Medication adherence among patients with chronic conditions in Italy

Francesco Napolitano, Paola Napolitano, Italo Francesco Angelillo, and Collaborative Working Group

Department of Experimental Medicine, Second University of Naples, Via Luciano Armanni, 5, 80138 Naples, Italy

Correspondence: Italo F. Angelillo, Department of Experimental Medicine, Second University of Naples, Via Luciano Armanni, 5, 80138 Naples, Italy, Tel: +39 081 5666031, Fax: +39 081 5666031, e-mail: italof.angelillo@unina2.it

Background: The aims of the cross-sectional study were to measure the extent of adherence to prescribed medications among patients affected by chronic diseases and to identify the predictors of the adherence. **Methods:** The study was conducted between March and December 2014 among 633 outpatients in four hospitals in Italy. Data were collected using a face to face interview at the time of their visit to the hospital. The Morisky Medication Adherence 4-item Scale was used to measure patients' self-reported adherence. **Results:** The majority of the patients were male (51.7%), the mean age was 63.2 years, one-third had at least a high school diploma or equivalent, 34.6% was employed, and the main diseases were hypertension, diabetes, and chronic obstructive pulmonary disease. A total of 39.3% patients reported themselves as being adherent to medications over the 4 weeks preceding their medical specialist's visit. Patients were more likely to adhere to medications if they had a college degree or higher level of education, a higher score of the Katz index, took a lower number of total pills per day, and did not use pill organizers. Patients who have never forgotten to take medications over the 4 weeks preceding their medical specialist's visit were 46.1%. **Conclusions:** The findings emphasize the need for improving information for the individuals affected by chronic diseases concerning the risks of non-adherence in order to encourage responsible behaviour to prescribed medications.
....

Introduction

A key component in the management of a patient with chronic health problem is the assessment of its adherence with therapeutic regimen. Low levels of patient adherence with disease plans compromise the effectiveness of the therapies and have been associated with an increased risk of adverse health outcomes, an increased health care expenditure through hospital admissions and hospital care, a lower quality of life, and a higher rate of mortality.[1,2]

Non-adherence of medications with proven efficacy among chronically ill subjects have been the focus of few studies in recent years on different diseases, such as diabetes,[3,4] heart failure,[5,6] neuropsychiatric disorders,[7–10] cardiovascular diseases,[11–16] and chronic obstructive pulmonary disease,[17,18] and also on the factors influencing the medication adherence.[16,19–21] These studies have suggested that the non-adherence frequently occurs for a variety of patient-related factors, including socio-demographic and socio-economic characteristics,[11,16,17] personal schedules, lack of understanding the diagnosis and treatment,[4,13,22] concerns about effectiveness and side effects of treatment, and the desire to manage the situation independent of the medical profession.[13,18,21] Possible barriers to adherence include characteristics of the medicines and their dosage and schedules,[16,17,19,20] practical issues related to access to medications,[23] medications costs, and physician-patient relationship.[14,22,24]

Prior to this study, to our knowledge no studies have evaluated the extent of medication non-adherence in patients with chronic diseases and factors that affect non-adherence in Italy. A greater understanding of this field would be of value so that avoidable risk factors can be identified and managed using appropriate interventions for improving medication-taking behaviour and economic outcomes. Therefore, the present investigation, among a sample of patients affected by chronic diseases in Italy, has been undertaken with two primary aims. The first aim was to measure the extent of adherence to prescribed medications, and the second aim was to identify the predictors of adherence to medication.

Methods

Recruitment

The cross-sectional study was conducted in the geographic area of Caserta and Naples, Italy, between March and December 2014. A two-stage sampling strategy was used to select a total of 770 participants. First, four public hospitals were selected by using a simple random sampling method. All hospital directors, who received an invitation letter with a description about the study and that the information would be anonymous and used for research purposes only, gave written approval to perform the study. Then the research team randomly approached potential participants presenting at each selected hospital for a clinical consultation in cardiology, metabolic disorders, and respiratory ambulatory centres. Patients were eligible if they were aged 18 years and above and if they had evidence of at least one chronic disease. Patients with cognitive impairment and psychiatric diseases have been excluded. On entry, participants were screened for eligibility and those eligible were recruited until the designated sample size has been reached.

The sample was estimated based on the following factors: expected proportion of the population not adhering to prescribed medications of 35%, keeping 95% confidence interval (CI), a 5% tolerated error and a design effect of two. With an allowance of 10% for non-response, the final sample size was calculated to be of 770 patients.

Interviews

A semistructured interview was designed for the study and a pilot test on 25 subjects was carried out before survey implementation to ensure clarity of the questionnaire.

Data were collected using a face to face structured interview of the subject at the time of their visit to the hospital by using a

questionnaire in the waiting room of the ambulatory centre by two investigators who were trained to understand the purpose and meaning of the study, be familiar with the contents, and be skilled with recruitment interview techniques. Prior to answering the questionnaire, the interviewer explained at each patient the intention of the study and the importance of their contribution, the pertinent information of the study, and allowed the subjects to ask any question. The patients were also informed that their participation was voluntary and that they could withdraw from the interview at any stage without any penalty if they did not wish to participate. Patients were told that their responses would be treated in confidence and complete anonymity was assured, and no information linked an individual's questionnaire to his or her identity. All patients signed an informed consent before commencing the interview. Patients did not receive any incentive for the time spent being interviewed.

The interview addressed five primary themes: (i) basic information (gender, age, highest level of education, marital status, number of children, employment status, medical history), pre-admission performance-based measure of independence in activities of daily living using the Katz Index,[25] and comorbidities measured by the Charlson *et al.* comorbidity Index score;[26] (ii) use of health-care services in the previous 12 months; (iii) drugs/drug groups used, the dosage and the length of medication; (iv) adherence to prescribed medications; and (v) main source of information on the use of medicines for their chronic diseases and the needs of additional information about such therapies.

Assessment of medication adherence

The Morisky Medication Adherence 4-item Scale (MMAS-4) was used to measure patients' self-reported adherence to their medications [27] over the 4 weeks preceding their medical specialist's visit in order to minimize potential recall bias. The instrument has been widely used and it has been demonstrated to be accurate to assess medication adherence in patients with chronic diseases.[10,21,23,28] This scale measures adherence through four questions: (a) Do you ever forget to take your medicine? (b) Are you careless at times about taking your medicine? (c) When you feel better do you sometimes stop taking your medicine? (d) Sometimes, if you feel worse when you take your medicine, do you stop taking it? Each item has a no/yes response option, and to each 'yes' response is assigned a score of one and to each 'no' response a score of zero, allowing a total possible score ranging from zero (full compliance) to four (worst compliance). A patient was considered to be adherent to the medications over the 4 weeks preceding their medical specialist's visit if there was a lack of a 'yes' response, and non-adherent if the score ranged from one to four. Moreover, a patient was considered to have never forget to take the therapies if he/she declared that he/she had always taken the therapies over the 4 weeks preceding the medical specialist's visit.

The study protocol was approved by the Ethics Committee of the Second University of Naples.

Statistical analysis

The statistical analysis has been completed in two stages. Initially, a bivariate analysis was carried out to evaluate the crude effect of each independent variable on the different study outcomes. Categorical variables were compared using the χ^2 test or Fisher's exact test and continuous variables were compared using Student's *t*-test and Mann–Whitney *U* test for independent samples. Variables with *P*-value less or equal than 0.25 from the bivariate analysis were included into multivariate logistic regression models. In a second step, multivariate analysis was performed to determine the independent correlates of the outcomes of interest by estimating the adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) using the logistic regression models. The models were

constructed using backwards stepwise selection procedure, wherein the criterion for the variable inclusion and exclusion in the model was respectively of *P*-value > 0.2 and *P*-value < 0.4. Two multivariate logistic regression models have been used to identify factors associated with the following outcomes of interest: adherence to the medications over the 4 weeks preceding their medical specialist's visit (Model 1); patient who have never forget to take the medicines over the 4 weeks preceding their medical specialist's visit (Model 2). The following characteristics of each respondent were included in all models: gender (male = 0; female = 1), age (continuous, in years), educational level (three categories: primary school or lower = 1; secondary school = 2; college degree or higher = 3), Katz index of pre-admission performance-based measure of independence in activities of daily living (0–5 = 0; 6 = 1), Charlson *et al.* comorbidity index score (<2 = 0; ≥2 = 1), disease with higher duration (three categories: cardiovascular disease = 1; metabolic diseases = 2; bronchopulmonary diseases = 3), number of medications per day (continuous), number of pills per day (continuous), having pill organizers (no = 0; yes = 1), have a cohabiting with the same illness (no = 0; yes = 1), duration of pharmacological treatment (continuous), number of medical specialist's visits in the preceding 12 months (continuous), physicians as source of information about therapies for their chronic diseases (no = 0; yes = 1), and need of additional information about therapies for their chronic diseases (no = 0; yes = 1). Moreover, marital status (single/separated/divorced/widowed = 0; married = 1), and occupation (unemployed = 0; employed = 1) were included in Model 2.

Statistical significance was defined as a *P*-value less than or equal to 0.05 based on two-sided statistical tests. The statistical software package Stata version 10.1 was used to carried out the analysis.[29]

Results

Of the 770 patients approached, 633 agreed to participate and enrolled with a response rate of 82.2%. The characteristics of the overall sample and the results of the bivariate analysis for the variables significantly associated with the outcomes are presented in Table 1. Demographically, the majority were male (51.7%), the mean age was 63.2 years, one-third (32.5%) had at least a high school diploma or equivalent, 34.6% was employed, the median Katz index of pre-admission performance-based measure of independence in activities of daily living and the median Charlson *et al.* comorbidity index score were respectively six and two, the patients were mainly affected by hypertension (81.8%), diabetes (34.4%), and chronic obstructive pulmonary disease (17.1%), and the duration of respondents' illness ranged from 1 to 50 years.

Among the study population, 39.3% patients reported themselves as being adherent to medications over the 4 weeks preceding their medical specialist's visit according to the Morisky score of 0, whereas 22.7%, 28.8%, 7.9%, and 1.3% had respectively a score of 1, 2, 3 or 4 (worst adherence). From the bivariate analysis, almost all factors were found to be associated with medication adherence. On the contrary, the multivariate stepwise logistic regression analysis with the ORs and 95% CIs of the independently associated variables indicated that only few variables affect medication adherence. Of the socio-demographic variables, only the level of education resulted significantly associated with self-reported medication adherence to therapy over the 4 weeks preceding their medical specialist's visit according to the Morisky score of 0. Indeed, patients with a college degree or higher level of education were more likely to adhere compared with those with a lower education (OR = 2.05; 95% CI 1.37–3.06). Medication-adherent respondents had a significantly higher score of the Katz index of pre-admission performance-based measure of independence in activities of daily living (OR = 1.8; 95% CI 1.03–3.15), took a lower number of total pills per day (OR = 0.75; 95% CI 0.66–0.87), and did not use any pill organizers (OR = 0.26; 95% CI 0.13–0.5) (Model 1 in Table 2). Almost half

Table 1 Characteristics of the study population of the adherent patients and of those who have never forget to take medications over the 4 weeks preceding medical specialist's visit

	Total $n = 633$		Adherent patients $n = 249$		Patients who have never forget to take medications $n = 292$	
	n	*%*	*n*	*%*	*n*	*%*
Gender						
Male	327	51.7	112	45	137	46.9
Age (years)	63.2 ± 11.9 (18–96)[a]		60.1 ± 12.4 (18–96)[a]		60.4 ± 12.2 (18–96)[a]	
Educational level*·**						
Primary school or lower	229	36.2	65	26.2	74	25.3
Secondary school	198	31.3	73	29.3	95	32.5
College degree or higher	206	32.5	111	44.5	123	42.2
Marital status						
Married	510	80.5	210	84.3	241	82.5
Katz index of independence in activities of daily living*·**						
0–5	128	20.2	22	8.8	33	11.3
6	505	79.8	227	91.2	259	88.7
Charlson *et al.* comorbidity index score*·**						
<2	185	29.2	107	43	121	41.4
≥2	448	70.8	142	57	171	58.6
Number of chronic conditions*·**	2.8 ± 1.3 (1–7)[a]		2.3 ± 1.1 (1–7)[a]		2.3 ± 1.2 (1–6)[a]	
Main diseases[b]						
Hypertension	518	81.8	201	80.7	235	80.5
Diabetes	218	34.4	55	22.1	72	24.6
Chronic obstructive pulmonary disease	108	17.1	25	9.9	36	12.3
Medical specialist's visits*·**						
Median (range)	3 (0–10)		3 (0–10)		3 (0–10)	
Medications per day*·**						
Median (range)	4 (1–12)		3 (1–10)		3 (1–10)	
Pills per day*·**						
Median (range)	5 (1–18)		3 (1–16)		3 (1–16)	
Duration of pharmacological treatment (years)	6.9 ± 4.8 (1–35)[a]		6.8 ± 4.7 (1–25)[a]		7.1 ± 4.9 (1–35)[a]	
Patients who have pill organizers*·**						
Yes	73	11.5	14	5.6	23	92.1
Physician as source of information about therapies for their chronic diseases*·**	314	49.6	144	57.8	168	57.5
Need of additional information about therapies for their chronic diseases*·**	203	32.1	62	24.9	69	23.6

a: Mean ± standard deviation (range).
b: Number for this item may exceeds the total number since patients could also have more than one disease.
*P-value ≤ 0.05 by comparison between adherent and non-adherent patients.
**P-value ≤ 0.05 by comparison between patients who have never forget to take medication and those who forget at least once to take medications.

(46.1%) of the patients have never forget to take medications over the 4 weeks preceding their medical specialist's visit. After multivariable logistic adjustments, the results regarding the patients who have never forget to take the medicines over the 4 weeks preceding their medical specialist's visit showed that, among the demographic characteristics, only educational level had a significant relationship with the outcome of interest. Those with secondary school (OR = 1.68; 95% CI 1.08–2.61) and with at least a college degree level of education (OR = 2.42; 95% CI 1.53–3.81) were more likely to remember to take the medicines than those with a primary school or lower level. Moreover, patients who have never forget to take the medicines were those who took a lower number of pills per day (OR = 0.79; 95% CI 0.75–0.84), those who did not use any pill organizers to remember to take the medicines (OR = 0.42; 95% CI 0.23–0.75), and those who did not need additional information about therapies for their chronic diseases (OR = 0.57; 95% CI 0.38–0.84) (Model 2 in Table 2).

Discussion

This study determined the level of adherence to prescribed medications and its predictors among adult people with chronic diseases and it has important implications to clinical practice and policy-making.

The comparison in the level of adherence with similar international literature from both developed and developing countries is difficult and the differences could be explained by the characteristics of the population, the data collection tools, operational definitions and measurements of adherence, and the disparities in health care systems such as, for example, access to health care and drug dispensing regulations. Comparisons with previous research across countries that have used the MMAS-4 indicated that the prevalence of adherence of 39.3% found in this study was consistent with the 42.5% in community-dwelling patients with schizophrenia in the US,[7] the 41.3% in a community patient cohort with cardiovascular risk factors who are at risk of developing heart failure in Ireland,[30] and the 37% in patients from a subspecialty epilepsy clinic attended by predominantly ethnic minority in the US.[8] The finding of the current study was higher than the 18% in patients with chronic conditions in Spain [19] and the 4.6% in adults with epilepsy in China.[31] High prevalence for the adherence to their medication regimens has been documented for interferon β-1b therapy among patients with multiple sclerosis in Spain with a value of 68.3%,[32] in a secondary care setting in Northern Ireland [18] and in Hungary [17] among chronic obstructive pulmonary disease patients with values of 60.5% and 58.2%, in patients under oral chronic medication treatment in community pharmacy settings in Turkey with 58%,[33] and in those with epilepsy in Vietnam with 57.6%.[34]

Table 2 Multivariate logistic regression analyses indicating associations between several variables and the different outcomes regarding medication adherence

Variable	OR	SE	95% CI	P-value
Model 1. Adherence to the medications over the 4 weeks preceding their medical specialist's visit (sample size = 633)				
Log likelihood = −344.88, χ^2 = 158.74 (9 df), P < 0.0001				
Educational level				
Primary school or lower	1[a]	–	–	–
College degree or higher	2.05	0.41	1.37–3.06	<0.001
Number of pills per day	0.75	0.05	0.66–0.87	<0.001
Having pill organizers	0.26	0.08	0.13–0.5	<0.001
Katz index of independence in activities of daily living	1.8	0.51	1.03–3.15	0.04
Need of additional information about therapies for their chronic diseases	0.69	0.14	0.46–1.03	0.07
Physician as source of information about therapies for their chronic diseases	1.37	0.26	0.95–1.98	0.09
Gender	1.31	0.25	0.89–1.91	0.16
Disease category with higher duration				
Cardiovascular diseases	1[a]	–	–	–
Bronchopulmonary diseases	0.73	0.2	0.42–1.25	0.25
Number of medications per day	1.08	0.09	0.91–1.29	0.39
Model 2. Patient who have never forget to take the medications over the 4 weeks preceding their medical specialist's visit (sample size = 633)				
Log likelihood = −359.49, χ^2 = 154.74 (7 df), P < 0.0001				
Number of pills per day	0.79	0.02	0.75–0.84	<0.001
Educational level				
Primary school or lower	1[a]	–	–	–
College degree or higher	2.42	0.56	1.53–3.81	<0.001
Secondary school	1.68	0.37	1.08–2.61	0.02
Having pill organizers	0.42	0.12	0.23–0.75	0.003
Need of additional information about therapies for their chronic diseases	0.57	0.11	0.38–0.84	0.005
Physician as source of information about therapies for their chronic diseases	1.41	0.25	0.98–2.01	0.06
Gender	1.24	0.23	0.86–1.79	0.25

a: Reference category.

The results of the multiple logistic regression analysis highlights the important effect that several factors may have in the adherence of patients with chronic diseases. The adherence to the medications over the 4 weeks preceding their medical specialist's visit was significantly higher among patients with the highest level of education when compared with those less educated. This is consistent with previous studies.[35,36] Moreover, people more educated were more likely to remember to take the medicines. In addition, medication-adherent patients took significantly a lower number of pills per day and this is in accordance with other research.[17,19,35] A possible explanation of this result is that when patients have to take a lower number of pills, they are less likely to forget to take them and hence become more cautious with their treatment. Moreover, the finding that patients who never forget to take their medications do not need additional information about therapies for their chronic diseases may be explained by the fact that they knew more completely their medications and that they should not discontinue the therapies.

Caution is required in interpreting the findings of this study in light of some limitations. The first limitation is linked to the adopted cross-sectional survey design, whereby claims about the directionality of causal relationships between the dependent and independent variables cannot be verified. Second, the use of self-report data and potential inaccurate participant report should be taken into consideration in interpreting the results. This means that the prevalence of adherence tend to be overestimated because some persons may be affected by forgetfulness and recall errors, patients do not know which medicines they used as their drug use is controlled by someone else, or some persons would be reluctant to confess openly that they have forget to take the medicines. To minimize the underestimation possibility, the medication adherence was measured over a short period of time of the 4 weeks preceding the clinic visit of the patient. Third, the administration of the questionnaire through face to face interview may increase likelihood of respondents' inclination to give socially acceptable answers. Although the nature of the study was not sensitive, this bias was reduced by ensuring confidentiality and privacy of the respondents. Despite this study endures these potential weaknesses, its strength is that assessed not only medication adherence, but also its relationship to several factors. Moreover, this sample was enriched by a high response rate, which provides a fairly good representation of the targeted population. Nevertheless, given that there is a paucity of previous research regarding the prevalence of non-adherence medicines on patients with chronic diseases in Italy, we strongly believe that these data contributes to increasing the knowledge about the topic in this population.

In conclusion, the results of this study provide evidence about the frequency of non-adherence to prescribed medications in individuals affected by chronic diseases. The findings emphasize the need for improving information for the people affected by chronic diseases concerning the risks of non-adherence in order to encourage responsible behaviour to prescribed medications. Health professionals, especially primary care physicians, have a crucial role to develop education programs aligned with the needs of these individuals.

Acknowledgements

Key points

- A key component in the management of a patient with chronic health problems is the assessment of its adherence with therapeutic regimen. Low levels of patient adherence

with disease plans compromise the effectiveness of medical conditions therapies.

- Patients with a college degree or higher level of education, with higher score of the Katz index, who took a lower number of total pills per day, and who did not use any pill organizers were more likely to adhere to prescribed medication for their chronic diseases.

- The results of this study provide evidence about the frequency of non-adherence to prescribed medications in individuals affected by chronic diseases. The findings emphasize the need for improving information for the people affected by chronic diseases concerning the risks of non-adherence in order to encourage responsible behaviour to prescribed medications. Health professionals, especially primary care physicians, have a crucial role to develop education programs aligned with the needs of these individuals.

References

1   Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;353:487–97.

2   Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care* 2005;43:521–30.

3   Jamous RM, Sweileh WM, Abu-Taha AS, et al. Adherence and satisfaction with oral hypoglycemic medications: a pilot study in Palestine. *Int J Clin Pharm* 2011;33:942–8.

4   Ahmad NS, Ramli A, Islahudin F, Paraidathathu T. Medication adherence in patients with type 2 diabetes mellitus treated at primary health clinics in Malaysia. *Patient Prefer Adherence* 2013;7:525–30.

5   Dunlay SM, Eveleth JM, Shah ND, et al. Medication adherence among community-dwelling patients with heart failure. *Mayo Clin Proc* 2011;86:273–81.

6   Wu JR, Lennie TA, Dekker RL, et al. Medication adherence, depressive symptoms, and cardiac event-free survival in patients with heart failure. *J Card Fail* 2013;19:317–24.

7   DiBonaventura M, Gabriel S, Dupclay L, et al. A patient perspective of the impact of medication side effects on adherence: results of a cross sectional nationwide survey of patients with schizophrenia. *BMC Psychiatry* 2012;12:20.

8   Nakhutina L, Gonzalez JS, Margolis SA, et al. Adherence to antiepileptic drugs and beliefs about medication among predominantly ethnic minority patients with epilepsy. *Epilepsy Behav* 2011;22:584–6.

9   Sweileh WM, Ihbesheh MS, Jarar IS, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. *Epilepsy Behav* 2011;21:301–5.

10 De las Cuevas C, Peñate W, Sanz EJ. Risk factors for non-adherence to antidepressant treatment in patients with mood disorders. *Eur J Clin Pharmacol* 2014;70:89–98.

11 Cooper DC, Trivedi RB, Nelson KM, et al. Antidepressant adherence and risk of coronary artery disease hospitalizations in older and younger adults with depression. *J Am Geriatr Soc* 2014;62:1238–45.

12 Hashmi SK, Afridi MB, Abbas K, et al. Factors associated with adherence to antihypertensive treatment in Pakistan. *PLoS One* 2007;2:e280.

13 Li WW, Kuo CT, Hwang SL, Hsu HT. Factors related to medication non-adherence for patients with hypertension in Taiwan. *J Clin Nurs* 2012;21:1816–24.

14 Holt E, Joyce C, Dornelles A, et al. Sex differences in barriers to antihypertensive medication adherence: findings from the cohort study of medication adherence among older adults. *J Am Geriatr Soc* 2013;61:558–64.

15 Lee GKY, Wang HHX, Liu KQL, et al. Determinants of medication adherence to antihypertensive medications among a Chinese population using Morisky medication adherence scale. *PLoS One* 2013;8:e62775.

16 Wang W, Lau Y, Loo A, et al. Medication adherence and its associated factors among Chinese community-dwelling older adults with hypertension. *Heart Lung* 2014;43:278–83.

17 Agh T, Inotai A, Meszaros A. Factors associated with medication adherence in patients with chronic obstructive pulmonary disease. *Respiration* 2011;82:328–34.

18 Khdour MR, Hawwa AF, Kidney JC, et al. Potential risk factors for medication non-adherence in patients with chronic obstructive pulmonary disease (COPD). *Eur J Clin Pharm* 2012;12:1279–85.

19 Jansà M, Hernández C, Vidal M, et al. Multidimensional analysis of treatment adherence in patients with multiple chronic conditions. A cross-sectional study in a tertiary hospital. *Patient Educ Couns* 2010;81:161–8.

20 Tsai KT, Chen JH, Wen CJ, et al. Medication adherence among geriatric outpatients prescribed multiple medications. *Am J Geriatr Pharmacother* 2012;10:61–8.

21 Rajpura J, Nayak R. Medication adherence in a sample of elderly suffering from hypertension: evaluating the influence of illness perceptions, treatment beliefs, and illness burden. *Manag Care Pharm* 2014;20:58–65.

22 Hashmi SK, Afridi MB, Abbas K, et al. Factors associated with adherence to anti-hypertensive treatment in Pakistan. *PLoS One* 2007;14:e280.

23 Sirey JA, Weinberger MI, Greenfield A, Bruce ML. Medication beliefs and self-reported adherence among community-dwelling older adults. *Clin Ther* 2013;35:153–60.

24 Kronish IM, Diefenbach MA, Edmondson DE, et al. Key barriers to medication adherence in survivors of strokes and transient ischemic attacks. *J Gen Intern Med* 2012;28:675–82.

25 Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc* 1983;31:721–7.

26 Charlson ME, Pompei P, Ales KL, McKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.

27 Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;1:67–74.

28 Natarajan N, Putnam W, Van Aarsen K, et al. Adherence to antihypertensive medications among family practice patients with diabetes mellitus and hypertension. *Can Fam Physician* 2013;59:e93–100.

29 Stata Corporation. Stata Reference Manual Release 10.1. College Station, TX, USA, 2007.

30 Bermingham M, Hayden J, Dawkins I, et al. Prospective analysis of LDL-C goal achievement and self-reported medication adherence among statin users in primary care. *Clin Ther* 2011;33:1180–9.

31 Tang F, Zhu G, Jiao Z, et al. Self-reported adherence in patients with epilepsy who missed their medications and reasons for nonadherence in China. *Epilepsy Behav* 2013;27:85–9.

32 Fernández O, Agüera E, Izquierdo G, et al. Adherence to interferon β-1b treatment in patients with multiple sclerosis in Spain. *PLoS One* 2012;7:e35600. Correction in *PLoS One* 2012;7:10.

33 Okuyan B, Sancar M, Izzettin FV. Assessment of medication knowledge and adherence among patients under oral chronic medication treatment in community pharmacy settings. *Pharmacoepidemiol Drug Saf* 2013;22:209–14.

34 Harimanana A, Chivorakul P, Souvong V, et al. Is insufficient knowledge of epilepsy the reason for low levels of healthcare in the Lao PDR? *BMC Health Serv Res* 2013;13:41.

35 Al-Qazaz HKH, Sulaiman SA, Hassali MA, et al. Diabetes knowledge, medication adherence and glycemic control among patients with type 2 diabetes. *Int J Clin Pharm* 2011;3:1028–35.

36 Paschal AM, Rusha SE, Sadler T. Factors associated with medication adherence in patients with epilepsy and recommendations for improvement. *Epilepsy Behav* 2014;31:346–50.