Beliefs about medicines and non-adherence in patients with stroke, diabetes mellitus and rheumatoid arthritis: A cross-sectional study in China

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Abstract

Objectives: To investigate beliefs about medicines and their association with medicine adherence in patients with chronic diseases in China.

Design: A cross-sectional questionnaire-based study

Setting: Two large urban hospitals in Hefei and Tianjin, China

Participants: Hospital inpatients (313 stroke patients) and outpatients (315 diabetic patients and 339 rheumatoid arthritis (RA) patients) were recruited between January 2014 and September 2014.

Outcome measures: The Beliefs about Medicines Questionnaire (BMQ), assessing patients' beliefs about the specific medicine (Specific-Necessity and Specific-Concerns) prescribed for their conditions (stroke/diabetes/RA) and more general background beliefs about pharmaceuticals as a class of treatment (BMQ-General Benefit, Harm and Overuse); the Perceived Sensitivity to Medicines scale (PSM) assessed patients' beliefs about how sensitive they were to the effects of medicines and the Medication Adherence Report Scale. The association between non-adherence and beliefs about medicines was assessed using a logistic regression model.

Results: Patients with diabetes mellitus had a stronger perceived need for treatment [mean (SD) Specific-Necessity score, 3.75 (0.40)] than patients with stroke [3.69 (0.53)] and RA [3.66 (0.44)] (p=0.049). Moderate correlations were observed between Specific-Concerns and General-Overuse, General-Harm and PSM (Pearson correlation coefficients, 0.39, 0.49 and 0.49, respectively, p<0.01). 311 patients were non-adherent to their medicine [159 (51.0%) in the stroke group, 60 (26.7%) in the diabetes mellitus group and 62 (19.8%) in the RA group, p<0.01]. Across the whole sample, after adjusting for demographic characteristics non-adherence was associated with patients who had higher concerns about their medicines (OR,

1.35, 95% CI 1.07-1.71) and patients who believed that they were personally sensitive to the effects of medications (OR 1.44, 95% CI 1.16-1.85).

Conclusion: The BMQ is a useful tool to identify patients at risk of non-adherence. In future, adherence intervention studies may use the BMQ to screen for patients who are at risk of non-adherence and to map interventional support.

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Strengths and limitations of this study

- First large study of beliefs about medicines in China
- High response rate, reflecting generalisability of the study finding
- A cross-sectional design implicating that the association between non-adherence and beliefs about medicines did not necessarily lead a causal relationship.
- Self-reported adherence may not be the best measurement for medicine adherence.

Introduction

Medicine plays an essential role in chronic disease management. However, it is recognised that only half of patients with chronic diseases take their medicines as prescribed. Stroke, diabetes mellitus and rheumatoid arthritis (RA) are three common chronic diseases which together affect over 10% of China's population of 1.40 billion. Stroke is the leading cause of adult death and disability in China with an annual mortality rate of approximately 1.6 million, or 157 per 100,000. Patients with chronic diseases often require multiple medicine treatments for their conditions and any associated symptoms and comorbidities. To obtain full benefit from treatment, patients need to adhere to these complex medicine regimens in order to control their disease and maintain health. However, in reality medicine management is sub-optimal and relates to physician inertia and patients' poor adherence with therapy. The elderly, with high rates of co-morbidity and co-prescribing, tend to have poor adherence and are at particular risk of unwanted adverse effects from drugs. Sec.

Studies outside China have identified patients' beliefs about medicines as an important determinant of non-adherence. A recent meta-analysis of 96 peer-reviewed studies involving over 24,000 patients across 24 long-term conditions and 18 countries showed that non-adherence was related to patients beliefs about medicines, measured by the Beliefs about Medicines Questionnaire (BMQ). These studies indicated that there was often a disconnect between the patients and prescribers view of the medicine. Many patients doubted their personal need for the treatment or harboured concerns and these beliefs are associated with non-adherence. Beliefs about medicines may also be relevant in China, particularly as there some evidence that trust between patients and health professionals may have diminished after China's economic reform. Patients often do not trust their doctors and doubt the treatment including therapeutic treatment they received. It is possible that this may translate into

scepticism about prescribed medicines and non-adherence. The aim of this study was to understand beliefs about medicines in Chinese patients with stroke, diabetes mellitus and RA and to investigate whether these beliefs are associated with medicine non-adherence.

Methods

A cross-sectional study was conducted in two large teaching hospitals in China between January 2014 and November 2014. The study was approved by the local research ethics committees.

Study populations and recruitment

Patients with stroke were recruited from The Second Hospital, Tianjin Medical University, Tianjin, China and patients with diabetes mellitus and RA were recruited from Anhui Provincial Hospital, Anhui Medical University, Hefei, China. Both hospitals are large teaching hospitals and are level 3 general hospitals, the highest classification for quality care given by the China's National Health and Family Planning Commission (NHFPC) for all public hospitals. Patients who had a clinical diagnosis of stroke, diabetes mellitus or RA who were judged by the healthcare professionals as able to answer questions were invited by the healthcare professionals to take part in the study when they were admitted to hospital (stroke patients) or came to hospital clinics (diabetic and RA patients) during the study period. Some patients may have co-morbidity. However, they were only included for the condition they were hospitalised or the condition from the specific outpatient clinics. They were asked to complete a questionnaire which took approximately 10-15 minutes. Study information was given to patients and verbal consent was obtained before they started to fill in the questionnaire. All invited patients returned their questionnaires. Since there is a lack of research on beliefs about medicines and medicine non-adherence in China, a target sample

size of 300 patients for each condition was chosen based on typical sample sizes used in similar surveys. A recent meta-analysis showed that small-moderate effect of psychological beliefs on medicine adherence was observed in 94 studies with an average sample size of 266. Data collection started in January 2014 and lasted around 4 months for each condition and was stopped once the target numbers were reached (November 2014).

Questionnaire measurement

The questionnaire consisted of demographic information, the BMQ questionnaire, ¹⁴ perceived sensitivity to medicines scale (PSM) and medicine adherence report scale (MARS). ¹⁵ All scales were translated and back translated in accordance with the Originator's conditions to create a Chinese version, (BMQ-Chinese © R Horne MARS-Chinese © R Horne, PSM-Chinese © R Horne). The BMQ and MARS were translated into Chinese by Dr Li Wei, the principal investigator for this study. They were then sent to the co-authors, Profs Xiaomei Li and Xin Li for comments and further adaptation resulting in a final Chinese version of the BMO.

Demographic information included name, age, gender, education, occupation and duration of the condition. The BMQ questionnaire has two parts: the BMQ-Specific assessing beliefs about medicine used for a particular condition and the BMQ-General assessing beliefs about medicines in general. The details of the BMQ questionnaire can be found in a previous publication. In brief, BMQ-Specific comprised two scales: a 5-item treatment necessity scale Specific-Necessity and a 6-item treatment concern scale Specific-Concern. BMQ-General used three subscales: 1) General-Overuse (4 items), 2) General-Harm (4 items), and 3) General-Benefit (4 items). Perceived Sensitivity to Medicines (PSM) scale contained 5 items assessing perceptions of personal susceptibility to the effects of medicines. All BMQ items

and PSM were scored on a Likert type scale (where 1 = strongly disagree, 2 = disagree, 3 = uncertain, 4 = agree and 5 = strongly agree). A mean item score was then calculated as the sum of each item score divided by the number of items [for example, mean score of Specific-Necessity= (N1+N2+N3+N4+N5)/5]. The Cronbach's α s indicated that all scale measures were internally consistent in the study sample¹⁶ with high value of $\alpha_{psm} = 0.85$, $\alpha_{concern} = 0.75$ and $\alpha_{necessity} = 0.64$, and low values of $\alpha_{overuse} = 0.54$, $\alpha_{harm} = 0.55$ and $\alpha_{benefit} = 0.58$. For BMQ-Specific, patients were only asked for the treatment prescribed for the diagnosed condition in the past 12 months. Medicine adherence was measured for the same period using the MARS scale consisting of 5 items with 25 score points in total. For example, one item is "I forget to take them".

Before the study commenced, 30 people including doctors, nurses, medical students and patients were asked to complete the questionnaire to assess whether the Chinese version of the BMQ, PSM and MARS would be easily understood by Chinese patients. Feedback was wholly positive; however we recognised that patients were likely to be elderly and may have poor literacy. Therefore, arrangements were made to provide help should patients have any difficulty completing the questionnaire. Patients in both centres completed the questionnaire either by themselves or with help from the healthcare professionals in the medical ward or clinic they attended. Healthcare professionals received a briefing from the local investigators on how to complete the questionnaire including instructions on how to explain the meaning of the questionnaire items without influencing patients' responses.

Definition of adherence and non-adherence

It is commonly accepted that it is not necessary to take 100% of a prescribed treatment, and 80% adherence is a commonly used cut-off to define adherence, especially in medicine

benefit/safety studies.¹⁷ While the MARS scale does not allow direct assessment of the percentage of prescribed treatment taken, we used a cut-off of 20 out of 25 on this scale to define adherence, indicating that patients are taking a large proportion of their prescribed doses. Adherence was calculated as sum of the scores from each item divided by the maximum points of 25 using the 5-item MARS scale. Non-adherent patients were defined as having a score <80% adherence to medicine.

Attitudinal analysis

Participants were categorized into attitudinal groups (i.e. Skeptical, Ambivalent, Indifferent and Accepting groups) based on whether they scored above or below the scale midpoint for BMQ necessity and concerns scales. Non-adherence was investigated between the groups.¹⁷

Statistical analysis

Data were presented as mean (SD) for continuous variables and as frequencies (%) for categorical variables. Chi-squared and analysis of variance (ANOVA) tests were performed to determine significant differences between the three diseases. Correlations were used to examine relationships between BMQ-General and BMQ-Specific subscales. Logistic regression analysis was employed to assess the association between non-adherence and medicine beliefs. Five percent of patients had at least one missing value in their BMQ answers and the total missing values were 0.3% for the whole BMQ items. A sensitivity analysis was done to include all patients with missing data replaced with imputed data in the multivariable analysis concluding all variables listed in Table 1. The multiple imputation analysis included all variables used in the final analysis with 10 imputations by using the Markov Chain Monte Carlo method to produce imputed data. All statistical analyses were carried out using SAS (version 9.4).

Results

Patient characteristics

There were 967 patients in the study (313 with stroke, 315 with diabetes mellitus and 339 with RA). Table 1 shows the demographic and clinical information by disease groups. Patients with RA were significantly younger than patients with stroke and diabetes mellitus (mean age 49.7 vs 65.8 and 62.5, respectively). The RA group was 85% female while only 44% of stroke patients and 45% of diabetes mellitus patients were female. Patients with RA were 5 times more likely to report having received no formal education than patients with stroke and diabetes mellitus (23.3% vs 4.8% and 4.1%, respectively). Over half of patients in the stroke group had less than 1 year disease duration while more than half of the patients in the RA and diabetes mellitus groups had more than 5 years disease duration.

BMQ results

The results of BMQ subscales are shown in Table 2. There were no significant differences in the mean scores of Specific-Concerns and General-Harm between the three groups. However, differences were observed for Specific-Necessity, General-Overuse, General-Benefit and PSM among the three groups. Patients with RA had the highest score of 3.75 (SD 0.40) for Specific-Necessity and lowest scores of 2.95 (SD 0.51) for General-Overuse and 3.55 (SD 0.45) for General-Benefit. The mean scores of PSM were 2.89 (SD 0.65), 2.35 (SD 0.64) and 2.70 (SD 0.68). The attitudinal analysis categorised patients into four groups (high/low necessity and high/low concerns) according to the midpoint of the Specific-Necessity Specific-Concerns scales shows that 45% of patients were classified as 'Ambivalent', 45% as 'Accepting', 4% as 'Skeptical' and 6% as 'Indifferent' (Figure 1).

Patients' general beliefs about medicines were associated with their evaluations of the specific treatments they were taking. Table 3 shows the correlation between BMQ-General and BMQ-Specific. Specific-Necessity was positively associated with General-Benefit (Pearson correlation coefficients = 0.31, p<0.01). Moderate correlations were observed between Specific-Concerns and General-Overuse, General-Harm and PSM (Pearson correlation coefficients, 0.39, 0.49 and 0.49, respectively, p<0.01). General-Overuse was also correlated with General-Harm and PSM (Pearson correlation coefficients, 0.45 and 0.39, respectively, p<0.01). The Pearson correlation coefficient was 0.39 (p<0.01) for General-Harm and PSM.

Association between beliefs about medicines and non-adherence

Three hundred and eleven patients were non-adherent to their medicine [159 (51.0%) in the stroke group, 60 (26.7%) in the diabetes mellitus group and 62 (19.8%) in the RA group, p<0.01]. After adjusting for demographic characteristics, Specific-Concerns and PSM were significantly associated with non-adherence (adjusted ORs, 1.35, 95% CI 1.07-1.71 and 1.44, 95% CI 1.16-1.80). Negative associations between non-adherence and Specific-Necessity and General-Benefit were not statistically significant (Table 4). The subgroup analyses showed that the point estimates of Specific-Concerns were positively associated with non-adherence across the three conditions i.e. the more concerns about the medicines, the more non-adherent to medicines, with adjusted ORs ranging from 1.15 (95% CI 0.67-1.98) for diabetes mellitus to 1.43 (95% CI 1.02-2.00) for stroke (Table 5). The unadjusted results showed similar results across the three disease conditions. The sensitivity analysis showed that Specific-Concerns and PSM were positively associated with non-adherence (adjusted ORs, 1.15 95% CI 1.04-1.26 and 1.40, 95% CI 1.04-1.26, respectively) and General-Benefit was negatively associated with non-adherence (adjusted OR 0.79, 95% CI 0.71-0.87). Compared with

patients in the Accepting group, patients in the other attitudinal groups were more likely to be the non-adherent (adjusted ORs, 1.50 95% CI 1.10-2.05 for the Ambivalent group, 1.27 95% CI 0.60-2.68 for the Skeptical group and 1.27 95% CI 0.69-2.34 for the Indifferent group. Only patients in the Ambivalent group showed a statistical significance.

Discussion

This is the first large study of this kind that investigates beliefs about medicines and medicine non-adherence in China in three common chronic diseases. Both unadjusted and adjusted results revealed that Specific-Concerns and PSM were significantly associated with non-adherence i.e. the higher the concern about the medicine or the higher perceived sensitivity to medicines. Using the continuous MARS-5 scores showed similar relationships to those reported in logistic regression (r=-0.09, p<0.01 for Specific-Concerns and r=-0.09, p<0.01 for PSM). We noted differences between groups that might indicate different attitudes towards the diseases and their treatments or be attributable to other factors. The hospital out-patients (diabetes mellitus and RA) included some patients who had previous hospitalisations and come back to hospital for regular monitoring.

Our findings were consistent with the evidence from a recent meta-analysis which showed that higher adherence was associated with fewer concerns about treatment ¹⁰ but not consistent with previous findings that higher belief in personal need for treatment was associated with higher adherence; Specific-Necessity was not associated with non-adherence in our overall analysis. Subgroup analyses showed that patients with stroke and diabetes mellitus showed the same direction association as previous studies i.e, patients with higher necessity were less likely to be non-adherent. However, an opposite non-statistically significant result of Specific-Necessity and adherence for patients with RA (Our result of 1.34 (95% CI 0.73-2.46) for non-adherence equals 0.75, 95% CI 0.41-1.38 for adherence) was observed in the

study in comparison with the meta-analysis result which had a pooled OR of 3.28, 95%CI 1.11-9.71 for adherence. 10 The point estimate could be due to chance and further studies need to confirm the finding. A recent study found that General-Benefit may be negatively associated with non-adherence among 398 patients with epilepsy from the UK primary care population (adjusted OR, 0.92, 95%CI 0.63-1.34)¹⁸ and this association was confirmed by our study with a borderline significant OR of 0.75 (95%CI 0.56-1.02). There was no correlation between Necessity and Concern (Table 2) in our study population and this was supported by a recent Swedish study conducted in 578 stroke patients.¹⁹ They reported a Spearman's correlation coefficient of 0.075 (p=0.08). Compared to patients with high necessity and low concerns, patients with high necessity and high concerns, low necessity and high concerns, and low necessity and low concerns were all associated with non-adherence and this was supported by studies conducted in patients with inflammatory bowel disease and renal dysfunction. ^{20 21} High perceived sensitivity to medicines was reported to be associated with non-adherence and higher medical care utilisation, increased symptom reporting and greater information-seeking about medication. 18, 22 Our study also showed PSM was associated with non-adherence.

Our study has some strengths. Firstly, this was the first large BMQ study conducted in China. Secondly, we choose two large teaching hospitals for this study and collected data continually until the target numbers were reached for each condition. Therefore, our study population was more likely to represent the disease population from each region as large teaching hospitals provide health care service to majority of Chinese patients. However, we acknowledge that some patients with Transient Ischemic Attacks (TIAs), a subtype of stroke may not be admitted to hospital. Therefore our stroke in-patients may under represent the TIA patients. Thirdly, China has higher prevalence rates of stoke and diabetes mellitus than Western Europe and stroke is also the leading cause of death in China. In light of the current

deteriorated relationship between health professional and patients (i.e. patients do not trust their doctors and other health professionals, doctors, nurses are often abused verbally and physically by patients, 11, 23, 24 more studies are needed from the patients' perspective. More consideration from the patient perspective should be taken into account in term of chronic disease management and the relationship between patients and health professionals. However, our study was an observational study. Therefore the results may be confounded by unmeasured factors such as comorbidity. Self-reported adherence may not be the best measurement for medicine adherence as patients may, for example, underestimate how often they forget their treatment. However, a strong correlation was found for medicine adherence measured by self-reported questionnaire, electronic prescriptions and serum biomarkers in a recent intervention study suggesting that self-report is a reliable measure. Also our study found relatively low reliability of the BMQ general scales and further investigation and refinement might be needed of these Chinese translations. The difference in non-adherence between stroke and other conditions needs to be explored in future studies as disease itself may play an important role in medicine adherence.

In conclusion, we found that the BMQ is a useful tool to identify psychological factors that are linked to non-adherence in patients with stroke, diabetes and RA. Future studies should use the BMQ to screen patients to identify those who are at high risk of non-adherence and map their treatment plan accordingly.

CONFLICT OF INTEREST/STUDY SUPPORT:

Specific author contributions: LW, RC and RH were involved in conception and design and interpretation of data. LW did the statistical analysis and wrote the first draft of the article. SC, RC and BN contributed to data analysis. LXM, LX and LSM collected data. SC, AC,

LXM, LX and LSM were involved in interpretation of data. All authors were responsible for re-drafting of the article and approved the final version.

Guarantor of the article: LW is the guarantor

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Potential competing interests: RH declares: (1) Speaker engagements with honoraria and consultancy payments from the pharmaceutical companies; (2) Founder and shareholder of a UCL-Business, university spin-out company (Spoonful of Sugar Ltd) providing consultancy on medication-related behaviours to healthcare policy makers, providers and industry; and (3) Originator of BMQ.

References:

- 1. Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence. https://www.nice.org.uk/guidance/cg76/chapter/introduction (accessed on 30 January 2017)
- 2. Liu L, Wang D, Wong KS, Wang Y. Stroke and stroke care in China: huge burden, significant workload, and a national priority. Stroke; a journal of cerebral circulation. 2011;42(12):3651-4.
- 3. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet. 2014;383(9913):245-54.

- 4. Li R, Sun J, Ren LM, Wang HY, Liu WH, Zhang XW, et al. Epidemiology of eight common rheumatic diseases in China: a large-scale cross-sectional survey in Beijing.

 Rheumatology (Oxford). 2012 Apr;51(4):721-9. doi: 10.1093/rheumatology/ker370. Epub 2011 Dec 16.
- 5. China Total population, 2015. http://www.who.int/countries/chn/en/ (accessed on 25 May 2017)
- 6. Wu X, Zhu B, Fu L, Wang H, Zhou B, Zou S, et al. Prevalence, incidence, and mortality of stroke in the chinese island populations: a systematic review. PLoS One. 2013 Nov 8;8(11):e78629. doi: 10.1371/journal.pone.0078629. eCollection 2013.
- 7. Will JC, Zhang Z, Ritchey MD, Loustalot F. Medication Adherence and Incident Preventable Hospitalizations for Hypertension. Am J Prev Med. 2016 Apr;50(4):489-99. doi: 10.1016/j.amepre.2015.08.021. Epub 2015 Oct 31.
- 8. Shore S, Carey EP, Turakhia MP, Jackevicius CA, Cunningham F, Pilote L, et al. Adherence to dabigatran therapy and longitudinal patient outcomes: insights from the veterans health administration. Am Heart J. 2014 Jun;167(6):810-7. doi: 10.1016/j.ahj.2014.03.023. Epub 2014 Apr 5.
- 9. Korhonen MJ, Ruokoniemi P, Ilomaki J, Meretoja A, Helin-Salmivaara A, Huupponen R. Adherence to statin therapy and the incidence of ischemic stroke in patients with diabetes. Pharmacoepidemiol Drug Saf. 2016 Feb;25(2):161-9. doi: 10.1002/pds.3936.
- 10. Horne, R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence –related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the necessity-concerns framework. Plos One. 2013 Dec 2;8(12)e80633. Doi:10.1371/journal.pone.0080633.
- 11. Tucker JD, Cheng Y, Wong B, Gong N, Nie JB, Zhu W, et al; Patient-Physician Trust Project Team. Patient-physician mistrust and violence against physicians in Guangdong

- Province, China: a qualitative study. BMJ Open. 2015 Oct 6;5(10):e008221. doi: 10.1136/bmjopen-2015-008221.
- 12. Chan CS, Cheng Y, Cong Y, Du Z, Hu S, Kerrigan A, et al. Patient-physician trust in China: a workshop summary. Lancet. 2016 Oct;388 Suppl 1:S72. doi: 10.1016/S0140-6736(16)31999-7.
- 13. National Health and Family Planning Commission of the PRC http://en.nhfpc.gov.cn/ (last access 30 January 2017)
- 14. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res. 1999 Dec;47(6):555-67.
- 15. Horne R. The nature, determinants and effects of medication beliefs in chronic illness (PhD thesis) University of London 1997.
- 16. Bland JM, Douglas G Altman, DG. Statistics notes: Cronbach's alpha. BMJ 1997; 314:572 doi: https://doi.org/10.1136/bmj.314.7080.572
- 17. Wei L, Wang J, Thompson P, Wong S, Struthers AD, MacDonald TM. Adherence to statin treatment and readmission of patients after myocardial infarction: a six year follow up study. Heart 2002;88:229-33.
- 18. Chapman SC, Horne R, Chater A, Hukins D, Smithson WH. Patients' perspectives on antiepileptic medication: relationships between beliefs about medicines and adherence among patients with epilepsy in UK primary care. Epilepsy Behav. 2014 Feb;31:312-20. doi: 10.1016/j.yebeh.2013.10.016. Epub 2013 Nov 27.
- 19. Sjolander M, Eriksson M, Glader EL. The association between patients' beliefs about medicines and adherence to drug treatment after stroke: a cross-sectional questionnaire survey. BMJ open. 2013;3(9):e003551.

- 20. Horne R, Parham R, Driscoll R, Robinson A. Patients' attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. Inflamm Bowel Dis. 2009 Jun;15(6):837-44. doi: 10.1002/ibd.20846.
- 21. Chater AM, Parham R, Riley S, Hutchison AJ, Horne R. Profiling patient attitudes to phosphate binding medication: a route to personalising treatment and adherence support. Psychol Health. 2014;29(12):1407-20. doi: 10.1080/08870446.2014.942663. Epub 2014 Aug. 22. Faasse K, Grey A, Horne R, Petrie KJ. High perceived sensitivity to medicines is associated with higher medical care utilisation, increased symptom reporting and greater information-seeking about medication. Pharmacoepidemiol Drug Saf. 2015 Jun;24(6):592-9. doi: 10.1002/pds.3751. Epub 2015 Apr 7.
- 23. Li ZG, Leng MX. Doctor-patient relationship research summary. Chinese Hospital Management. 2009;29(332):40-3.
- 24. Doctors face verbal abuse or violence. http://www.cmdae.org/en/index.php (Accessed 30 January 2017).
- 25. Lyons I, Barber N, Raynor DK, Wei L. The Medicines Advice Service Evaluation (MASE): a randomised controlled trial of a pharmacist-led telephone based intervention designed to improve medication adherence. BMJ Qual Saf. 2016 Oct;25(10):759-69. doi: 10.1136/bmjqs-2015-004670.

Table 1. Patient characteristics by conditions

	Stroke Diabetes		RA		
	n=313 (100%)	n=315 (100%)	n=339 (100%)		
Age, mean (SD) *	65.8 (13.7)	62.5 (13.9)	49.7 (12.8)		
Gender [†] *					
Women	136 (43.5%)	141 (44.8%)	287 (85.2%)		
Men	177 (56.5%)	174 (55.2%)	50 (14.8%)		
Education*					
Illiteracy (no formal	15 (4.8%)	13 (4.1%)	79 (23.3%)		
education)					
Primary school	66 (21.1%)	62 (19.7%)	93 (27.4%)		
Junior high school	60 (19.2%)	91 (28.9%)	91 (26.8%)		
High school/college	116 (37.1%)	77 (24.4%)	48 (14.2%)		
University or above	54 (17.2%)	70 (22.2%)	25 (7.4%)		
Unknown	2 (0.6%)	2 (0.6%)	3 (0.9%)		
Occupation*					
Farmer	5 (1.6%)	22 (7.0%)	110 (32.5%)		
Worker/clerk	83 (26.5%)	117 (37.1%)	38 (11.2%)		
Housewife/unemployment	45 (14.4%)	12 (3.8%)	113 (33.3%)		
Retirement	129 (41.2%)	54 (17.1%)	40 (11.8%)		
Health professional	19 (6.1%)	29 (9.2%)	15 (4.4%)		
Civil service	29 (9.3%)	72 (22.9%)	11 (3.2%)		
Unknown	3 (1.0%)	9 (2.9%)	12 (3.5%)		
Duration of the disease*					
<= 1 year	178 (56.9%)	20 (6.4%)	55 (16.2%)		
1-5 years	91 (29.1%)	74 (23.5%)	104 (30.7%)		
> 5 year	44 (14.1%)	220 (69.8%)	177 (52.2%)		
unknown	0 (0.0%)	1 (0.3%)	3 (0.9%)		

†Excluding missing data; *<0.05

Table 2. Results of BMQ and PSM by disease conditions

	Stroke	Diabetes	RA
	n=313	n=315	n=339
Specific-Necessity (mean, SD) †*	3.69 (0.53)	3.75 (0.40)	3.66 (0.44)
Specific-Concerns (mean, SD) [†]	3.03 (0.71)	3.15 (0.58)	3.07 (0.58)
General-Overuse (mean, SD) †*	3.22 (0.62)	3.12 (0.50)	2.95 (0.51)
General-Harm (mean, SD) †	2.94 (0.78)	2.95 (0.50)	2.99 (0.43)
General-Benefit (mean, SD) †*	3.70 (0.53)	3.69 (0.42)	3.55 (0.45)
PSM (mean, SD) †*	2.89 (0.65)	2.35 (0.64)	2.70 (0.68)
MARS score (mean, SD*)	18.81 (4.16)	21.51 (3.07)	21.47 (3.86)

[†]Excluding missing data; PSM=Perceived Sensitivity to Medicines; *<0.05

Table 3. Correlation matrix between BMQ-Specific, BMQ-General and PSM

	Necessity	Concerns Overuse		Harm	Benefit	PSM
Overall						
Necessity	1.00					
Concern	0.02(0.45)	1.00				
Overuse	-0.01 (0.87)	0.39 (<0.01)	1.00			
Harm	-0.05 (0.16)	0.49 (<0.01)	0.45 (<0.01)	1.00		
Benefit	0.31(<0.01)	-0.09 (0.01)	0.11 (<0.01)	0.04 (0.21)	1.00	
PSM	0.04 (0.22)	0.45 (<0.01)	0.39 (<0.01)	0.38<0.01)	0.05 (0.14)	1.00
Stroke						
Necessity	1.00					
Concern	0.04 (0.43)	1.00				
Overuse	0.06 (0.31)	0.50 (<0.01)	1.00			
Harm	-0.06 (0.27)	0.66 (<0.01)	0.57 (<0.01)	1.00		
Benefit	0.36 (<0.01)	0.01 (0.88)	0.24 (<0.01)	0.13 (0.12)	1.00	
PSM	0.23 (<0.01)	0.52 (<0.01)	0.51 (<0.01)	0.50 (<0.01)	0.22 (<0.01)	1.00
Diabetes me	llitus					
Necessity	1.00					
Concern	0.02 (0.59)	1.00				
Overuse	-0.05 (0.40)	0.26 (<0.01)	1.00			
Harm	-0.08 (0.20)	0.21 (<0.01)	0.44 (< 0.01) 1.00			
Benefit	0.19 (<0.01)	-0.07 (0.26)	0.18 (<0.01)	0.08 (0.19)	1.00	
PSM	-0.08 (0.20)	0.36 (<0.01)	0.38 (<0.01)	0.44 (<0.01)	0.07 (0.23)	1.00
RA						
Necessity	1.00					
Concerns	0.01 (0.91)	1.00				
Overuse	-0.08 (0.13)	0.41 (<0.01)	1.00			
Harm	0.02 (0.72)	0.42 (<0.01)	0.30 (<0.01)	1.00		
Benefit	0.30 (<0.01)	-0.21 (<0.01)	-0.20 (<0.01)	-0.15 (0.21)	1.00	
PSM	-0.04 (0.52)	0.54 (<0.01)	0.29 (<0.01)	0.27 (<0.01)	-0.13 (0.02)	1.00

Table 4. Odd ratios of medicine non-adherence

	Unadjusted	Adjusted*
	OR, 95% CI	OR, 95% CI
Specific-Necessity	0.90, 0.67-1.21	0.93, 0.68-1.27
Specific-Concerns	1.27, 1.02-1.58	1.35, 1.07-1.71
General-Overuse	1.32, 1.04-1.69	1.15, 0.88-1.50
General-Harm	1.09, 0.87-1.38	1.12, 0.89-1.43
General-Benefit	0.84, 0.63-1.12	0.75, 0.56-1.02
PSM	1.72, 1.41-2.09	1.44, 1.16-1.85

^{*}Adjusted for age, gender, education, occupation, duration of the disease and different diseases

Table 5. Odd ratios of medication non-adherence by disease groups

	Stroke		Diabetes			RA		
	Unadjusted	Adjusted*	Unadjusted	Adjusted*		Unadjusted	Adjusted*	
	OR, 95% CI	OR, 95% CI	OR, 95% CI	OR, 95% CI		OR, 95% CI	OR, 95% CI	
Specific- Necessity	0.83, 0.54-1.26	0.92, 0.59-1.43	0.71, 0.35-1.40	0.92, 0.43-1.97		1.31, 0.75-2.27	1.34, 0.73-2.46	
Specific- Concerns	1.43, 1.04-1.96	1.43, 1.02-2.00	1.16, 0.71-1.88	1.15, 0.67-1.98		1.38, 0.91-2.12	1.32, 0.84-2.10	
General- Overuse	1.26, 0.88-1.81	1.24, 0.85-1.82	1.12, 0.64-1.96	1.10, 0.61-2.00		1.06, 0.66-1.71	0.98, 0.60-1.60	
General- Harm	1.26, 0.95-1.68	1.30, 0.96-1.77	0.58, 0.32-1.05	0.59, 0.32-1.11		1.27, 0.72-2.24	1.27, 0.70-2.30	
General- Benefit	0.87, 0.57-1.32	0.83, 0.53-1.29	0.78, 0.41-1.50	0.83, 0.41-1.69		0.64, 0.37-1.09	0.65, 0.37-1.13	
PSM	1.76, 1.22-2.53	1.79, 1.23-2.60	1.60, 1.05-2.44	1.73, 1.10-2.70		1.06, 0.74-1.51	1.01, 0.70-1.48	

^{*}Adjusted for age, gender, education, occupation, duration of the disease

Figure legend

Figure 1. Attitudinal analysis of BMQ-Specific.