specifying) the cost context or the class distribution; an AUC ≥ 0.70 implies good discrimination capability of the selected tool (Metz, 1978, Fawcett, 2006). This result of the ROC analysis was significant. Similarly, an additional ROC analysis using PHQ-9 score as a test for HTN condition also had a significant result with AUC=0.75, 95% confidence interval (0.74, 0.76).

Logistic regression models with significant depressive symptoms as outcome

A logistic regression model with significant depressive symptoms as outcome and SBP, HTN conditions (controlled vs. uncontrolled), age and sex as predictors was conducted (see Table 3). Age, SBP, and HTN conditions were significantly related to the incidence of having significant depressive symptoms. The model selection suggested that there may be interactions between age, SBP and HTN condition in predicting the outcome.

To test for the interaction effects, we created a product term of age group (≥ 70 vs. 60-70) and HTN conditions (controlled vs. not controlled). Table 4 presents the estimates of the logistic regression model that included the product term with the younger group as the reference group. The results indicate significant interaction effects between age and HTN conditions on the likelihood of having significant depressive symptoms. Specifically, those in the older age group (≥ 70) and with uncontrolled HTN were particularly at risk of having significant depressive symptoms, relative to those who are younger (age 60 to < 70) and with controlled HTN.

DISCUSSION

The principal finding of this study is that 12.8% of older patients with HTN (controlled and uncontrolled) and 32.8% of patients with uncontrolled HTN had clinically significant depressive symptoms in rural China. In contrast, the prevalence of depressive disorders among general older adults in China community was 6% (Ma et al., 2008, Chen et al., 2005). To our knowledge, this is the first study investigating the prevalence of clinically significant depressive symptoms among older patients with hypertension in rural China and exploring its relationship with blood pressure control.

Hypertension has a very high prevalence in rural China elderly, affecting more than 40% of older adults in rural areas (Li et al., 2010, He, 2016, Li et al., 2016), and only 45% of these older adults with hypertension were recognized (Prince et al., 2012). HTN has been listed as the top priority of the chronic diseases management system in the national health policy of China (Kwan et al., 2008). With its limited mental health resources, depression among Chinese patients with HTN has been inadequately addressed in China especially in rural areas. The large percentage of patients with both uncontrolled HTN and clinically significant depressive symptoms in our study suggests the interplay between the two conditions—patients with HTN may be more likely to develop depression, and depression may be a risk factor for hypertension. In addition, the significant positive correlation between BP and PHQ-9 scores indicated that patients with high BP are likely to have high PHQ-9 scores and vice versa. Furthermore, the results of ROC analyses suggest that SBP could be a predictor for depressive symptoms and that PHQ-9 score could be a predictor for uncontrolled HTN. Results of this study support the complex relationship between depression and HTN. In previous studies, SBP was found to be associated with mortality risks (Weidung et al., 2015, Weidung et al., 2016) which was also highly related to depression (Barefoot et al., 1996, Bush et al., 2001). Further studies focusing on the relationships between depression, SBP and mortality risk are recommended.

We also found significant interaction effects of age group and HTN conditions in predicting having significant depressive symptoms. This finding indicates that those who have uncontrolled HTN and are 70 year old or older have higher odds of having significant depressive symptoms compared to individuals in other age group and HTN conditions combinations. The combination of HTN and depression, therefore, as the first and second leading causes of disability adjusted life years by 2020 (Murray and Lopez, 1997), requires special attention and the development of effective preventive intervention strategies for depression in this large subgroup of older adults are needed.

Mental illnesses account for a large proportion of the global burden of disease (Mathers et al., 2008), and they commonly co-occur with chronic medical illnesses and interact in complex ways to increase the severity, impede treatment, and worsen the outcomes of both disorders. Integrated care (e.g. co-locating mental health providers in primary care settings) has been shown to help improve clinical outcomes and reduce costs (Smith et al., 2007a). Evidence suggests that patients may be more engaged when mental health is integrated into care for physical health than other forms of care provision (Katon et al., 2010). Approaches to integrating the healthcare of co-occurring mental and physical disorders in high-income countries have shown great promise to improve outcomes (Smith et al., 2007b). Their effectiveness, however, has rarely been studied in low and middle-income countries, which is the objective of the ongoing COACH study, screening data for which were used here. The present analysis of the baseline data showed significant correlations between depressive symptom severity and HTN especially uncontrolled HTN among older adults in rural China. These outcomes support the need to integrate the management of depression into chronic disease management for HTN in rural China.

This study has limitations. The sample was from one out of 55 counties in rural Zhejiang Province, so our findings may not be generalizable to urban or other rural areas. The data in this study were cross-sectional, which limited the analysis of the long-term associations between depression and HTN. Longitudinal studies would help to sort out the relationship between the two conditions.

Measuring blood pressure in outpatient settings is challenging, because many factors including individuals' mood status can affect the readings. It is unclear whether our measure of blood pressure was biased; for example, people with depression may experience greater anxiety during visits to the doctor, and therefore have higher blood pressure readings. Caution, therefore, should be exercised in interpreting the findings. In order to minimize measurement error, we used the average value of three measurements.

Other limitations include the fact that we used no diagnostic assessment of depression. Nonetheless, the PHQ-9 is a valid measure of depressive symptom severity that is highly correlated with the diagnosis of major affective illness using the cut off of ≥ 10 . Both symptom severity and categorical diagnosis of depression are important to consider in their relationships to HTN. Future research should include a more complete diagnostic assessment of depression.

Finally, we had no information about the comorbidities including complications of HTN among this sample, which could influence the independence of the data from possible confounders, such as stroke, that are highly related with depression. We also did not have data about prescribed treatment or adherence to treatment for depression and HTN. Antidepressant medications can influence blood pressure and the results of the PHQ-9 could be influenced by the use of those drugs. We

acknowledge that medication use can potentially confound the relationship between HTN conditions and depression symptoms.

In conclusion, our investigation adds new evidence to the literature on depressive symptoms in older adults with HTN. The prevalence of depressive symptoms in this group is high in rural China, and there is a significant association between HTN and depressive symptoms. Patients with uncontrolled HTN are much more likely to develop clinically significant depressive symptoms. Depressive symptoms may complicate HTN management, posing a significant clinical and public health challenge in rural China. Additional research is needed in the design and implementation of integrated care for management of older patients with comorbid HTN and depression.

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Conflict of Interest: None

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Graphics**Table 1 Demographic characteristics of participants**

Demographics characteristics	Participants
Mean age, y \pm SD	71.5 \pm 8.1
Women, N (%)	5942 (57.2)
Uncontrolled blood pressure, N (%)	2825 (27.2)
Depression in whole group, N (%)	1329 (12.8)

Depression in uncontrolled HTN, N (%) 926 (32.8)

Depression in controlled HTN, N (%) 403 (5.3)

HTN, hypertension

Table 2 Pearson (Spearman) Correlation coefficients between blood pressure and the PHQ-9 score

	Diastolic blood pressure	Systolic blood pressure	PHQ-9 Score
Diastolic blood pressure	1.00	0.37*** (0.37***)	0.16*** (0.11***)

Systolic blood pressure	0.37*** (0.37***)	1.00	0.30*** (0.31***)
PHQ-9 Score	0.16*** (0.11***)	0.30*** (0.31***)	1.00

***, $p < 0.001$.

PHQ-9, nine-item Patient Health Questionnaire

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Table3 Estimates from logistic regression using SBP, age, sex, HTN condition as predictors for significant depressive symptoms^a

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	<i>P</i>
Intercept	1	-9.277	0.528	308.825	<0.001
SBP ^b	1	0.017	0.003	23.736	<0.001
Age (in years)	1	0.062	0.004	250.485	<0.001
Sex (male=1)	1	-0.150	0.065	5.332	0.020
HTN conditions ^c (not controlled=1)	1	1.755	0.099	317.524	<0.001

Note: ^aSignificant depressive symptoms was defined as PHQ 9 scores ≥ 10 , coded 1 (vs. 0=PHQ 9 <10).

^bSBP=systolic blood pressure, used as a continuous variable.

^cHTN=hypertension.

Table 4 Logistic regression model modeling significant depressive symptoms^a

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	P
Intercept	1	-3.713	0.149	618.792	<0.001
Age group^b	1	1.610	0.126	164.675	<0.001
HTN conditions^c	1	2.781	0.129	467.284	<0.001
Age group * HTN	1	-0.948	0.151	39.579	<0.001
Sex	1	-0.111	0.064	2.978	0.084

Note: ^aSignificant depressive symptoms was defined as PHQ-9 scores ≥ 10 , coded 1 (vs. 0=PHQ-9 <10).

^bAge group was dichotomously coded (1= >70 years vs. 0= 60 to ≤ 70). The younger group is the reference group.

^cHTN=hypertension, HTN conditions were dichotomously coded (1=not controlled, 0=controlled).

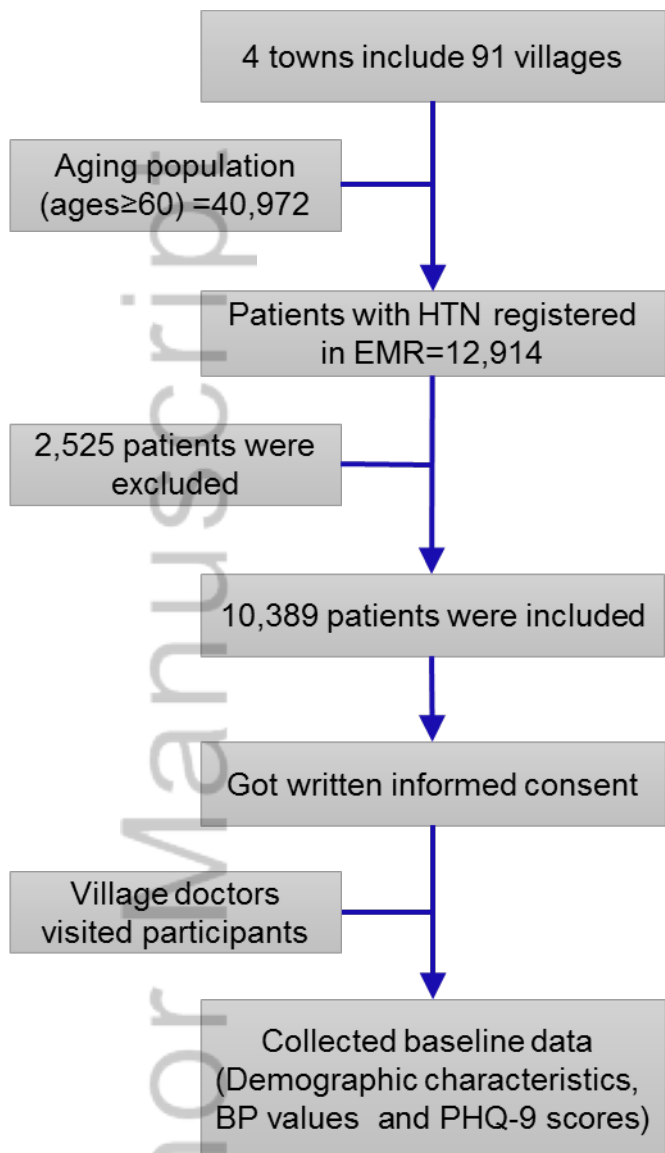


Figure 1 Participant procedure

HTN, hypertension; EMR, electronic medical record system; BP, blood pressure; PHQ-9, nine-item Patient Health Questionnaire.

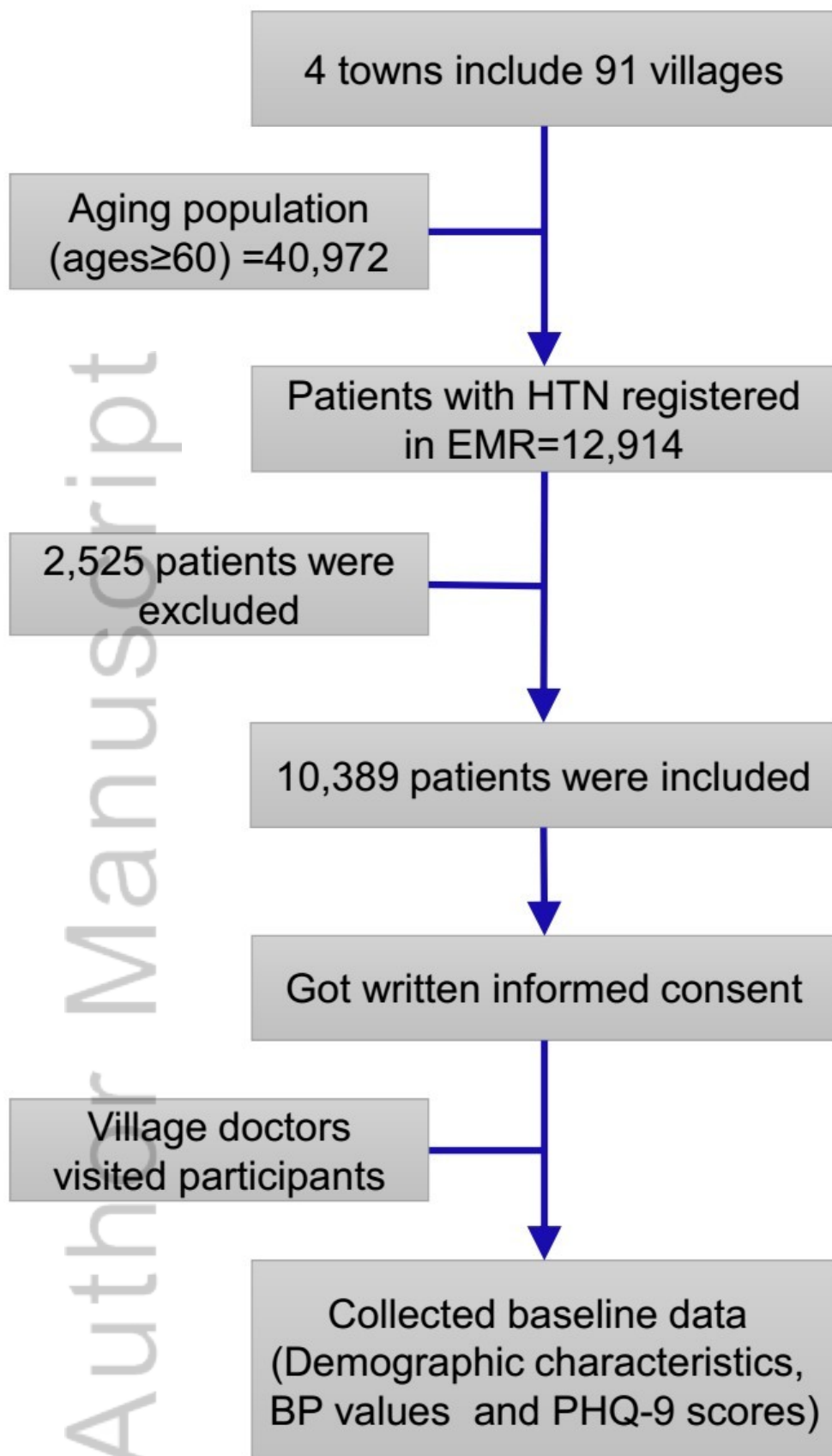


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HTN, hypertension; EMR, electronic medical record system; BP, blood pressure; PHQ-9, nine-item Patient Health Questionnaire.