SENSITIVITY AND SPECIFICITY OF THAI-VERSION BRIEF MEDICATION QUESTIONNAIRE

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ABSTRACT: Self-reported medication adherence tools are useful to screen non-adherence and barriers to non-adherence of patients in clinical practice. Having a reliable tool would facilitate pharmacists in monitoring patient drug use behavior. The purposes of this study were to develop the Thai-version Brief Medication Questionnaire (BMQ) and to validate it by examining sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy using pill count method as the comparison. The study recruited 229 patients with at least one chronic condition of diabetic, cardiovascular disease, or dyslipidemia who have been on their prescriptions for at least 4 weeks. The medication adherence of each patient was measured by 2 methods, i.e., BMQ and pill count method, at patient's home approximately 2 weeks after receiving the most recent prescriptions. The results showed that the 7-item regimen screen of Thai-version BMQ had 100% sensitivity with 0.37% specificity for repeated non-adherence, and 100 % sensitivity with 0.27% specificity for sporadic non-adherence while the 6-item regimen screen had 59.26-62.04% sensitivity with 82.68-86.31% specificity for repeated non-adherence, and 22.65-29.13% sensitivity with 80.51-82.35% specificity for sporadic non-adherence. Kappa coefficient revealed the high relationship between 7-day and 14-day patient reports on non-adherence at 0.861 (95% CI 0.816 - 0.907). In conclusion, the Thai-version of BMQ could be used to detect patient medication non-adherence both repeated and sporadic.

Keywords: medication adherence tool, self-report, validity, sensitivity, specificity

INTRODUCTION: Patient medication non-adherence of chronic conditions increases mortality and morbidity rates. Non-adhered patients with hypertension are reported having higher cardiovascular complication rate and cardio-vascular-related death rate than adhered patients. Non-adherence to HMG-Co A reductase inhibitor after hospitalization for myocardial infarction is associated with increasing mortality rate[1)]. Non-adherence of type II diabetic patients is significantly more likely to be hospitalized[2)]. Adherence to the medical regimen is an important factor contributing to treatment success. Previous studies reported the low average adherence rate of 37 to 78 percent among patients with chronic diseases was caused by several barriers including forgetfulness, complex regimens, lack of knowledge about disease and treatment, adverse drug reaction, and negative beliefs in medication[3,4)]. Many methods have been suggested for measuring patient's medication adherence such as directly observed therapy, drug or metabolite level in blood measurement, Medication Electronics Monitoring (MEMS), pill count, patient self-reports rates of prescription refills, and others[5)]. Each method has its advantages and disadvantages but no method is regarded as the gold standard. Directly observed therapy is inconvenient for measuring adherence in clinical practice since it is time consuming and requires more manpower[5,6)]. Adherences detected via the drug or metabolite measurement method are interfered by pharmacokinetics factors such as the variation of metabolic rate of each patient and food-drug interaction. The drug or metabolite measurement method could only measure medication adherence for short interval and involves complicated process of blood or urine collection[7-9)]. Pill counts obtaining good quantitative data still need patients' cooperation to bring their pills to the hospital[6,10)]. Self-reports using questionnaires are simple, fast, inexpensive, and able to detect medication adherence barriers. However, adherence measured from self-reports is subjective data. Untested tools can have poor validity due to response biases from socials desirability, fearing the consequences, memory,

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language, and timeframe of assessment such as using long timeframe or unspecified recall period [6,9,11-13]. Previous studies found that self-report tools had 14-100 percent sensitivity and 30-100 percent specificity by using MEMS or pill count as the standard method[14-18]. BMQ is a high sensitivity and specificity self-report tool for screening non-adherence patients and useful in exploring adherence problems from different causes including complex regimen, patient negative belief, and difficulty of recall[18]. Svarstad and colleagues (1999) have reported 80% sensitivity and 100% specificity of BMQ when used to detect repeated non-adherence in patients with at least 20 percent over or under use of prescribed medication[18].

To date, there is no Thai-version BMQ for screening non-adherence in patients with chronic disease. The purpose of this study was to develop and validate Thai-version BMQ in chronic patients.

METHODS:

Instrumentation

The original English version BMQ was forward translated with permission into Thai language and reconciled by two Thai translators together with a coordinator. The reconciled forward BMQ was backward translated into English by a bilingual English speaking native to confirm equivalent of two forms. The Thai-version BMQ was then cognitive debriefed with 30 Thai chronic patients before the final Thai-version BMQ was further validated.

BMQ was a 4-part medication adherence tools including (1) regimen screen (2) belief screen (3) recall screen and (4) access screen. The regimen screen consisted of 7 items checking how and whether patients took the medication according to what was prescribed. The original version BMQ asked patients to recall back for 7 days however, in this study the patients were asked to think back for both 7 days and 14 days. The belief screen, the recall screen, and the access screen contained 2 items each to detect different types of barriers to medication non-adherence. For each medication, patients answering yes to at least 1 item in any part were screened as positive for non-adherence.

Participants

To test the sensitivity and specificity of the Thai-version BMQ, 229 patients from chronic outpatient Sattahip Primary Care Unit were enrolled into the study. Inclusion criteria are patients with at least 1 disease of diabetic, cardiovascular disease, or dyslipidemia and being prescribed medications for chronic conditions including antihypertensive drug or antidiabetic drug for at least 4 weeks. Patients who consented to participate in the study after receiving their prescribed medications were given the instruction to start taking refilled medications from the new bottles. They were also told in advance that the follow up interview would be conducted at their home by the researcher after 2 weeks.

Adherence measurement by pill count method

The patients were face to face interviewed for their medication adherence using BMQ approximately 2 weeks after enrollment. After the interview, the researcher also counted medications remained in the bottles as another measure of patients' adherence. Medication adherence measuring from the pill count method was calculated as percentage of medication adherence and absolute percentage of medication non-adherence using the following formulas:

$$\%\ \text{medication adherence} = \frac{(\text{amount of tablets received} - \text{amount of tablets remained})}{\text{amount of tablets should be taken}} \times 100$$

$$\%\ \text{medication non-adherence} = |100 - \%\ \text{medication adherence}|$$

Data analysis

The participants' characteristics were analyzed using descriptive statistics. Validity of the Thai-version BMQ was assessed by sensitivity, specificity, positive predictive value (PPV), and accuracy (formulas as shown in table 1). Kappa coefficient was calculated to determine level of agreement of patients' self-reports on missed doses during 7-day and 14-day recall periods. The statistical package for social science (SPSS) software, version 13.0 for Windows® was used in all analyses.

RESULTS:

Patients' characteristics

From 229 patients, there were 853 prescription drugs being screened for non-adherence problems. The demographic data of patients were presented in table 2. The majority of patients were 73.8% female. The participants' age range was 19-84 years with the average of 61.11 ± 10.75 years. Most patients took medications without a caregiver and 79.2% were scheduled to take medications more than 2 times per day.

Medication adherence

The mean percentage of medication adherence ± SD was 94.02 ± 16.86%. From pill counting of 853 drug items, medication non-adherence could be classified into 3 groups as (1) no non-adherence meaning that patients were not detected for any non-adherence or absolute medication non-adherence = 0, (2) sporadic non-adherence meaning that patients had absolute medication non-adherence > 0 and < 20, and (3) repeated non-adherence meaning that patients had absolute of medication non- adherence ≥ 20. Figure 1 presented proportions of drug items of 3 medication adherence groups using pill count method. The patients were categorized into 6 groups by pill count method and BMQ. (Table 3)

Validity of BMQ

Table 4 showed sensitivity, specificity, PPV, NPV, and accuracy of BMQ across types of non-adherence, both repeated and sporadic. Since each patients were interviewed using BMQ twice, one for 7-day and the other for 14-day recall periods, the result of both recall periods were also compared. The regimen screening items of BMQ contained 7 items. However, the first item asked whether patients could name the medication prescribed. It was not common and literacy impossible for the studied subjects to name their medication in English. Thus the recall screening of 6 items was also analyzed for comparison. Both recall periods of 7 items had similar result with high sensitivity (100%, 100%), but low specificity (0.27%, 0.37%) and accuracy (2.90%, 36.46%) in screening repeated non-adherence and sporadic non-adherence, respectively. The 6-item regimen screen (Item 2-7) showed better results for

Table 1 Validity of the Thai-version BMQ formulas

Type of adherence from pill count	BMQ	
	adherence	Non-adherence
adherence	a	b
Sporadic non-adherence	c	d
Repeated non-adherence	e	f

Repeated non-adherence

Sensitivity	= f/(e+f) x 100
Specificity	= [(a+c)/ (a+b+c+d)] x 100
PPV	= [f/(b+d+f)] x 100
NPV	= [(a+c)/(a+c+e)] x 100
Accuracy	= [(a+c+f)/ (a+b+c+d+e+f)] x 100

Sporadic non-adherence

Sensitivity	= [d/(c+d)] x 100
Specificity	= [(a+e)/ (a+b+e+f)] x 100
PPV	= [d/ (b+d+f)] x 100
NPV	= [(a+e)/(a+c+e)] x 100
Accuracy	= [(a+d+e)/ (a+b+c+d+e+f)] x 100

Table 2 Demographic data of patients

Variable	**number (%)**
Gender, female	169 (73.8)
Age, mean years	61.11 ± 10.75
Education	
none	16 (7.0)
primary education	163 (71.2)
secondary education	40 (17.5)
diploma	4 (1.7)
bachelor's degree	6 (2.6)
Income (bath)	
0	24 (10.5)
1-500	71 (31.0)
501-5000	62 (27.1)
5001-10,000	48 (21.0)
10,001-20,000	14 (6.1)
20,001-30,000	4 (1.7)
≥ 30,000	1 (0.4)
Not available	5 (2.2)
Living alone	24 (10.5)
Taking drug by themselves	203 (88.6)
Disease	
Diabetics	95 (41.5)
Dyslipidemia	84 (36.7)
Hypertension	202 (88.2)
Angina pectoris	6 (2.6)
Atrial fibrillation	3 (1.3)
Heart failure	2 (0.9)
Myocardial infarction	1 (0.4)
Take drug ≥ 2 times/day	179 (78.2)
Number of drug	
1	13 (5.7)
2	42 (18.3)
3	54 (23.6)
4	56 (24.4)
5	32 (14.0)
6	18 (7.9)
7	10 (4.4)
8	4 (1.7)

both recall periods compared to 7-item screening. We found high agreement of patient's report about dose omission between 7 days and 14 days (shown in Table 5). Kappa coefficient showing the level of agreement between 7 days and 14 days was 0.861 (95% CI 0.816 - 0.907). The 2-item recall screen showed higher sensitivity for sporadic and repeated non- adherence than that of the 2-item belief screen. The 2-item access screen had only 10.19% and 11.33% sensitivity to detect repeated and sporadic non-adherence respectively.

DISCUSSION: Validity of the Thai-version BMQ was different from the original version. The regimen screen had higher sensitivity and lower specificity, accuracy, and PPV than the result from the study by Svarstad BL *et al.*, which showed regimen screen at 80.0% sensitivity, 100.0% specificity, 100% PPV, and 95.0% accuracy[18]. Almost all of participants of this study had failed to mention or name prescribed drug without prompting. It was partly due to lack of English proficiency of patients. This resulted in 100% sensitivity but only 0.27% specificity since all patients were identified as non-adherence according to the 7-item scale. When the first item, asking patients to name the medication, was excluded, the 6-item regimen screen showed decreased sensitivity and revealed increased specificity. When comparing between 7-day and 14-day recall periods, the 6-item regimen presented higher sensitivity for 14-day period since more non-adherence were detected than the 7-day period. During the first 7 days after receiving medications, patients still took all medications as directed. However, when the period was extended to 14 days, some patients started to miss some doses. This was why the result showed higher non-adherence rate during the 14 days.

The belief screen was more related to repeated non-adherence. The result of this study also revealed higher sensitivity in screening repeated non-adherence than sporadic non-adherence which was consistent with the study by Svarstad BL and colleagues[18]. Several studies showed that belief about drug treatment, such as experience of adverse drug reaction and failure of treatment was a factor of drug non-adherence[19-20]. However,

Table 3 Number of patients in medication adherence grouping by BMQ and pill count

Pill count	BMQ 7-item regimen screen[a]	
	Adherence	Non-adherence
Adherence	2	434
Sporadic non-adherence	0	309
Repeated non-adherence	0	108
Pill count	**BMQ 6-item regimen screen[a]**	
	Adherence	Non-adherence
Adherence	404	32
Sporadic non-adherence	239	70
Repeated non-adherence	44	64
Pill count	**BMQ 7-item regimen screen[b]**	
	Adherence	Non-adherence
Adherence	2	434
Sporadic non-adherence	0	309
Repeated non-adherence	0	108
Pill count	**BMQ 6-item regimen screen[b]**	
	Adherence	Non-adherence
Adherence	397	39
Sporadic non-adherence	219	90
Repeated non-adherence	41	67
Pill count	**BMQ 2-item belief screen**	
	Adherence	Non-adherence
Adherence	345	91
Sporadic non-adherence	234	75
Repeated non-adherence	66	42
Pill count	**BMQ 2-item recall screen**	
	Adherence	Non-adherence
Adherence	308	128
Sporadic non-adherence	164	145
Repeated non-adherence	59	49
Pill count	**BMQ 2-item access screen**	
	Adherence	Non-adherence
Adherence	412	24
Sporadic non-adherence	274	35
Repeated non-adherence	97	11

[a]7 days timeframe, [b]14 days timeframe

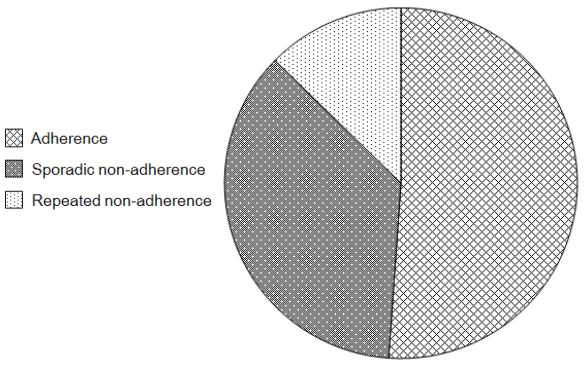

Figure 1 Medication adherence categorized by pill count

the belief screen in this study could detect less non-adherence rate or had lower sensitivity than Svarstad BL study. This could be caused by different social status of the interviewer. Patients would tend to hinder their non-adherence behavior from health care professions. The recall screen was more sensitive to sporadic than repeated non-adherence, which was consistent with the result from Svarstad BL and colleagues but lower sensitivity percentage was reported in this study. While 7.4% of participants in this study reported having difficultly in remembering taking drugs but 27.3% of participants in Svarstad BL and colleagues' study. Seventy-eight percent of patients in this study had ≥ 2 times per day drug regimen and this could influence memory problems. The under report of memory problems could cause low sensitivity in this study since the participants were more elderly with the average age of 61.11 ± 10.75 years. The higher age was associated with higher memory problem. Since this study had tested 2 periods of recall, 7-day and 14-day, the 7-day recall used in the Thai-version BMQ was recommended to avoid memory problem causing increased difficulty level in answering the questionnaire. Also, the result of the study did not show much different in validity indicators between both periods.

CONCLUSION: The 6-item regimen screen could be used to detect medication non-adherence for Thai patients. The 7-day regimen screening for screening repeated non-adherence had 59.26% sensitivity and 86.31% specificity, while the 14-day had 62.04% sensitivity and 82.68% specificity. The belief screen with higher sensitivity to repeated non-adherence, the recall screen with higher sensitivity to sporadic non-adherence, and the access screen were recommended tools, which could assist health care practitioners to identify barriers to medication adherence leading to the appropriate measures selected for each individual patient to improve treatment outcomes.

Table 4 Validity of Thai-version BMQ

Screen (Timeframe)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
The 7-item regimen screen (7 days)					
repeated non-adherence	100.0	0.27	12.69	100.0	12.90
sporadic non-adherence	100.0	0.37	36.31	100.0	36.46
The 6-item regimen screen (7 days)					
repeated non-adherence	59.26	86.31	38.55	93.59	82.88
sporadic non-adherence	22.65	82.35	42.17	65.21	60.73
The 7-item regimen screen (14 days)					
repeated non-adherence	100.0	0.27	12.69	100.0	12.90
sporadic non-adherence	100.0	0.37	36.31	100.0	36.46
The 6 item regimen screen (14 days)					
repeated non-adherence	62.04	82.68	34.18	93.76	80.07
sporadic non-adherence	29.13	80.51	45.92	66.67	61.90
Belief screen					
repeated non-adherence	38.89	77.72	20.19	89.77	72.80
sporadic non-adherence	24.27	75.55	36.06	63.72	56.98
Recall screen					
repeated non-adherence	45.37	63.36	15.22	88.89	61.08
sporadic non-adherence	46.93	67.46	45.03	69.11	60.02
Access screen					
repeated non-adherence	10.19	92.08	15.71	87.61	81.71
sporadic non-adherence	11.33	93.57	50.00	65.01	63.77

Table 5 Level of agreement between 7-day and 14-day periods on self-report adherence

7-day recall	14-day recall		*Kappa*	*T*	
	take all doses	don't take sometimes		*value*	*Prob.*
take all doses	668	34	*0.861*	*5.404*	*0.000*
don't take sometimes	0	131			

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