Utilization of the Beliefs about Medicine Questionnaire and Prediction of Medication Adherence in China: A Systematic Review and Meta-Analysis

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1

1. Introduction

Chronic disease, characterized by long duration and slow progression, affect around 260 million Chinese people [1]. Cardiovascular diseases, hypertension, diabetes and other chronic diseases contribute to approximately 8.8 million deaths annually, 89% of all deaths in China [2]. The Chinese government has estimated that almost half of the elderly Chinese population suffer one or more chronic diseases [3]. As population ageing has accelerated, mainly due to the one-child policy between 1979 to 2016, the percentage of the Chinese population aged 60 years or over increased to 12.4% by 2010 and is estimated to reach to 28% by 2040 [4].

For patients diagnosed with chronic disease, taking appropriate medication as prescribed is typically necessary to control symptoms and prevent complications. This 'adherence', has been defined by the WHO [5] as 'the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider'. However, medication adherence varies widely across individuals, treatments and medical conditions [6, 7]. For example, in China, only 67.8% of diabetic patients, 65.1% of hypertension patients and 15.3% of myocardial infarction patients are estimated to adhere to prescribed treatment [8-10].

Among numerous factors that have been found to reduce medication adherence, patients' beliefs about medicines are one of the most fully researched [11]. It has been posited that adherence arises from a judgment that personal need for a particular treatment outweighs any concerns about the potential risks of using it, known as the 'NecessityConcern Framework' [11, 12]. These beliefs about specific medicines derive in part from beliefs about pharmaceuticals overall. People who believe that pharmaceutical treatments are typically harmful or overused by healthcare professionals tend to have more concerns about a newly prescribed treatment, whereas people who believe pharmaceutical treatments are typically beneficial are more likely to feel that they personally need particular treatments. Therefore, the BMQ contains two subscales: BMQ-Specific and BMQ-General, assessing both beliefs about medicines in general and specific beliefs about particular medicines [12, 13]. The BMQ-Specific subscale assesses beliefs about the necessity of a particular medication for a particular condition (Specific Necessity) and concerns about the treatment's potential adverse consequences (Specific Concerns). The BMQ-General includes assessing perceptions about whether pharmaceutical medicines and typically harmful, overused by healthcare practitioners and beneficial for individuals and society [13, 14].

According to Horne's meta-analysis, there were ninety-four studies involving 25,072 patients indicating that patients who believe in their personal need for a specific medication and have few concerns about it typically are more adherent to their treatment [11]. Since being published, the BMQ has been widely used across different patient groups in 18 countries. There has been a recent interest in its use in the Chinese context [15-17]; however, the most extensive review of relationships between BMQ-Specific scores and adherence [11] did not search Chinese language databases and was conducted before many of the Chinese studies were published. There are many differences between the UK context in which the BMQ was first designed and the China context including differences in the

structure of the healthcare system, variations in trust in healthcare professionals, and use of Traditional Chinese Medicine [18]. Although we could assume that the Necessity-Concerns Framework also applies in the Chinese context and that similar general beliefs about pharmaceuticals are relevant in the Chinese population, the application of the BMQ in China has not been systematically reviewed.

Therefore, the present review primarily aimed to systematically review all quantitative studies measuring Chinese people's beliefs about medicines using the BMQ; and secondly, to evaluate the association between beliefs about medicines and medication adherence in Chinese population through meta-analysis.

2. Methods

This systematic review and meta-analysis were conducted in accordance with the statement of *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA)[19] and the *Meta-analysis of Observational Studies in Epidemiology* (MOOSE) guidelines [20].

2.1 Data sources and search strategy

Three commonly used databases indexing English language publications in medical and psychological areas (PubMed, EMBASE & PsycINFO), and the two largest general Chinese databases (CNKI & WANFANG DATA), were searched in October 2017 and updated in February 2019. The literature search covered publications from 1997, the year in which the BMQ was published.

Search strategy were conducted using Mesh terms (or other index terms) and keywords in full text. Phrases related to the concepts of 'beliefs about medicines' and 'questionnaire/survey' were searched in all databases. In the non-Chinese databases, the concept of 'Chinese population' was also added to the search. Moreover, we hand searched reference lists of all included papers to identify further studies. The full search strategy using in PubMed is presented below, and the searches and results in each database can be found in **Appendix A-C**.

("China" [Mesh] OR "Taiwan" [Mesh] OR China [Text Word] OR Chinese [Text Word] OR Taiwan [Text Word] OR Taiwanese [Text Word] OR Hong Kong [Text Word] OR Macao [Text Word] OR Macau [Text Word]) AND ((("perception" [Mesh] OR belief\$[Text Word] OR perception\$[Text Word]) AND ("medicine" [Mesh] OR medicine\$[Text Word] OR perception\$[Text Word]) AND ("medicine" [Mesh] OR medicine\$[Text Word] OR medication\$[Text Word] OR drug\$[Text Word])) OR "beliefs about medicine" [Text Word] OR BMQ [Text Word]) AND ("Surveys and Questionnaires" [Mesh] OR questionnaire\$[Text Word] OR scale\$[Text Word])

2.2 Selection criteria

Studies were included, if: 1) participants aged 18 years old or over; 2) participants were residents of mainland China, Hong Kong, Macao or Taiwan; 3) Measured beliefs about medicine using a standard version of BMQ; 4) studies were clinical trials (randomized/nonrandomized clinical trials) or observational studies (longitudinal or crosssectional studies). Studies were excluded if: 1) they did not have quantitative or mixedmethods designs; 2) the full-text could not be obtained; 3) the disease was treated by nonpharmaceutical methods.

Where data from same study or overlapping sample were reported in multiple publications, peer-reviewed journal articles were used above other reports e.g. degree theses unless more data was reported in the other publication. For studies published in both English and Chinese, the English version was used unless the Chinese version provided more data.

2.3 Identification of studies

Titles and abstracts of publications in the first-round search were screened by two reviewers (BN & ZC) independently, and the additional publications in update session were screened by reviewers BN and XLW. The overall agreement between reviewers was 94%. Differences between reviewers were resolved through discussion. Where an article was deemed as potentially relevant by any reviewer, the full article was obtained. Any remaining disagreements were resolved by a fourth reviewer LW.

2.4 Data extraction

Data were extracted by the first reviewer BN using a standardised form and checked by the second reviewer ZC. Where data were reported at multiple time points, the point with the fewest missing data was selected. For trial studies, if the overall baseline data across intervention groups and control groups were unavailable, only the data of control group were extracted. The following data were extracted and coded:

- Study information: authors' names, publication year, article title, lead author's institution, study design (such as cross-sectional or randomized control trail (RCT)), sampling strategy, and type of publication (journal article or degree thesis).
- Participant characteristics: age, gender, sample size, response rate, and diagnosis.
- Beliefs about medicines questionnaire: questionnaire type (BMQ-Special and/or BMQ-General); the source of the questionnaire (existing version or self-translated); the internal consistency reliability of BMQ (Cronbach's α) specific to the participants of each study; and the mean and standard deviation of the scores of each BMQ subscale including across multiple subgroups if available. The mean and standard deviation of the necessity-concerns differential (NCD) score, which is calculated by subtracting the Concerns score from the Necessity was also extracted where available.
- Medication adherence: the measurement used, adherence results (percentage of adherent participants and/or mean score), effect size of the relationship between adherence and BMQ scores (correlation coefficient (r), regression coefficient (β) and/or odds ratio (OR)), and P value or confidence intervals (CI). For studies assessed with tripartite measure, such as Morisky Medication Adherence Scale, the high and middle level were defined as 'adherence', and the low level was defined as 'non-adherence' in this study. [21-23].

7

2.5 Quality assessment

Two reviewers (BN & ZC or BN & XLW) independently assessed studies' quality using an assessment tool (see *Appendix D*), based on the U.S. National Institute of Health [24] and Hagstromer's checklists [25]. It assessed the quality of participant sampling, outcome measurement and statistical analyses. An additional section on medication adherence measurement was designed and applied where relevant. The quality of each study was presented using a percentage of potential quality items the study obtained scores on. For this total, scores of 80% and 60% were used as cut-off points to determine 'Good', 'Moderate', and 'Poor' quality. Disagreements between reviewers were resolved through discussion with the third reviewer LW.

2.6 Data analysis

Effect sizes and 95% CI for associations between beliefs about medicines and medication adherence were pooled in meta-analyses using RevMan 5.3 software (the Cochrane Collaboration, 2014, Nordic Cochrane Centre, Copenhagen, Denmark). Both β and r were used as the effect size separately and reported in the meta-analysis in subgroups.

Heterogeneity was examined using the Chi-squared statistic (Q) and presented as the ratio of true heterogeneity to total observed variation (I²) [26]. The I² higher than 50% indicated a high heterogeneity. A random-effects model was applied due to the variability between studies in terms of participant characteristics, disease categories, and study designs. The potential publication bias was detected using funnel plot.

3. Results

3.1 Overview

Figure **1** shows the process and results of the systematic search. The search produced 1770 results from the non-Chinese databases and 1201 results from the Chinese databases. One additional article was identified through hand-searching. Duplicates (n=656) were removed before reviewing. After review of titles and abstracts, 2129 records were removed due to their non-quantitative nature, adolescent participants or other exclusion criteria (see *Figure* **1**). 187 full-texts were examined, of which 58 (44 journal articles and 14 theses) met the inclusion criteria and were included in the systematic review. Forty-five of the studies had a cross-sectional design, and eleven were RCTs. There were also one longitudinal study and one study with mixed method. All included studies were published between 2012 and 2019. Eight articles were in English and 50 were in Chinese. (See *Table* **1 & 2**)

3.2 Participants characteristics

Sample sizes ranged from 48 to 967, representing 12,595 participants in total. Nine studies did not report the mean age. The reported mean ages of participants in the remaining 49 studies ranged from 37.6 to 69.4 years old, with an overall mean age of 57.1 years old weighted by the sample size. These participants came from 28 cities of 17 provinces or regions, mainly located in coastal developed areas. The three most common conditions in the reviewed studies were cardiac-cerebral vascular disease (16 studies), mental disorder (12 studies), cancer (8 studies) and kidney disease (5 studies). (See Table 1

& 2).



Figure 1 Flow chart of study selection

Characteristics	Number of studies or ranges
Article type	
Journal articles	44
Theses	14
Publication date	
2012	1
2013	4
2014	4
2015	10
2016	10
2017	12
2018	16
2019	1
Language	
English	8
Chinese	50
Research quality	
Good	12
Moderate	36
Poor	10
Study design	10
Cross-sectional	45
Clinical trial (RCT Nonrandomized clinical	11
trial & Open-label trail)	11
	1
Mixed method	1
Sample size	18-967
Posponso rato	48-507
Moon ago	27.6.60.4
Conder	37.0-09.4
Gender	0%-82.8%
	10
Cardiac-cerebrai vascular disease	16
	12
	8
Ridney disease	5
Other disease	1/
BiviQ measurement	44
BMQ-S & BMQ-G	11
BMQ-S only	47
Mean sum scores of BMQ components	
Mean sum score of Necessity	10./-22.2
Mean sum score of Concern	9.8-19.6
Mean NCD score	-5.6-11.1
Mean sum score of Harm	10.4-14.3
Mean sum score of Overuse	9.1-12.9
Mean sum score of Benefit	14.2-14.8
BMQ version	
Self-translated	11

Table 1 Summary of characteristics of the included studies and participants

Cited Si's version	21	
Cited Lu's version	12	
Cited Wu's version	3	
Unknown	11	
Adherence rate	33.4-100.0%	
Adherence measurement		
MMAS (4-item/8-item)	34	
BAASIS	3	
MARS	2	
MCS	1	
Self-designed questionnaire	1	
VAS (combined use)	1	
Electronic medicine bottles (combined use)	1	
Did not measure adherence	17	

MMAS: Morisky Medication Adherence Scale; BAASIS: Basel Assessment of Adherence with Immunosuppressive medication Scales; MARS: Medication Adherence Report Scale; VAS: Visual Analogue Scale; MCS: Medical Compliance Scale. Table 2 Detailed information of included studies in the systematic review

Author	Illness group	N	Mean Age ± SD	Gender (% male)	Response rate (%)	Study Design
BKF Wan et al. (Jan-2017) [27]*	Chronic diseases	698	60.04±15.89	46%	Not reported	Cross-sectional
C Rui (May-2017) [28]	HIV	150	45	68.7%	95%	Cross-sectional
CF Yen et al. (Dec-2014) [29]*	Insomnia	392	48.0±13.9	38.3%	Not reported	Cross-sectional
CM Geng et al. (Jun-2018) [30]	Kidney transplant	86	43.81±8.59	61.6%	95.56%	Cross-sectional
CY Du et al. (Sep-2017) [31]	Liver transplant	278	53.32±10.20	75.90%	92.70%	Cross-sectional
DJ Ying & XX Zhang (Nov-2015) [32]	Cerebral stroke	212	63.72±7.59	64.6%	96.36%	Cross-sectional
F Xu et al. (Apr-2018) [33]	Decompensated cirrhosis	32 of 64	18-64	Not reported	Not reported	RCT
H Jiang et al. (Feb-2017) [23]	Primary glaucoma	156	61.3±8.3	23.7%	Not reported	Cross-sectional
H Sun (Oct-2017) [34]	Coronary artery disease	58 of 118	62.33±10.57	74.1%	96.67%	Nonrandomized clinical trial
HB Jin et al. (Aug-2015) [35]	Cerebral Infarction	326	63.15±7.33	64.7%	93.14%	Cross-sectional
HD Tian et al. (Nov-2018) [36]	Postpartum depression	128	Not reported	0%	100%	Cross-sectional
HF Xie et al (Nov-2016) [37]	Depression	48	38.67±9.91	35.42%	97.96%	Mixed method
HF Xie et al. (Mar-2018) [38]	Depression	108	38.66±9.90	52.8%	100%	Open-label trial
HM Liu et al. (Jan-2016) [39]	Type 2 diabetes	373	62.3±7.3	42.9%	87.15%	Cross-sectional
J Chen (Jan-2015) [40]	Osteoporosis	365	68.35±8.21	54.2%	96.05%	Cross-sectional
J Zhang et al. (Oct-2016) [41]	Breast cancer	192	51.34	0%	96.0%	Cross-sectional
JL Shao et al. (Oct-2015) [42]	Acute myocardial infarction	151	62.65±11.15	82.8%	100%	Cross-sectional
JW Wu et al. (Apr-2016) [43]	Atrial fibrillation	213	64.12±7.82	64.79%	96.80%	Cross-sectional
L Dong et al. (Apr-2016) [44]	Ulcerative colitis	42 of 85	42.77±12.28	58.89%	93.33%	RCT
L Wang (Jun-2015) [45]	HVR	60 of 120	52±12	54.2%	100%	RCT
L Yuan et al. (Jun-2018) [46]	Cerebral infarction	300	Not reported	68.3%	100%	Cross-sectional
L Zhang et al. (May-2018) [47]	Depression	106	42.1±12.8	32.1%	Not reported	Cross-sectional

LQ Ning et al. (Sep-2016) [48]	Deep venous thrombosis	101	53.33±37.84	42.6%	93.52%	Cross-sectional
Author	Illness group	Ν	Mean Age ± SD	Gender (% male)	Response rate (%)	Study Design
L Wei et al. (Jul-2017)[17] *	Overall Stroke Diabetes Rheumatoid arthritis	967 313, 315 339	59.08±13.5 65.8±13.7 62.5±13.9 49.7±12.8	41.5% 56.5% 55.2% 14.8%	100%	Cross-sectional
M Yuan et al. (Feb-2018) [49]	Parkinson's disease	49 of 97	66.20±8.18	59.2%	98.0%	RCT
M Yuan et al. (Oct-2018) [50]	Parkinson's disease	155	65.68±8.54	58.1%	96.9%	Cross-sectional
MB Wu (May-2013) [51]	Breast cancer	154 of 311	52.61±9.39	0%	94.8%	RCT
MB Wu et al. (Jan-2014) [52]	Breast cancer	204	53.74±9.72	0%	99.5%	Cross-sectional
Q Cai et al. (Jan-2019) [53]*	Asthma	217	48.05±16.33	46.5%	Not reported	Cross-sectional
Q Guo et al. (May-2017) [54]	Acute coronary	213	Not reported	55.9%	85.2%	Cross-sectional
QX Zhang et al (Jul-2018) [55]	Anxiety disorder	45 of 87	37.56±12.69	37.8%	97.8%	RCT
S Teng (Jun-2016) [56]	Liver transplant	293	61.48±5.22	76.11%	97.67%	Cross-sectional
S Teng et al. (Sep-2015) [57]	Renal transplant	255	47.1±12.3	59.2%	94.44%	Cross-sectional
SH Liu et al. (Jan-2018) [58]	HVR	154	46.62±10.52	50%	Not reported	Cross-sectional
SJ Zhao et al. (Feb-2017) [59]*	Atrial fibrillation	288	59.2±12.2	62.2%	84.71%	Cross-sectional
SL Guo (Nov-2014) [60]*	Lung or colorectal cancer	151	63.8±11.2	51%	99.3%	Cross-sectional
SY Liu et al. (Aug-2017) [61]	Breast cancer	237	50.77±9.742	0%	77.70%	Cross-sectional
SY Yang & ZQ Lu (Feb-2016) [62]	Cancer	129	Not reported	53.5%	99.2%	Cross-sectional
SY Yang et al. (Apr-2018) [63]	Colorectal cancer	104	57.11±9.22	58.0%	87.4%	Longitudinal
TT Chen et al. (Nov-2015) [64]*	Anxiety	148	42.2±8.8	45.90%	85.50%	Cross-sectional
W Yan et al. (Apr-2015) [65]	Hypertension	108	60~80	43.5%	85.70%	Cross-sectional
WY Ni et al. (Jul-2018) [66]	Breast cancer	52 of 106	Not reported	0%	96.3%	RCT
X Liu et al. (Mar-2012) [67]	Nephritic syndrome	97	41.35±16.81	46.4%	100%	Cross-sectional
X Wang (May-2018) [68]	Functional dyspepsia	269	41.34±9.57	47.2%	82.3%	Open-label trial
XX Qiao et al. (Jul-2017) [69]	Chronic diseases	820	69.38±6.53	30.85%	97.70%	Cross-sectional

XX Zhang & DJ Ying (Sep-2016) [70]	Chronic renal failure	217	60.12±11.98	54.8%	96.8%	Cross-sectional
Author	Illness group	Ν	Mean Age ± SD	Gender (% male)	Response rate (%)	Study Design
XY Liu et al. (Nov-2015) [71]	Chronic nephrosis III-IV stage	242	59.32±11.73	55.8%	96.8%	Cross-sectional
XY Yu & W Zeng (Dec-2016) [72]	Permanent atrial fibrillation	92	61.28±13.08	43.5%	100%	Cross-sectional
XY Zhao (May-2017) [73]	Ischemic stroke	200	64.86±10.83	61.5%	96.15%	Cross-sectional
Y Lu et al. (Apr-2014) [74]	Depression	102	68.63±5.51	31.4%	100%	Cross-sectional
Y Lu et al. (Feb-2016) [15]*	Depression	135	68.31±5.75	34.1%	85.4%	Cross-sectional
YF Wang (Nov-2013) [22]	Primary glaucoma	213	60.85±9.47	29.1%	Not reported	Cross-sectional
YJ Zhu (May-2017) [75]	HIV	150	44	68.7%	100%	Cross-sectional
YS Zhao (Feb-2018) [76]	Depression	56 of 114	53.07±12.27	46.4%	93.3%	RCT
YY Dong (Jun-2018) [77]	Allergic rhinitis	205	Not reported	62.4%	82.0%	Cross-sectional
YY Yao (Jun-2018) [78]	Chronic diseases	399	Not reported	45.6%	95%	Cross-sectional
ZX Si (May-2013) [79]	HVR	182	46.71±10.75	50%	89.22%	Cross-sectional
ZX Si et al. (Feb-2013) [80]	HVR	164	47.02±10.52	50.6%	91.11%	Cross-sectional

* Published in English

3.3 Beliefs about medicines

The first Chinese BMQ study was published in 2012 [81]. Several Chinese versions of BMQ were identified from the included studies. The top-three commonly used versions, used in 36 of the 58 studies, were specific for patients with CHD (Si's version) [80], depression (Lu's version) [74] and breast cancer (Wu's version) [52]. Most studies followed a standard scoring methodology for the BMQ, except for Wu [52], who calculated new subscale scores based on the results of a factor analysis.

All studies measured participants' specific beliefs about medicines, but seven studies did not subsequently report these results. Tian [36] measured patients' concerns about medicines using 5 items, but only reported scores of two items that was marked as an error data. Mean sum scores of necessity beliefs, concerns and their differential scores ranged between 10.7-22.2, 9.8-19.6, and -5.6-11.1, respectively. Eleven studies also measured participants' general beliefs about medicines. The ranges for each factor in BMQ-General subscale were 10.4-14.3 (Harm), and 9.1-12.9 (Overuse), and 14.2-14.8 (Benefit). (See **Table 3**).

Seventeen studies reported the tested internal consistency (Cronbach's α) of the BMQ items. Cronbach's α for overall and each subscale were 0.67-0.94 (Overall), 0.60-0.92 (Necessity), 0.58-0.91 (Concerns), 0.55-0.73 (Harm), 0.47-0.79 (Overuse), and 0.51-0.58 (Benefit).

Table 3 BMQ and medication adherence results of the included studies

Author and date	BMQ subscales-	Beliefs about Medicine (Mean± SD)	Adherence Measure	Adherence (%)	Correlation between BMQ and Adherence
BKF Wan et al. (Jan-2017)	BMQ-G,	N=16.6±3.3; C=13.5±3.1	MMAS-8	Not reported	Not reported
	BMQ-S	NCD=3.1±4.2; H=11.4±2.4			
		O=11.9±2.2; B=14.7±1.9			
C Rui (May-2017)	BMQ-S	N ₁ =19.84±3.00; N ₂ =18.64±2.51	MMAS-4	Overall:	β _N =0.44, SE=0.22 (P=.046);
		C ₁ =16.21±3.13; C ₂ =15.68 ±2.77		66.7%	OR _N =1.56 (1.01, 2.41);
		NCD ₁ =3.63±3.88;			β _c =-0.03, SE=0.21 (P=.87);
		NCD ₂ =2.96±3.33			ORc=0.97 (0.65, 1.45)
CF Yen et al. (Dec-2014)	BMQ-S	N=10.7±3.8; C=16.3±4.4	N/A	N/A	N/A
CM Geng et al. (Jun-2018)	BMQ-G,	N=20.62 ±2.58; C=17.03 ±3.59	BAASIS	60.47%	Not reported
	BMQ-S	H=10.35 ±2.67; O=11.45 ±2.94			
CY Du et al. (Sep-2017)	BMQ-G,	N=20.1±1.7; C=15.1±2.4	N/A	N/A	N/A
	BMQ-S	H=11.2±1.9; O=10.4±1.9			
DJ Ying et al. (Nov-2015)	BMQ-S	N=16.2±2.1; C=10.1±1.7	N/A	N/A	N/A
		NCD=6.1±1.9			
F Xu et al. (Apr-2018)	BMQ-S	NCD=9.42±2.98	MMAS-8	Not reported	Not reported
H Jiang et al. (Feb-2017)	BMQ-S	Not reported	MMAS-8	53.2%	r _N =0.09 (P>.05); r _c =-0.47 (P<.01)
H Sun (Oct-2017)	BMQ-S	N=17.1 ± 2.0; C=14.5 ± 3.0	MMAS-8	55.2%	Not reported
HB Jin et al. (Aug-2015)	BMQ-S	N=16.3±1.9; C=9.8±1.7	N/A	N/A	N/A
		NCD =6.4±1.8			
HD Tian et al. (Nov-2018)	BMQ-S	N=17.61±0.89; C: Error data	MMAS-4	76.6%	Not reported
HF Xie et al (Nov-2016)	BMQ-S	N=16.0±2.1; C=19.6±1.4	MMAS-4	64.6%	Not reported
HF Xie et al.(Mar-2018)	BMQ-S	(Average score)	MMAS-4	75%	Not reported
		N=3.20±0.41, C=3.91±0.27			
HM Liu et al. (Jan-2016)	BMQ-S	N=19.3±2.4; C=13.3±3.0	MMAS-8 &	88.2%	r _{NCD} =0.26 (P<.001)
		NCD=6.0±4.0	ED	64.9%	
J Chen (Jan-2015)	BMQ-S	N=17.7±3.4; C=13.7±3.1	N/A	N/A	N/A

		NCD=4.0±0.4			
Author and date	BMQ	Beliefs about Medicine	Adherence	Adherence	Correlation between BMQ and Adherence
	subscales-	(Mean± SD)	Measure	(%)	
J Zhang et al. (Oct-2016)	BMQ-S,	N=13.8±2.5; C=12.2±2.3	N/A	N/A	N/A
	BMQ-G	NCD=1.6±0.4; H=11.7±1.5			
		O=9.1±1.3			
L Dong et al. (Apr-2016)	BMQ-S	N=18.5±1.7; C=18.6±1.5	MMAS-8	Not reported	Not reported
JL Shao et al. (Oct-2015)	BMQ-S	NCD=3.9±3.6	MMAS-8	92.7%	r _N =0.17 (P=.04); r _C =-0.48 (P<.001)
					r _{NCD} =0.47 (P<.001)
					β _N =0.13 (P<.05); β _C =-0.31 (P<.001)
JW Wu et al. (Apr-2016)	BMQ-S	N=16.1±2.2; C=9.9±1.8	N/A	N/A	N/A
		NCD=6.1±1.9			
L Wang (Jun-2015)	BMQ-S	N=20.9±2.7; C=10.7±3.5	MMAS-8	100.0%,	Not reported
		NCD=10.2±4.4			
L Wei et al. (Jul-2017)	BMQ-S,	(Average score)	MARS	49.0%	(Non-adherence) OR _N = 0.92 (0.59,1.43);
Stroke group	BMQ-G	N ₁ =3.69 ± 0.53; C ₁ =3.03 ± 0.71			OR _c = 1.43 (1.02,2.00); OR _H = 1.30 (0.96.1.77);
		$H_1=2.94 \pm 0.78; O_1=3.22 \pm 0.62$			OR ₀ = 1.24 (0.85,1.82); OR _B = 0.83 (0.53,1.29)
	_	B ₁ = 3.70 ± 0.53	_		
Rheumatoid arthritis		N ₃ =3.66 ± 0.44; C ₃ =3.07 ± 0.58	_	80.2%	OR _N = 1.34 (0.73,2.46); OR _c = 1.32 (0.84,2.10);
group		H₃=2.99 ± 0.43; O₃=2.95 ± 0.51			OR _H = 1.27 (0.70,2.30); OR ₀ = 0.98 (0.60,1.60);
		B ₃ =3.55 ± 0.45			OR _B = 0.65 (0.37,1.13)
Diabetes group	-	N ₂ =3.75 ± 0.40; C ₂ =3.15 ± 0.58	-	73.3%	OR _N = 0.92 (0.43,1.97); OR _c = 1.15 (0.67,1.98);
		$H_2=2.95 \pm 0.50; O_2=3.12 \pm 0.50$			OR _H = 0.59 (0.32,1.11); OR ₀ = 1.10 (0.61,2.00);
		B ₂ =3.69 ± 0.42			OR _B = 0.83 (0.41,1.69)
L Yuan et al. (Jun-2018)	BMQ-S	N=16.79±1.84; C=9.69±1.53	N/A	N/A	N/A
		NCD=6.47±1.52			
L Zhang et al. (May-2018)	BMQ-S	(Average score)	N/A	N/A	N/A
		NCD _{Male} =0.88±1.25;			
		NCD _{Female} =0.81±1.34			

M Yuan et al. (Feb-2018)	BMQ-S	NCD=4.69±4.11	MMAS-4	79.6%	Not reported
Author and date	BMQ subscales-	Beliefs about Medicine (Mean± SD)	Adherence Measure	Adherence (%)	Correlation between BMQ and Adherence
LQ Ning et al. (Sep-2016)	BMQ-S	NCD=8.2±6.4	MMAS-8	73.3%	r _N >0 (P<.05); r _c <0 (P<.05); r _{NCD} >0 (P<.05); β _N =0.278 (P<.01)
M Yuan et al. (Oct-2018)	BMQ-S	N=19.05±2.90; C=13.39±2.41 NCD=6.12±4.05	MMAS-4	86.45%	r _N =0.22 (P<.01); r _C =-0.23 (P<.01) r _{NCD} =0.28 (P<.01)
MB Wu (May-2013)	BMQ-S, BMQ-G	N=12.9±3.0 ;C=13.9±2.8	MMAS-8 & VAS	Not reported	Not reported
MB Wu et al. (Jan-2014)	BMQ-S, BMQ-G	N=12.2±3.1; C=12.2±2.4 O=9.2±1.7; Toxicity =10.7±2.3 Long-term effect=4.7±1.5	N/A	N/A	N/A
Q Cai et al. (Jan-2019)	BMQ-S	N=17.34±2.80; C=15.98±3.04	MMAS-8	50.2%	Not reported
Q Guo et al. (May-2017)	BMQ-S	N=18.42±2.72; C=13.02±3.56; NCD=5.40±1.47	N/A	N/A	N/A
QX Zhang et al (Jul-2018)	BMQ-S	(Average score) N=2.91±0.57; C=3.31±0.59	MMAS-4	84.4%	Not reported
S Teng (Jun-2016)	BMQ-S, BMQ-G	N=20.0±3.1; C=15.2±4.2 NCD=4.8± 1.1	BAASIS-4	43.0%	r _N =-0.28 (P<.01); r _C =0.03 (P>.05) r _{NCD} =0.18 (P<.01)
S Teng et al. (Sep-2015)	BMQ-S, BMQ-G	N=20.4±2.8; C=16.9±3.7 NCD=3.5±4.1; H=11.2±2.9; O=10.3±2.9	BAASIS-4	45.1%	Not reported
SH Liu et al. (Jan-2018)	BMQ-S	Not reported	MMAS-8	Not reported	r _N =0.31 (P<.01); r _C =-0.38 (P<.01) r _{NCD} =0.44 (P<.01)
SL Guo (Nov-2014)	BMQ-S, BMQ-G	N=18.9±4.5; C=16.6±5.4; NCD=2.3±7.0; H=14.3±3.8; O=12.5±2.9	MARS-5	43.4%	Not reported
SY Liu et al. (Aug-2017)	BMQ-S	N=15.7±3.8; C=15.7±3.7; NCD=-0.0±4.4	MMAS-8	64.9%	β _{NCD} =0.32 (P<.001)

SY Yang & ZQ Lu (Feb-	BMQ-S	Not reported	MMAS-8	80.6%	$r_N=0.18 (P<.05); r_C=-0.17 (P<.05);$
2016)					r _{NCD} =0.24 (P<.05)
Author and date	BMQ	Beliefs about Medicine	Adherence	Adherence	Correlation between BMQ and Adherence
	subscales-	(Mean± SD)	Measure	(%)	
SJ Zhao et al. (Feb-2017)	BMQ-S,	N=18.3±2.5;	MMAS-8	67.7%	β _N =0.16 (P<.01), SE=0.05, OR=1.17 (1.06-1.29);
	BMQ-G	C=14.4±3.5;			β _c =-0.27 (P<.001), SE=0.05, OR=0.76 (0.69-
		NCD=3.9±4.7;			0.84); β _{NCD} =0.27 (P<.001), SE=0.05, OR=1.31
		H=10.6±2.5;			(1.19-1.45); β _H =-0.20 (P=.001), SE=0.06,
		O=10.2±2.3			OR=0.82 (0.73-0.92)
SY Yang et al. (Apr-2018)	BMQ-S	NCD=0.11±3.94	MMAS-8	Not reported	r_{NCD} =0.30 (P<.01); β_{NCD} =0.07, SE=0.02 (P=.008)
TT Chen et al. (Nov-2015)	BMQ-S	N=17.2±5.2; C=13.7±4.4	N/A	N/A	N/A
W Yan et al. (Apr-2015)	BMQ-S	N=19.0±2.8; C=16.3±4.3	MMAS-8	33.4%	r _N =0.38 (P<.01); r _C =-0.54 (P<.01);
					r _{NCD} =-0.40 (P<.01)
WY Ni et al. (Jun-2018)	BMQ-S	N+C=47.00±2.52	MMAS	Not reported	Not reported
X Liu et al. (Mar-2012)	BMQ-S	N=17.6±3.2; C=16.0±3.5	MMAS-8	72.2%	r _{NCD} =0.20 (P<.05)
X Wang (May-2018)	BMQ-S	N=16.26±1.96; C=15.48±2.08	N/A	N/A	N/A
XX Qiao et al. (Jul-2017)	BMQ-S	N=17.6±2.9; C=13.9±3.1	MMAS-8	67.8%	β _N =0.17 SE=0.02 (P<.001);
					βc=-0.32 SE=0.02 (P<.01)
XX Zhang & DJ Ying (Sep-	BMQ-S	N=17.3±3.2; C=13.1±2.9;	N/A	N/A	N/A
2016)		NCD=4.2±0.4			
XY Liu et al. (Nov-2015)	BMQ-S	N=17.2±3.3; C=13.0±2.9;	N/A	N/A	N/A
		NCD=4.2±0.4			
XY Yu & W Zeng (Dec-	BMQ-S	N=18.0±1.0; C=13.3±0.9	MMAS-8	54.4%	r _N =0.46 (P<.05); r _c =-0.34 (P<.05);
2016)					r _{NCD} =0.06 (P<.05)
XY Zhao (May-2017)	BMQ-S	N=17.59±1.77; C=14.08±1.41;	MMAS-8	41.5%	r _N =0.67 (P<.01); r _c =-0.37 (P<.01);
		NCD=3.87±2.51			r_{NCD} =0.68 (P<.01); β_{NCD} =0.18, SE=0.20 (P=.003)
Y Lu et al. (Apr-2014)	BMQ-S	Not reported	N/A	N/A	N/A
Y Lu et al. (Feb-2016)	BMQ-S	N=17.1±3.6; C=14.9±3.4	MMAS-4	77.0%	β _N =1.25 (P<.001), OR=3.48 (1.89-6.42)
· ·					β _c =-0.92 (P<.01), OR=0.40 (0.21-0.77)

YF Wang (Nov-2013)	BMQ-S	Not reported	MMAS-8	43.7%	r _N =0.03 (P>.05); r _c =-0.41 (P<.01); r _{NCD} =0.38 (P<.01); β _c =-0.33 (P<.001)
Author and date	BMQ	Beliefs about Medicine	Adherence	Adherence	Correlation between BMQ and Adherence
	subscales-	(Mean±SD)	weasure	(%)	
YJ Zhu (May-2017)	BMQ-S	N=19.44 ± 2.90; C=12.27 ±	MMAS-4	84.7%	β=0.03 (P=.30)
		2.79			
YS Zhao (Feb-2018)	BMQ-S	NCD=4.89±2.69	MMAS-4	Not reported	Not reported
YY Dong (Jun-2018)	BMQ-S	Not reported	Self-designed	23.4%	β=0.13, (P=.02)
YY Yao (Jun-2018)	BMQ-S	N=18.56±3.01; C=12.76±3.03	MCS	89.7%	r _№ =0.33 (P<.01); r _c =-0.12 (P<.05)
		NCD=5.78±4.37			r _{NCD} =0.31 (P<.01)
ZX Si (May-2013)	BMQ-S	N=22.2±2.3; C=11.2±2.6;	MMAS-8	87.4%	r _N =0.46 (P<.01); r _C =-0.33 (P<.01)
		NCD=11.1± 3.9			r _{NCD} =0.51 (P<.01); β _C =-0.14 (P=.03)
ZX Si et al. (Feb-2013)	BMQ-S	Not reported	N/A	N/A	N/A

1) Correlation between BMQ and adherence: r (p-value), β (p-value) or OR (95% CI); 2) N: Necessity, C: Concern, NCD: Necessity-Concern differential, H: Harm, O: Overuse, B: Benefit; 3) MMAS-8: 8-item Morisky Medication Adherence Scale; MMAS-4: 4-item Morisky Medication Adherence Scale; MARS-5: 5item Medication Adherence Report Scale; BAASIS-4: 4-item Basel Assessment of Adherence with Immunosuppressive medication Scales; VAS: Visual Analogue Scale; ED: Electronic device.

3.4 Medication adherence

Forty-one out of 58 studies measured participants' medication adherence using at least one self-reported scale. The majority of them (34/41) used a MMAS [82]. Two of them [51, 83] combined a visual analogue scale (VAS) [84] or an electronic monitoring device as additional measurements. The Basel Assessment of Adherence with Immunosuppressive medication Scales (BAASIS) [85], the 5-item Medication Adherence Report Scale (MARS-5) [86], Medical Compliance Scale [87] and one self-designed questionnaire were also used in a small number of studies [56, 57, 60] [17, 30] [77][78]. Total 41 studies measured participants' medication adherence, while 8 of them did not report the adherence rate. The proportions of adherent patients in the remaining 33 studies ranged from 33.4% to 100%. (*See Table 1 & 3*).

3.5 Relationship between BMQ scores and adherence

Twenty-four studies reported association between BMQ components and medication adherence with correlation coefficient r (16 studies), regression index β (13 studies), odds ratio (OR) with 95% CI (4 studies), or both. Two studies were excluded due to missing exact value [48] or inconsistence of the values reported in the text [56]. More details can be found in **Table 4**.

23

Table 4 The source of effect size

	r _N	r _c	r _{NCD}	β_{N}	$\boldsymbol{\beta}_{\mathrm{C}}$	β_{NCD}
C Rui (May-2017)				√	\checkmark	
H Jiang et al. (Feb-2017)	\checkmark	\checkmark				
HM Liu et al. (Jan-2016)			\checkmark			
JL Shao et al. (Oct-2015)	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	
LQ Ning et al. (Sep-2016)				\checkmark		
M Yuan et al. (Oct-2018)	\checkmark	\checkmark	\checkmark			
SH Liu et al. (Jan-2018)	\checkmark	\checkmark	\checkmark			
SJ Zhao et al. (Feb-2017)				\checkmark	\checkmark	\checkmark
SY Liu et al. (Aug-2017)						\checkmark
SY Yang & ZQ Lu (Feb-2016)	\checkmark	\checkmark	\checkmark			
SY Yang et al. (Apr-2018)			\checkmark			\checkmark
W Yan et al. (Apr-2015)	\checkmark	\checkmark	\checkmark			
X Liu et al. (Mar-2012)			\checkmark			
XX Qiao et al. (Jul-2017)				\checkmark	\checkmark	
XY Yu & W Zeng (Dec-2016)	\checkmark	\checkmark	\checkmark			
XY Zhao (May-2017)	\checkmark	\checkmark	\checkmark			\checkmark
Y Lu et al. (Feb-2016)				\checkmark	\checkmark	
YF Wang (Nov-2013)	\checkmark	\checkmark	\checkmark		\checkmark	
YJ Zhu (May-2017)						\checkmark
YY Dong (Jun-2018)						\checkmark
YY Yao (Jun-2018)	\checkmark	\checkmark	\checkmark			
ZX Si (May-2013)	\checkmark	\checkmark	\checkmark		\checkmark	

Figure 2 shows the significant positive correlations between adherence and necessity beliefs in overall meta-analysis (pooled effect size=0.32, 95% CI: 0.21, 0.43) and two subgroups (pooled r= 0.30, 95% CI: 0.16, 0.43; pooled β = 0.37, 95% CI: 0.17, 0.57). Negative correlations between specific concerns and adherence were observed in both overall meta-analysis (pooled effect size=-0.35, 95% CI: -0.42, -0.28) and subgroup analyses (pooled r= -0.35, 95% CI: -0.43, -0.27; pooled β = -0.35, 95% CI: -0.49, -0.21) (**Figure 3**). Moreover, a weak significant positive correlation was found between the NCD score and adherence (pooled effect size=0.25, 95% CI: 0.15, 0.36) (*Figure 4*).

There was significant heterogeneity between studies for the Necessity belief analysis (Q (16) =232.60, P<.01, I^2 =93%), the Concern analysis (Q (17) =101.37, P<.001, I^2 =83%) and their differential score (Q (18) =336.55, P<.01, I^2 =95%).

We tested the influence of heterogeneity by excluding the most extreme outliers. After excluding 4 out 11 studies (Necessity), 2 out 11 studies (Concerns) and 4 out 13 studies (NCD) from three meta-analyses, heterogeneity reduced (I²<50%). However, the effect direction and significance of correlation remained similar to the initial results. Moreover, we tested the influence of translation quality by excluding the studies which did not use a validated BMQ (Necessity/Concern 2 studies & NCD 5 studies). The effects sizes also were similar in these sensitivity analyses (see *Table 5*).

				Correlation with Necessity	Correlation with Necessity
Study or Subgroup	Correlation with Necessity	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.1.1 Correlation coe	efficient (r)				
11 JL Shao 2015	0.165	0.0794	5.9%	0.17 [0.01, 0.32]	
13 W Yan 2015	0.375	0.0831	5.9%	0.38 [0.21, 0.54]	
18 YF Wang 2013	0.031	0.0686	6.1%	0.03 [-0.10, 0.17]	
26 H Jiang 2017	0.009	0.0803	5.9%	0.01 [-0.15, 0.17]	-
30 XY Yu 2016	0.463	0.0824	5.9%	0.46 [0.30, 0.62]	
31 SY Yang 2016	0.179	0.0856	5.8%	0.18 [0.01, 0.35]	
34 ZX Si 2013b	0.46	0.0586	6.3%	0.46 [0.35, 0.57]	
54 XY Zhao 2017	0.67	0.0391	6.5%	0.67 [0.59, 0.75]	-
59 SH Liu 2018	0.31	0.0731	6.0%	0.31 [0.17, 0.45]	
61 M Yuan 2018	0.22	0.0767	6.0%	0.22 [0.07, 0.37]	
63 YY Yao 2018	0.33	0.0447	6.4%	0.33 [0.24, 0.42]	
Subtotal (95% CI)			66.8%	0.30 [0.16, 0.43]	•
Heterogeneity: Tau ² =	= 0.05; Chi ² = 124.07, df = 10	(P < 0.00)	0001); I ²	= 92%	
Test for overall effect	Z = 4.28 (P < 0.0001)				
4.1.2 Regression coe	fficient (Beta)				
11 JL Shao 2015	0.13	0.0657	6.2%	0.13 [0.00, 0.26]	
23 SJ Zhao 2017	0.16	0.05	6.4%	0.16 [0.06, 0.26]	-
32 LQ Ning 2016	0.278	0.0923	5.7%	0.28 [0.10, 0.46]	
36 Y Lu 2016-China	1.247	0.129	5.0%	1.25 [0.99, 1.50]	
37 XX Qiao 2017	0.173	0.024	6.6%	0.17 [0.13, 0.22]	-
53 C Rui 2017	0.44	0.22	3.3%	0.44 [0.01, 0.87]	
Subtotal (95% CI)			33.2%	0.37 [0.17, 0.57]	
Heterogeneity: Tau ² =	= 0.05; Chi ² = 70.82, df = 5 (P	< 0.000	01); $I^2 =$	93%	
Test for overall effect	Z = 3.67 (P = 0.0002)				
Total (95% CI)			100.0%	0.32 [0.21, 0.43]	•
Heterogeneity: Tau ² =	= 0.05; Chi ² = 232.60, df = 16	(P < 0.00	0001); I ²	= 93%	
Test for overall effect	Z = 5.64 (P < 0.00001)		.,		-1 -0.5 0 0.5 1
Test for subgroup dif	ferences: $Chi^2 = 0.37$, $df = 1$ (1)	P = 0.54	$1^2 = 0\%$		

Figure 2 Forest plot of correlations between Necessity beliefs and medication adherence

Correlation with Concern Correlation with Co	ncern				
Study or Subgroup Correlation with Concern SE Weight IV, Random, 95% CI IV, Random, 95%	CI				
4.3.1 Correlation coefficient (r)					
11 JL Shao 2015 -0.479 0.0629 5.9% -0.48 [-0.60, -0.36]					
13 W Yan 2015 -0.542 0.0683 5.7% -0.54 [-0.68, -0.41]					
18 YF Wang 2013 -0.406 0.0574 6.1% -0.41 [-0.52, -0.29]					
26 H Jiang 2017 -0.47 0.0626 5.9% -0.47 [-0.59, -0.35]					
30 XY Yu 2016 -0.342 0.0926 4.9% -0.34 [-0.52, -0.16]					
31 SY Yang 2016 -0.166 0.086 5.1% -0.17 [-0.33, 0.00]					
34 ZX Si 2013b -0.332 0.0661 5.8% -0.33 [-0.46, -0.20]					
54 XY Zhao 2017 -0.37 0.0612 6.0% -0.37 [-0.49, -0.25]					
59 SH Liu 2018 -0.38 0.0692 5.7% -0.38 [-0.52, -0.24]					
61 M Yuan 2018 -0.23 0.0763 5.4% -0.23 [-0.38, -0.08]					
63 YY Yao 2018 -0.12 0.0494 6.4% -0.12 [-0.22, -0.02]					
Subtotal (95% CI) 62.8% -0.35 [-0.43, -0.27]					
Heterogeneity: Tau ² = 0.02; Chi ² = 45.79, df = 10 (P < 0.00001); $I^2 = 78\%$					
Test for overall effect: Z = 8.17 (P < 0.00001)					
4.3.2 Regression coefficient (Beta)					
11 IL Shao 2015 -0.31 0.0737 5.5% -0.31 [-0.45, -0.17]					
18 YF Wang 2013 -0.331 0.0612 6.0% -0.33 [-0.45, -0.21]					
23 SJ Zhao 2017 -0.27 0.0592 6.0% -0.27 [-0.39, -0.15]					
34 ZX Si 2013b -0.14 0.0747 5.5% -0.14 [-0.29, 0.01]					
36 Y Lu 2016-China -0.916 0.087 5.1% -0.92 [-1.09, -0.75]					
37 XX Qiao 2017 -0.32 0.022 7.0% -0.32 [-0.36, -0.28] -					
53 C Rui 2017 -0.03 0.21 2.1% -0.03 [-0.44, 0.38]	-				
Subtotal (95% Cl) 37.2% -0.35 [-0.49, -0.21]					
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 55.18$, $df = 6$ (P < 0.00001); $I^2 = 89\%$					
Test for overall effect: Z = 4.87 (P < 0.00001)					
Total (95% Cl) $100.0\% -0.35 [-0.42, -0.28] \qquad \clubsuit$					
Total (95% Cl) 100.0% -0.35 [-0.42, -0.28] Heterogeneity: Tau ² = 0.02; Chi ² = 101.37, df = 17 (P < 0.00001); l ² = 83%					
Total (95% CI) Heterogeneity: Tau ² = 0.02; Chi ² = 101.37, df = 17 (P < 0.00001); I ² = 83% Test for overall effect: $Z = 9.82$ (P < 0.00001)	0.5 1				

Figure 3 Forest plot of correlations between Concerns beliefs and medication adherence

			C	orrelation with NCD	Correlation with NCD
Study or Subgroup	Correlation with NCD	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.5.1 Correlation co	efficient (r)				
11 JL Shao 2015	0.469	0.0637	5.3%	0.47 [0.34, 0.59]	
13 W Yan 2015	-0.402	0.0976	4.8%	-0.40 [-0.59, -0.21]	
18 YF Wang 2013	0.383	0.0586	5.4%	0.38 [0.27, 0.50]	
27 HM Liu 2016	0.26	0.0483	5.5%	0.26 [0.17, 0.35]	
30 XY Yu 2016	0.057	0.1045	4.7%	0.06 [-0.15, 0.26]	
31 SY Yang 2016	0.237	0.0834	5.0%	0.24 [0.07, 0.40]	
34 ZX Si 2013b	0.509	0.0551	5.4%	0.51 [0.40, 0.62]	
5 X Liu 2012	0.203	0.0979	4.8%	0.20 [0.01, 0.39]	
54 XY Zhao 2017	0.68	0.0381	5.6%	0.68 [0.61, 0.75]	
59 SH Liu 2018	0.44	0.0652	5.3%	0.44 [0.31, 0.57]	
51 M Yuan 2018	0.28	0.0743	5.1%	0.28 [0.13, 0.43]	
53 YY Yao 2018	0.31	0.0453	5.5%	0.31 [0.22, 0.40]	· · · ·
56 SY Yang 2018	0.3	0.0897	4.9%	0.30 [0.12, 0.48]	
Subtotal (95% CI)			67.2%	0.30 [0.17, 0.42]	
Test for overall effec	t: Z = 4.61 (P < 0.00001) efficient (Beta)				
23 SI Zhao 2017	0.27	0.0547	5.4%	0.27 [0.16, 0.38]	
45 SY Liu 2017	0.32	0.0584	5.4%	0.32 [0.21, 0.43]	
52 YI Zhu 2017	0.03	0.0289	5.6%	0.03 [-0.03, 0.09]	+
54 XY Zhao 2017	0.18	0.0607	5.3%	0.18 [0.06, 0.30]	— -
56 SY Yang 2018	0.07	0.0264	5.7%	0.07 [0.02, 0.12]	
70 YY Dong 2018	0.13	0.0559	5.4%	0.13 [0.02, 0.24]	
Subtotal (95% CI)			32.8%	0.16 [0.07, 0.25]	
Heterogeneity: Tau ² Test for overall effec	= 0.01; Chi ² = 32.86, df = t: Z = 3.52 (P = 0.0004)	= 5 (P < 0	0.00001);	$e^{2} = 85\%$	
Total (95% CI)			100.0%	0.25 [0.15, 0.36]	•
Heterogeneity: Tau ²	= 0.05; Chi ² = 336.55. df	= 18 (P	< 0.00001	.); $I^2 = 95\%$ —	
Fest for overall effec	t: $Z = 4.81 (P < 0.00001)$				-0.5 -0.25 0 0.25 0.5

Figure 4 Forest plot of correlations between NCD scores and medication adherence

	Pooled r (95% CI)	Pooled β (95% Cl)	Overall pooled effect
			size (95% CI)
Necessity			
Before	0.30 (0.16, 0.43)	0.37 (0.17, 0.57)	0.32 (0.21, 0.43)
After	0.28 (0.12, 0.45)	0.37 (0.17, 0.57)	0.32 (0.19, 0.44)
Concern			
Before	-0.35 (-0.43 <i>,</i> -0.27)	-0.35 (-0.49, -0.21)	-0.35 (-0.42, -0.28)
After	-0.33 (-0.42, -0.23)	-0.35 (-0.49, -0.21)	-0.34 (-0.41, -0.26)
NCD			
Before	0.30 (0.17, 0.42)	0.16 (0.07, 0.25)	0.25 (0.15, 0.36)
After	0.37 (0.24, 0.49)	0.16 (0.06, 0.27)	0.29 (0.17, 0.42)

Table 5 Pooled effect sizes of meta-analyses before and after removing outliers

3.6 Research quality

The quality assessment indicated that twelve studies were rated as good quality, thirty-six as moderate quality, and ten as poor quality (see Table 1 & 2). The element of study quality, which seemed to be the weakest overall, was a lack of sample size calculation, with only sixteen studies including this information. Regarding participants, most studies clearly described the inclusion criterial of participants, except Yan's study [65]. The reported response rates varied between 77.7% and 100%. Eight studies did not report participants' response rate. Liu's study [61] had a considerable dropout rate (>20%), but did not discuss the impact of these missing data. For sampling strategies, the majority of studies (41/58) applied a non-probability sampling method, such as convenient sampling, stratified sampling and opportunity sampling. Another 14 studies did not describe their sampling strategies. Only three studies [27, 72] [76] applied random sampling method. Around half of studies (28/58) clearly defined how they had assessed beliefs about medicines and explained what they had measures. Eleven studies used self-translated versions of BMQ, three most commonly cited versions were translated and validated following the appropriate guideline. However, another eleven studies did not provide any details of translation, meaning unable to detect whether they followed an appropriate methodology. Although items on general benefit beliefs had been added into BMQ since 2001[14], few included study cited the new

version, except Wan [27] and Wei [17]. The funnel plots (*Figure 5*) showed that there was a slight publication bias among studies reporting regression beta [88].



Figure 5. Panel (a): Funnel plot of studies for Necessity belief analysis. Panel (b): Funnel plot of studies for Concern analysis. Panel (c): Funnel plot of studies for NCD analysis.

4. Discussion

This was the first study systematically review studies which have measured Chinese patients' beliefs about medicines using the BMQ. The results showed that the BMQ has been widely used in a wide range of Chinese patient groups. Several different versions of the BMQ had been used. The meta-analysis results indicated that the Chinese population had same cognitive and behavioural patterns with Western population: patients who believed that they needed their medication and had fewer concerns about potential risks of treatment were more likely to be adherent.

4.1 The use of BMQ in China

We found that the BMQ was first introduced and applied in the Chinese population in 2012 [67], despite having been available from 1999 and widely used in different patient groups and cultures [11, 13]. Cardiac-cerebral vascular disease (16 out of 58) was the main focused condition in BMQ studies in China.

4.2 The reliability of translation of BMQ

A commonly accepted Cronbach's α indicate sufficient reliability for questionnaires is 0.7 [89]. Eight out of nine tested Cronbach's α of overall BMQ reported by studies were over than 0.7, indicating these Chinese versions had acceptable internal consistency reliability. However, nearly half (18 out of 43) reported Cronbach's α for subscales were lower than 0.7. It might be ascribed to a small number of items and heterogeneity of participants. The Cronbach's α is easily influenced by the size of the questionnaire, therefore the reliability of subscales made up of 4 or 5 items was highly possible underestimated.

4.3 Correlation between beliefs about medicines and medication adherence

The results suggested that patients with stronger necessity beliefs about medication might adhere more to prescribed medication. Whereas, patients who are more concerned about potential risks of their medication, might be less likely to adhere to treatment. With the significant positive correlation between adherence and the NCD score which is also in line with predictions, these findings indicate the Necessity-Concern Framework is an effective model to predict adherence behaviour. Our findings were consistent with previous reviews of studies using the BMQ [11]. In Horne's meta-analyses, the converted correlation coefficients (r) between specific beliefs about medicines and medication adherence were $r_n=0.15$, and $r_c=-0.19$ [90, 91], which had same direction with pooled results in the current meta-analyses (r_n =0.32, and r_c =-0.35). The results also indicated that the correlations between specific beliefs about medicines and medication adherence in Chinese population seemed stronger than them among the Western population.

Regarding the heterogeneity, there was substantial heterogeneity among included studies across the three meta-analyses. However, this was expected due to the many complex factors that contribute to medication adherence behaviour [92]. The effect direction and correlation significance remained similar after removing outlier cases, indicating that these outliers did not bias our estimates of the effects of beliefs on adherence.

4.4 Study quality

The majority of included studies (48 out of 58) had a moderate or good quality. However, there were several common limitations to study quality identified by our review. Firstly, more than half of the included studies (41 out of 58) applied a non-probability sampling method, such as convenience sampling, which is a simple and pragmatic way to recruit participants but could lead to sampling bias and harm both the internal and external validity of the study. Moreover, the response rate varied between studies and selection bias could be introduced. These patients who were highly engaged with the survey might also adhere their treatment. The findings may not be generalizable to the whole population [93, 94]. In addition, most of the included studies measured participants' medication adherence with self-report scales, which may be influenced by recall bias, social desirability bias and errors in self-observation [95]. We also noted that the definition of nonadherence used varied across studies with different cut-off points and measurements being used which might identify different groups of patients. Several of the studies did not report data clearly,

31

with seven studies measuring but not reporting data on the medicine beliefs, and eight studies [27, 33, 44, 51, 58, 63, 66, 76] measuring but not reporting adherence rate, as well.

4.5 Strengthens and limitations

This is the first study that systematically reviewed all studies using the BMQ to evaluate medication beliefs in China. The review not only focused the studies published conducted in databases in English indexing, but also some Chinese databases as most of the studies published in Chinese. This review highlights that beliefs about medicine are associated with medication adherence in the Chinese population as has been found in other reviews. The results also offer targets for intervention. The associations were evaluated using both correlation coefficient and regression index. The latter one was adjusted by some confounding factors, which may contribute to the influence of beliefs about medicines on adherence and their correlation. Potentially, clinicians may be able to assess patients' beliefs about medicines in order to identify those at risk of nonadherence.

There were also several limitations of this review. Firstly, although there were a reasonable number of studies focused on participants' specific beliefs about medicines, there was a lack of evidence about the influence of general beliefs on medication adherence. Similarly, there was a limited range of patient groups/diseases on which data had been collected meaning that we were unable to generalize our finding to the entire Chinese population. The majority of studies identified were also cross-sectional, meaning that we could not evaluate whether medication beliefs predicted outcomes prospectively. Finally, the correlations between each BMQ subscale and different translated versions were not explored in the present study and were worthy detecting in the future study.

32

5. Conclusion

Our review found that the BMQ has been widely applied in the Chinese population. The Necessity-Concerns Framework and specific beliefs about medicines appears to be a useful conceptual model to explain Chinese patients' medication adherence behaviour, as has been found in previous reviews in other population. Further high-quality studies examining medication beliefs and adherence in Chinese populations with a wide range of conditions are warranted.

Authorship

Bo Nie: Contributed to study design, Conducted the study, analysed the data and wrote the first draft of the manuscript.

Sarah Chapman: Contributed to study design, data analysis, and interpretation of the results and approved the final version of the manuscript.

Zhe Chen: Contributed to data extraction and quality assessment and approved the final version of the manuscript.

Xiuli Wang: Contributed to data screening and quality assessment and approved the final version of the manuscript.

Li Wei: Contributed to study design, data analysis, and interpretation of the results and approved the final version of the manuscript.

Author declaration

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Appendixes

Appendix A Search strategy and searching results in PubMed

No.	Search term	Result of single	Result of combined
		search term	search terms
#1	"China" [Mesh]	163,095	
#2	"Taiwan"[Mesh]	33,702	170,674
#3	China[Text Word]	209,324	220,970
#4	Chinese[Text Word]	213,762	350,269
#5	Taiwan[Text Word]	46,923	359,916
#6	Taiwanese[Text Word]	9,415	361,591
#7	Hong Kong[Text Word]	21,642	365,694
#8	Macao[Text Word]	283	365,751
#9	Macau[Text Word]	324	365,772
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7		413,279
	OR #8 OR #9		
#11	"medicine"[Mesh]	1,060,607	
#12	medicine\$[Text Word]	789,887	1,412,351
#13	medication\$[Text Word]	222,203	1,598,281
#14	drug\$[Text Word]	5,353,008	6,428,996
#15	#11 OR #12 OR #13 OR #14		6,767,845
#16	"perception"[Mesh]	404,614	
#17	belief\$[Text Word]	30,394	409,040
#18	perception\$[Text Word]	332,401	494,179
#19	#16 OR #17 OR #18		527,809
#20	#15 AND #19		75,912
#21	"beliefs about medicine" [Text Word]	65	
#22	BMQ[Text Word]	200	188
#23	#20 OR #21 OR #22		76,075
#24	"Surveys and Questionnaires"[Mesh]	939,504	
#25	questionnaire\$[Text Word]	364,457	1,004,749
#26	scale\$[Text Word]	640,779	1,461,580
#27	#24 OR #25 OR #26		1,621,859
#28	#10 AND #23 AND #27		306

Appendix B Search strategy and searching results in EMBASE and PsycINFO

No.	Search term	EMBASE	PsycINFO
#1	exp China/	193,219	N/A
#2	exp Chinese/	53,194	N/A
#3	exp Han Chinese	4,508	
	exp Chinese Cultural Groups/		6,075
#4	exp Taiwan/	43,161	N/A
#5	exp Taiwanese/	2,437	N/A
#6	exp Hong Kong/	20,310	N/A
#7	exp Macao/	356	N/A
#8	China.sh,mp.	265,575	26,867
#9	Chinese.sh,mp.	262,619	47,318
#10	Taiwan.sh,mp.	58,611	10,949
#11	Taiwanese.sh,mp.	12,105	4,702
#12	Hong Kong.sh,mp.	27,369	10,592
#13	Macau.sh,mp.	288	252
#14	Macao.sh,mp.	543	172
#15	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	529,026	73,472
	OR #9 OR #10 OR #11 #12 OR #13 OR #14		
#16	exp medicine/	2,868,523	274,420
#17	exp medication/	2,372,064	136,949
#18	exp drug/	2,644,073	
	exp drugs/		297,022
#19	medicine\$.sh,mp.	1,113,530	66,032
#20	medication\$.sh,mp.	483,869	84,314
#21	drug\$.sh,mp.	9,712,890	370,435
#22	#16 OR #17 OR #18 #19 OR #20 OR #21	12,514,847	773,399
#23	belief\$.sh,mp.	95,069	132,595
#24	exp perception/	299,942	321,104
#25	perception\$.sh,mp.	370,595	450,065
#26	#23 OR #24 OR #25	581,698	647,046
#27	#22 AND #26	156,584	56,545
#28	BMQ.sh,mp.	482	67
#29	#27 OR #28	156,644	56,552
#30	exp questionnaire/	626,004	17,859
#31	questionnaire\$.sh,mp.	839,832	378,710
#32	scale\$.sh,mp.	1,095,661	633,228
#33	#30 OR #31 OR #32	1,747,647	845,670
#34	#15 AND #29 AND #33	1,124	340

No.	Search term	CNKI	WANFANG
#1	TI/AB ='药物'	851,943	1,128,762
#2	TI/AB ='药品'	90,574	183,182
#3	TI/AB ='服药'	51,397	61,188
#4	TI/AB ='用药'	346,652	413,487
#5	#1 OR #2 OR #3 OR #4	1,138,804	1,545,959
#6	TI/AB ='信念'	5,264	101,716
#7	TI/AB ='问卷'	194,332	639,969
#8	TI/AB ='量表'	180,193	283,713
#9	#7 OR #8	337,079	848,577
#10	#5 AND #6 AND #9	381	370
#11	FT='BMQ'	184	179
#12	FT='belief about medicine'	1	4
#13	FT='beliefs about medicine'	15	24
#14	FT='belief about medicines'	1	8
#15	FT='beliefs about medicines'	76	155
#16	#10 OR #11 OR #12 OR #13 OR #14 OR #15	555	646

Appendix C Search strategy and the number of results in ZHIWANG and WANFANG

Search term in Chinese databases:

CNKI: (((TI='药物'+'药品'+'服药'+'用药') OR (AB='药物'+'药品'+'服药'+'用药')) AND (TI='信念' OR AB='信念') AND ((TI='量表'+'问卷') OR (AB='量表'+'问卷'))) OR (FT= 'BMQ'+'belief about medicine'+'beliefs about medicine'+'belief about medicines'+'beliefs about medicines')

WANFANG: ((题名或关键词:("用药"+"药品"+"药物"+"服药") OR 摘要:("用药"+"药品"+"药 物"+"服药")) AND (题名或关键词:("量表"+"问卷") OR 摘要:("量表"+"问卷")) AND ((题 名或关键词:"信念") OR 摘要:("信念"))) OR 全部:("BMQ"+"belief about medicine"+"beliefs about medicine"+"belief about medicines"+"beliefs about medicines")

Appendix D Quality Assessment Tool

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Sampling & Participants (/5)				
Questions 1. Were the charac	teristics of the participants	included in the study clearly		
described? (Inclusion and/or e	exclusion criteria should be	listed, and answered the		
questions of who, where, and	when)			
Yes (1)	No			
Questions 2. Were the charac	teristics of participants with	n missing, incomplete, and/or		
invalid data been described?	This should be answered ye	es where the rate of exclusions		
based on missing or poor data	was less than 20%. This sh	ould be answered no, where a		
study did not describe or repo	ort the number of participar	nts excluded based on missing or		
poor data)				
Yes (1)	No	Unable to determine		
Questions 3. How did authors	sampling?			
Probability sampling (e.g.	Non-probability sampling	No description of the sampling		
random sampling) (2)	(e.g. convenience			
	sampling) (1)			
Questions 4. Was a sample siz	e justification, or variance a	and effect estimates provided?		
Study had a clear	The authors gave the	No sample size		
calculation/explanation, and	estimates of variance	calculation/explanation, or did		
a satisfied sample size (1)	and/or estimates of	not recruit enough participants		
	effect size (1)			
Deliafa about medicines (/C	1			
Beliefs about medicines (76) 	fine all and include a stand		
Questions 5. were the beliefs	about medicines clearly de	nned, and implemented		
Voc (1)	No			
Questions 6 Did author cite t	no he original reference of the	BMO2		
Ves (1)				
Questions 7 Did authors trans	slate the BMO following a s	tandard translation method (e.g.		
Brislin's translation model)? (I	f study cited the translated	BMO the question should be		
answered as ves)	r study cited the translated	bind the question should be		
Yes (1)	No	Unable to determine		
Ouestions 8. Did authors report the reliability/validity coefficient of the version they				
used?		,		
Yes (1)	No			
Questions 9. Were the metho	ds of data reduction for BM	IQ clearly described?		
Yes (1)	No			
Questions 10. Did authors clea	arly report the BMQ scores	for overall and each subgroup?		
Yes (1)	No	<u> </u>		
Medication adherence (/4)				
Questions 11. Were the medication/treatment adherence defined in detail, and				
implemented consistently across all participants?				
Yes (1)	No			
Questions 12. Did authors use	an objective measurement	t?		
Objective method (e.g. pill	Subjective tools (e.g.	No description of measure		
count or prescription-refill	self-reported scale) (1)	tools, or used inaccurate		
records) (2)		method		

Questions 13. Did authors clearly report the adherence results for overall and each subgroup?				
Yes (1)	No			
Statistical analysis (/5)				
Questions 14. How was the st	atistical power of the study	?		
≥ 80% (1)	<80%	No discussion of power calculation		
Questions 15. Were principal	confounders clearly measu	red and described? (Distributions		
of sex, age et al should be pre	sented)			
Yes (1)	No			
Questions 16. Were principal confounders adjusted statistically for their impact on the relationship between independent variable(s) and outcome(s)?				
Yes (1)	No			
Questions 17. Did authors select accurate statistical methods to solve the research questions?				
Yes (1)	No			
Questions 18. Have limits of agreement and/or confidence intervals been reported for the main analyses?				
Yes (1)	No			