




BMJ Open Influencing factors and their relationships of risk perception and decision-making behaviour of polypharmacy in patients with chronic diseases: a qualitative descriptive study

Yuxin Liu ¹, Ruoxi Wang ², Rui Huang,¹ Yan Cao,¹ Jia Wang ¹, Da Feng ¹

To cite: Liu Y, Wang R, Huang R, *et al*. Influencing factors and their relationships of risk perception and decision-making behaviour of polypharmacy in patients with chronic diseases: a qualitative descriptive study. *BMJ Open* 2021;**11**:e043557. doi:10.1136/bmjopen-2020-043557

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-043557>).

Received 11 August 2020
Revised 16 March 2021
Accepted 19 March 2021



© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Tongji Medical College, School of Pharmacy, Huazhong University of Science and Technology, Wuhan, China

²Tongji Medical College, School of Medicine and Health Management, Huazhong University of Science and Technology, Wuhan, China

Correspondence to

Da Feng; fengda@hust.edu.cn

ABSTRACT

Objectives In order to understand the influencing factors of the medication-taking behaviour in patients with chronic diseases, reveal the deep-seated causes underlying the phenomenon of polypharmacy, explore the formation rules of the risk perception of polypharmacy and how risk perception affect the medication decision-making behaviour of patients with chronic diseases.

Design A qualitative descriptive design was used. Study data were collected through semi-structured interviews with patients and physicians. We used the grounded theory approach to refine influencing factors, followed by interpretative structural modelling that analysed the interaction between these factors.

Setting Patients from two hospitals, two nursing homes and two communities. Physicians from two community hospitals in Wuhan, China.

Participants Patients with chronic diseases with high willingness to cooperate and good communication ability. Physicians with rich experience in the treatment of chronic diseases.

Results Twenty-nine interviews were conducted (20 patients and 9 physicians). A total of 35 influencing factors of the medication-taking behaviours in patients with chronic diseases were extracted from the interview data, further integrated into 10 integrated influencing factors and ultimately clustered into three aspects: ‘medication benefit’, ‘medication risk’ and ‘medication strategy’. Medication risk can be divided into four specific dimensions: economic risk, physical risk, psychosocial risk and time risk. 10 integrated influencing factors constituted the interpretative structural model of the medication decision-making behaviours in patients with chronic diseases.

Conclusions The causes underlying the medication decision-making behaviour of patients with chronic diseases are complex, involving a series of influencing factors such as their risk perception of the medication-taking behaviour. In order to alleviate the adverse effects of polypharmacy on patients’ health and medical costs, further safety measures should be proposed to improve the medication-taking behaviour in patients with chronic diseases based on the relationship and internal mechanism of the influencing factors of the medication decision-making behaviour.

Strengths and limitations of this study

- This is the first study to explore influencing factors of risk perception and decision-making behaviour of polypharmacy in patients with chronic diseases in the context of the Chinese health system.
- Participants were included based on the information system resources of community public health to ensure the credibility and acceptability of the results.
- The use of semi-structured interviews with both patients and physicians provided an opportunity to elicit comprehensive information about patients’ risk perception and decision-making behaviours, and interpretative structural modelling can transform the influencing factors of patients’ medication decision-making behaviours into a clearer model.
- The interview and inductive content analysis was conducted in Wuhan, China, and all study participants were Chinese, which may be considered as a limitation of the transferability of the study results in different cultural contexts.

INTRODUCTION

Non-communicable chronic disease is a general term for a class of diseases with hidden onset, long incubation period, long and slow course, unsustainable condition, no clear indication of ‘curing’. ‘Medium and Long-Term Planning for the Prevention and Treatment of Chronic Diseases in China (2017–2025)’ shows that the number of people dying of chronic diseases in China accounts for 86% of the total deaths, and the disease burden caused by chronic diseases accounts for more than 70% of the total disease burden, which has seriously affected the health of Chinese residents. Additionally, it has been reported that patients with chronic diseases often coexist with multiple diseases.¹ The results of the *National Health Services Survey in China (2013)* show that the prevalence of chronic diseases among middle



and older-aged Chinese continued to increase in the past years, and comorbidities have become a prominent challenge to the general health in senior Chinese.² Defined as the presence of additional diseases in relation to an index disease in one individual, comorbidity is associated with more complex clinical management.³ Comorbidities have a significant impact on treatment regimens.⁴ Clinically, patients with multiple chronic conditions are in poorer health status than those with a single condition.⁵ As an important method of control and treatment, taking a combination of medications is necessary in many cases,⁶ which leads to the phenomenon of polypharmacy.

There is not a unified definition of the term 'polypharmacy',⁷ it has been given in different definitions including but not limited to 'unnecessary drug use', 'medication use without indication' and 'use four/five or more medications'.⁸⁻¹⁰ Extant literature reveals that the incidence of drug interactions and adverse drug reactions increase significantly with the increase in the types and quantity of medications taken by patients with chronic diseases.¹¹ This is especially true in the senior population¹² whose liver and kidney functions are more prone to be damaged by the age growing.^{13 14} Besides, polypharmacy is also associated with adverse outcomes including falls, mortality rate, length of hospital stay, readmission rate soon after discharge, quality of life and healthcare cost.¹⁵⁻¹⁹ Common reasons of polypharmacy include misprescribing and overprescribing.²⁰ In addition, self-medication is another potential cause of polypharmacy, especially for older population.²¹ Additional contributing factors include misunderstanding of medical orders and mistaking drugs, both of which also arise more often in older age groups.¹²

The concept of risk perception was originally extended in psychology to study consumer behaviour. It was defined as people's ability to perceive the risks posed by their decision-making results. Risk perception is a complex multifactorial process built on the experiences that are influenced by socioeconomic, political and cultural contexts.²² Different theories about the mechanism of risk perception process have been proposed such as behaviours and skills,²³ health beliefs,²⁴ social learning.²⁵ According to relevant research, one's health behaviours may be driven by their risk perception.²⁶ However, there is no research that studied the correlation between risk perception and decision-making behaviour of polypharmacy in patients with chronic diseases at present.

As such, this study was designed and conducted to reveal the causes behind the phenomenon of polypharmacy and explore how risk perception affects the medication decision-making behaviour in patients with chronic diseases.

The aims of this study were to: (1) understand the influencing factors of the medication-taking behaviour in patients with chronic diseases and find out the deep-seated causes behind the phenomenon of polypharmacy from patients' and physicians' perspectives, respectively; (2) explore the relationship among the influencing

factors and reveal how risk perception influences the medication decision-making behaviour in patients. The focus of this study was patients with multiple chronic conditions, who tend to take multiple medications.

METHODS

Study design

A qualitative descriptive design-grounded theory was adopted. A qualitative descriptive design was employed in this study since the intention was to understand the risk perception and decision-making behaviour of polypharmacy directly from those patients who suffer from chronic diseases and their physicians,²⁷ and address the research questions from their standpoints and experiences.²⁸ Grounded theory was recognised as a rigorous method to facilitate the emergence of new themes, issues and opportunities from study data.²⁹ The data collection framework involved semi-structured interviews that elicit information, whereas also enable patients and physicians to elaborate on their comprehension of polypharmacy at the same time.³⁰ After refining the influencing factors, we integrated them into an appropriate quantity to construct the interpretative structural model of the medication decision-making behaviour in patients with chronic diseases. The main idea of the interpretative structural modelling method is to decompose a complex system into several subsystems according to experts' knowledge and practical experience, and to construct a multilevel hierarchical structure model,³¹ which helps to clarify the interaction among system elements.³² This method has been widely used to study the relationship between different variables in a complex system.³³

Setting

The study was undertaken in Wuhan, the capital of Hubei province, China. Two hospitals (Tianyou Hospital Affiliated to Wuhan University of Science and Technology, Union Jiangbei Hospital), two community hospitals (Hanjiadun Street Community Health Service Center, Baishazhou Street Community Health Service Center), two nursing homes (Zhongtai nursing home of Didong Community, Kangjian nursing home of Jiefangqiao Community) and two communities (Community of Hanjiadun Street, Community of Baishazhou Street) were purposively selected to meet the appropriate sample size of both patients and physicians. Data related to participants' risk perception and decision-making behaviour of polypharmacy were collected by semi-structured interviews, the collection of participants' demographic characteristics also completed at this phase.

Participants

The main participants of the study were health service users. However, considering that health service providers have established close contact with patients at work, they can provide rich information from another perspective, this study included physicians in the interview as well. As a

result, the study participants were patients suffering at least two types of chronic diseases who tend to take multiple medications and physicians with rich experience in the management and treatment of chronic diseases. Based on the information system resources of community public health, convenience sampling was used to select individuals who met the inclusion criteria as participants in this research. Any individual who was unwilling to participate in the interview as well as those with poor cooperation or communication with the interviewer were excluded. The researcher explained the subject of the study to participants in plain language, provided a written literal statement and completed a formal written consent process for attending the study to gain the trust of the participants and conduct the interviews with a high degree of cooperation. The process of including participants was in full compliance with the guidelines of the Ethics Committee of the Tongji Medical College of Huazhong University of Science and Technology. To reach a comprehensive understanding of different aspects of polypharmacy, a number of factors were taken into consideration during the selection process such as age, gender, socioeconomic level and comorbid chronic conditions of patients. For example, to achieve maximum variation in terms of comorbidity, different types of diseases were taken into consideration in the selection of patients to include a combination of diseases common among older people such as diabetes, hypertension, hyperlipidaemia and coronary disease. For physicians, the professional titles, education background and working years were taken into consideration as well. Based on the general sample size of qualitative research,³⁴ this study initially determined the sample size as about 30 people. Patients were the focus of the interview in this study, and physicians were the supplementary sources of information. In the end, a total of 29 participants were included in the study, including 20 patients and 9 physicians.

Patient and public involvement

Patients and the public were not involved in this study. Patients were not invited to comment on the study design or the study findings, and no patients were invited to contribute to the writing or editing of this document.

Data collection

The study data were collected from October 2019 to December 2019 using semi-structured face-to-face interviews and field notes. All interviews were conducted by the first author who is a trained interviewer with years of experience in communicating with patients and physicians. The interviews were conducted at locations approved by the participants such as their residences, nursing homes for patients or hospitals for physicians. Only the interviewer was present to ensure the privacy of the study and participants were able to interact comfortably about their experiences. The interviewer asked for audio recording before the interview started, and after the participants' informed consent, the interview was

formally started and recorded. Two interview outlines (online supplemental appendices 1 and 2) for patients and physicians separately were used to guide the interviews. These interview guides were informed based on literatures and previous work related to polypharmacy, and were fine-tuned by researcher of this study with the support of some relevant specialist. The questions in the interview guides were set as open-ended questions and can be flexibly adjusted according to the actual situation to encourage the participants to express their true thoughts. A total of 80% of the collected data were used for analysis and the other 20% were used for saturation testing. The interview numbers were deemed sufficient when data saturation had been reached which defined as no new information was emerging from the content of the interviews.

Data analysis

Data analysis was performed based on the grounded theory approach and the interpretative structural modeling method. In the grounded theory approach, the concepts are extracted directly from data rather than previous knowledge. Qualitative data analysis software (NVivo V.11) was used to facilitate data analysis. All recordings were transcribed verbatim after the interview, which were then thoroughly reviewed for several times. The original sentences in interview materials related to the research subject were identified as meaning units. These meaning units were coded as concepts based on their hidden contents. Codes with similar contents were further integrated into subcategories at higher levels of abstraction. Finally, categories were determined by comparing subcategories and reflecting on their potential contents. After refining and integrating the influencing factors into the appropriate quantity, 10 specialists in relevant fields were invited to form a group to analyse the inter-relationship among these influencing factors. A structured questionnaire is designed to obtain the opinions of the specialists. The specialists conducted a pairwise comparison of factors by answering the questions 'Do you think factor i directly affects factor j ?'. The questionnaire included explanations of factors to ensure an accurate and consistent understanding. As different experts may judge the pairwise comparison of two factors differently, the principle of 'the minority gives way to the majority' was adopted to address this issue.^{33 35} In this research, the contextual relationship between factors was determined if eight or more specialists agree. Subsequently, the opinions of specialists were transformed into an adjacency matrix, and computation tool (MATLAB R2017a) was used to develop a reachability matrix based on the obtained adjacency matrix according to the Boolean rules.

RESULTS

A total of 29 participants were included in this study, 13 men and 16 women; 20 of them were patients with

Table 1 Characteristics of patients in this study

Variables	N (%)
Gender	
Male	8 (40)
Female	12 (60)
Age (years)	
<60	3 (15)
60–64	5 (25)
65–69	2 (10)
70–74	2 (10)
75–79	3 (15)
>80	5 (25)
Education level	
Elementary	7 (35)
Middle	12 (60)
College	1 (5)
Number of medications used	
Mean (SD)	4.65 (2.39)

chronic diseases and 9 of them were physicians. The mean age of patients was 69.85 ± 11.34 years, and the mean age of physicians was 54.11 ± 18.98 years. Among patients, 7 had elementary school education, 12 had middle school education and 1 had college education. A total of eight physicians held a bachelor degree and one held a master's degree. The number of comorbidities among patients ranged between 2 and 6 and the number of medications (prescribed and non-prescribed) used by patients ranged from a minimum of 2 to a maximum of 11 per day. According to the most commonly reported definition of polypharmacy as numerical definition of five or more medications daily,³⁶ 12 of the 20 participating patients are experiencing now or had experienced polypharmacy. The characteristics of participants are presented in tables 1 and 2. The length of the interviews ranged from a minimum of 21 min to a maximum of 80 min.

A total of 35 influencing factors of the medication decision-making behaviour of patients with chronic

Table 2 Characteristics of physicians in this study

Variables	N (%)
Gender	
Male	5 (55.56)
Female	4 (44.44)
Age (years)	
30–60	4 (44.44)
>60	5 (55.56)
Education level	
College	8 (88.89)
Postgraduate	1 (11.11)

diseases were extracted from the interview data. The emerged influencing factors were further clustered into three aspects that ultimately determines the medication-taking behaviour in patients with chronic diseases, including 'medication benefit', 'medication risk' and 'medication strategy'. As to the medication risk, economic risk, physical risk, psychosocial risk and time risk were four dimensions of the risk perception of the medication-taking behaviour of patients with chronic diseases. They are discussed in the following sections. Complete influencing factors can be found in table 3.

Medication benefit

Subcategories forming the 'medication benefit' category were 'control of disease' and 'quality of life'. As an effective means to control chronic diseases, some patients chose to take multiple medications to control their diseases.

Now I have hypertension and diabetes. There are two kinds of medications for each disease, as well as the prostate medication and the stomach medication. (Patient No. 08)

When I started taking insulin, it was very effective at first. Then gradually my blood sugar went up again. My doctor advised me to take Pioglitazone Hydrochloride Tablets to help insulin but the effectiveness was not good, so I also added another Metformin. (Patient No. 15)

Another motivation for patients with chronic diseases to take multiple medications is to improve their quality of life, such as extending their life spans or protecting their organs.

I want to live longer, so I dare not reduce the medications I take now. (Patient No. 11)

Since I took too many medications, I was worried about the influence of the medications on my kidneys, so I took another medication to protect my kidneys. (Patient No. 16)

Medication risk

The potential risk of medications is another important factor affecting the medication taking behaviour of patients. In this study, it was found that the medication risk perceived by patients with chronic diseases can be divided into four dimensions: economic risk, physical risk, psychosocial risk and time risk.

Economic risk refers to the possibility that taking medications may cause economic loss to patients with chronic diseases.

Medications I take now are quite expensive, especially the medication for diabetes. The price of the medication for diabetes is too high. Now I am taking the general medication, the more effective medication is even more expensive. (Patient No. 07)

I used to take imported Plavix. That medication was too expensive. Now I asked the doctor to replace it

Table 3 Influencing factors of the medication-taking behaviour of patients with chronic diseases

Concept	Subcategory	Category
Variety of disease	Control of disease	Medication benefit
Severity of disease		
Course of disease		
Lengthen the span of life		
Protect organ	Quality of life	
Economic condition	Economic risk	Medication risk
Price of medication		
Medical insurance subsidy	Physical risk	
Severe medical subsidy		
Will to live		
Medication knowledge		
Medication experience	Psychosocial risk	
Physician–patient trust		
Treatment attitude		
Route of administration		
Family support	Time risk	
Length of spare time		
Convenience of medication purchase		
Convenience of medication pretreatment		
Prescription knowledge	Prescription of physician	Medication strategy
Clinical experience		
Hospital inventory	Medication recommendation	
Hospital regulation		
Physician–patient communication		
Suggestion from family		
Suggestion from neighbour	Subjective thought of patient	
Suggestion from colleague		
Suggestion from other patient		
Suggestion from drugstore		
Preference for medication	Medication substitute	
Effect of medication		
Multiple prescriptions		
Therapeutic equipment		
Physical exercise		
Diet control		

with a domestic one because the imported one costs too much. (Patient No. 18)

Physical risk refers to the possibility that taking medications may cause loss of physical health to patients with chronic diseases.

Of course I have concerns about the adverse effects of taking medications on my body. Anyone with a

certain level of education can realize this problem. (Patient No. 17)

Medications certainly affect the human body. Medications have an impact on the human body function and a great damage to the stomach. My stomach used to be in good condition. However, after I started taking medications, the function of my stomach was not as good as before and I have to take stomach medications, which shows that taking medications is definitely bad for my stomach. (Patient No.08)

Psychosocial risk refers to the possibility that taking medications may cause loss of social reputation to patients with chronic diseases.

Insulin needs to be injected on time, but patients with diabetes will always avoid other people when they take insulin. (Physician No. 06)

My family gave me a lot of support in my medication-taking behavior. They all supported me. (Patient No.14)

Time risk refers to the possibility that taking medications may cause loss of time to patients with chronic diseases.

I am retired now and I do not think it is troublesome to buy or take medications. Anyway, I'll buy the medications I should take and leave them at home every month. (Patient No. 16)

To buy medications in the hospital, I need to queue up to register first, then queue up to see the doctor. Finally, I still have to wait in line to get my medications. (Patient No. 15)

Medication strategy

Based on the experiences expressed in this study, medication strategies also contribute to the medication taking behaviour of patients. Four subcategories of 'prescription of physician', 'medication recommendation', 'subjective thought of patient' and 'medication substitute' formed this category. In general, patients take medications according to the prescriptions issued by physicians, so physician's prescription is an important factor affecting the medication-taking behaviour of patients with chronic diseases.

When I prescribe for patients with chronic diseases, I will use the knowledge of medication I have learned to prescribe for them. I never violate the knowledge I have learned. (Physician No. 05)

Most of the time, patients will be prescribed based on what medications are available in the hospital. Otherwise, it is not realistic to make patients seek another place to buy medicines I prescribe. (Physician No. 04)

There are also some patients who will listen to the medication recommendations provided by others other

than physicians, such as their family members, colleagues and other patients.

My grandson brought me a new medication these days, but I did not stop taking the medicines I had taken before. I take them both now. (Patient No. 11)

After the diagnosis of hypertension, I started to take Nifedipine Sustained-release Tablets, which was recommended by a pharmacy assistant. (Patient No. 04)

Some other patients choose to take medications based on their own subjective ideas.

I can't take Metformin. After taking Metformin, I feel sick and uncomfortable. So I told the doctor about the situation and stopped taking Metformin. (Patient No. 02)

The medications prescribed in the hospital did not work and had no effect, so I do not take the medications prescribed in the hospital now. (Patient No. 04)

There are also some patients who choose to treat chronic diseases with alternative means instead of taking medications.

As for statins, I think I have paid enough attention to my diet, so I cut them off. (Patient No. 17)

For patients with borderline hypertension, I will not advocate them to take medications, I will encourage them doing exercises instead of taking medications. (Physician No. 01)

Interpretative structural model of factors affecting medication decision-making behaviour of patients with chronic diseases

Underpinned by the grounded theory approach, the influencing factors of the medication decision-making behaviour of patients with chronic diseases were divided into 35 concepts, 10 subcategories and 3 categories, respectively, according to their grades. Among them, the number of subcategories is most suitable for constructing a clear and convincing interpretative structural model, rather than an overly simple or complex one. Based on this principle, 10 subcategories were chosen as the systematic elements in the interpretative structural model of factors affecting medication decision-making behaviour of patients with chronic diseases. As shown in table 4, S_i stands for the No. i influencing factor.

After identifying the 10 main factors, the opinions of the specialist group on the inter-relationship between the influencing factors were collected, and the results were divided into the following four types, which are shown in table 5.

Type V: the row factor S_i has a direct effect on the column factor S_j

Type A: the column factor S_j has a direct effect on the row factor S_i

Type X: the row factor S_i has a reciprocal effect on the column factor S_j

Type O: the row factor S_i has no effect on the column factor S_j and vice versa

Table 4 Factors affecting the medication decision-making behaviour in patients with chronic diseases

No.	Factors	S_i
1	Control of disease	S_1
2	Quality of life	S_2
3	Economic risk	S_3
4	Physical risk	S_4
5	Psychosocial risk	S_5
6	Time risk	S_6
7	Prescription of physician	S_7
8	Medication recommendation	S_8
9	Subjective thought of patient	S_9
10	Medication substitute	S_{10}

The relationships among the aforementioned factors are then converted into an adjacency matrix A as shown in table 6, in which a '1' in row i and column j indicates that the row factor S_i has an effect on the column factor S_j while a '0' indicates that the row factor S_i has no effect on the column factor S_j .

Then the reachability matrix of A is calculated according to the following Boolean rules, as shown in table 7.

$$M = (A + I)^{r+1} = (A + I)^r (A + I)^{r-1} (A + I)^3 (A + I)^2 (A + I)^1$$

In the equation, A is the adjacency matrix, I is the unit matrix and M is the reachability matrix. According to the equation, the final reachability matrix is calculated using MATLAB R2017a.

In order to understand the hierarchical relationship of influencing factors, the reachable set $R(S_i)$ and the antecedent set $A(S_i)$ of each factor are listed. Reachable collection is the collection of factors that factor S_i can affect. In reachability matrix, the reachable set $R(S_i)$ represents factors whose corresponding value is 1 on row i . Antecedent collection is the collection of factors that can affect S_j . And the antecedent set $A(S_i)$ represents factors whose corresponding value is 1 on column i in reachability matrix. $C(S_i)$ contains factors that affect S_i and also be affected by S_i . If $R(S_i) = C(S_i) = R(S_i) \cap A(S_i)$,

Table 5 Pairwise relationship of the factors

No.	S_{10}	S_9	S_8	S_7	S_6	S_5	S_4	S_3	S_2	S_1
S_1	O	O	O	A	O	O	A	A	X	
S_2	O	O	O	A	O	O	O	O		
S_3	X	O	O	A	O	O	O			
S_4	O	A	O	O	O	O				
S_5	O	O	O	O	O					
S_6	V	O	O	O						
S_7	O	O	O							
S_8	O	O								
S_9	O									
S_{10}										

Table 6 Adjacency matrix

No.	S ₁	S ₂	S ₃	S ₄	S ₅	S ₆	S ₇	S ₈	S ₉	S ₁₀
S ₁	0	1	0	0	0	0	0	0	0	0
S ₂	1	0	0	0	0	0	0	0	0	0
S ₃	1	0	0	0	0	0	0	0	0	1
S ₄	1	0	0	0	0	0	0	0	0	0
S ₅	0	0	0	0	0	0	0	0	0	0
S ₆	0	0	0	0	0	0	0	0	0	1
S ₇	1	1	1	0	0	0	0	0	0	0
S ₈	0	0	0	0	0	0	0	0	0	0
S ₉	0	0	0	1	0	0	0	0	0	0
S ₁₀	0	0	1	0	0	0	0	0	0	0

then $R(S_i)$ is the highest factor collection, define factors in $R(S_i)$ as the first level. Then delete the corresponding rows and columns of the first level factors, and the remaining factors form a new reachability matrix, find out factors in which $R(S_i)$ is equal to $C(S_i)$ as the second level. The rest can be done in the same manner to find out factors contained in each level. The result showed that the factors can be divided into three levels as follows: $L_1=\{S_1, S_2, S_5, S_8\}$; $L_2=\{S_3, S_4, S_{10}\}$; $L_3=\{S_6, S_7, S_9\}$. The process of hierarchical division of the factors is shown in [table 8](#).

According to the result of the above-mentioned hierarchical division, the interpretative structural model for influencing factors of medication decision-making behaviour in patients with chronic diseases can be formed as shown in [figure 1](#). In this model, factors at the same level are placed in the same layer. The relationships between factors affecting medication decision-making behaviour of patients with chronic diseases can be seen directly from the model. The two factors connected by an arrow exist influential ties, and the direction the arrow goes refers to the factor that affected by other factors.

The interpretative structural model of the medication decision-making behaviour of patients with chronic diseases can be divided into three layers. The top influencing factors, namely direct factors include control of

Table 7 Reachability matrix

No.	S ₁	S ₂	S ₃	S ₄	S ₅	S ₆	S ₇	S ₈	S ₉	S ₁₀
S ₁	1	1	0	0	0	0	0	0	0	0
S ₂	1	1	0	0	0	0	0	0	0	0
S ₃	1	1	1	0	0	0	0	0	0	1
S ₄	1	1	0	1	0	0	0	0	0	0
S ₅	0	0	0	0	1	0	0	0	0	0
S ₆	1	1	1	0	0	1	0	0	0	1
S ₇	1	1	1	0	0	0	1	0	0	1
S ₈	0	0	0	0	0	0	0	1	0	0
S ₉	1	1	0	1	0	0	0	0	1	0
S ₁₀	1	1	1	0	0	0	0	0	0	1

disease, quality of life, psychosocial risk and medication recommendation. The factors in this level directly affected the medication-taking behaviour of patients. The second-level influencing factors, namely key factors include economic risk, physical risk and medication substitute. These factors indirectly affected the medication-taking behaviour of patients by affecting the direct factors. They affected the up-level factors directly and are also affected by down-level factors. The third-level influencing factors, namely root factors, included time risk, prescription of physician and subjective thought of patient. These factors indirectly affected the medication-taking behaviour of patients through affecting the key factors. As the fundamental factors, root factors are the origin of patients' medication decision-making behaviour.

DISCUSSION

The results of this study revealed that the medication decision-making behaviour in patients with chronic diseases involves multiple influencing factors. A total of 35 influencing factors were extracted from the interview data, further integrated into 10 integrated influencing factors and ultimately clustered into 3 aspects, including the benefit, risk and strategy of medication-taking behaviour, respectively. The benefits of taking medications are factors that encourage patients to take medications, including the control of their diseases and the improvement of their quality of lives. In contrast, the risks of taking medications are factors that prevent patients from taking medications. The potential risks of medications perceived by patients cover four dimensions, namely economic, physical, psychosocial and time risk. In addition, the medication strategy includes factors that affect patients' specific medication-taking behaviour. Patients formulated the specific medication plan based on physicians' prescriptions, others' recommendations, their own subjective thoughts and possible medication substitutes. All the motivations of the patients with chronic diseases we interviewed for medication decision-making behaviour were included in the above 10 integrated influencing factors. The interaction of these factors is presented in the three-layer interpretative structural model.

Medication benefit

One of the categories that emerged in this study was medication benefit, which played a direct role in promoting polypharmacy in patients with chronic diseases. Benefits of taking medications are the original motivation for patients with chronic diseases to take medications. Current research suggests that the prescribing of multiple medications can be entirely appropriate when patients' clinical context is taken into consideration. For patients suffering from several chronic diseases or serious chronic diseases, inadequate number of medications may lead to the omission of potentially beneficial medications, which pose risks to patients' safety and well-being.³⁷

Table 8 Hierarchical division

S_i	$R(S_i)$	$A(S_i)$	$C(S_i)$	$C(S_i)=R(S_i)$	Level
1	1, 2	1, 2, 3, 4, 6, 7, 9, 10	1, 2	√	$L_1=\{S_1, S_2, S_5, S_8\}$
2	1, 2	1, 2, 3, 4, 6, 7, 9, 10	1, 2	√	
3	1, 2, 3, 10	3, 6, 7, 10	3, 10		
4	1, 2, 4	4, 9	4		
5	5	5	5	√	
6	1, 2, 3, 6, 10	6	6		
7	1, 2, 3, 7, 10	7	7		
8	8	8	8	√	
9	1, 2, 4, 9	9	9		
10	1, 2, 3, 10	3, 6, 7, 10	3, 10		
3	3, 10	3, 6, 7, 10	3, 10	√	$L_2=\{S_3, S_4, S_{10}\}$
4	4	4, 9	4	√	
6	3, 6, 10	6	6		
7	3, 7, 10	7	7		
9	4, 9	9	9		
10	3, 10	3, 6, 7, 10	3, 10	√	
6	6	6	6	√	$L_3=\{S_6, S_7, S_9\}$
7	7	7	7	√	
9	9	9	9	√	

Obliviously, one of the key risk factors for polypharmacy is the number of chronic diseases. Older people are exposed to polypharmacy because of multiple chronic conditions.³⁸ The ageing process is characterised by a high level of comorbidity, which often leads to the concomitant use of multiple medications for prophylaxis and treatment, so called polypharmacy.³⁹ Besides, severity and course of diseases are emerged as predictors

of polypharmacy in this study as well. In clinical practice, the dose of drugs increases along with the severity of the disease.⁴⁰ Similarly, results of the study by Franssen *et al* on patients with chronic obstructive pulmonary disease shows that not only the severity of the disease, but also the health status is an independent predictor of polypharmacy.⁴¹ Physicians should carefully consider the variety, severity and course of any chronic diseases since older

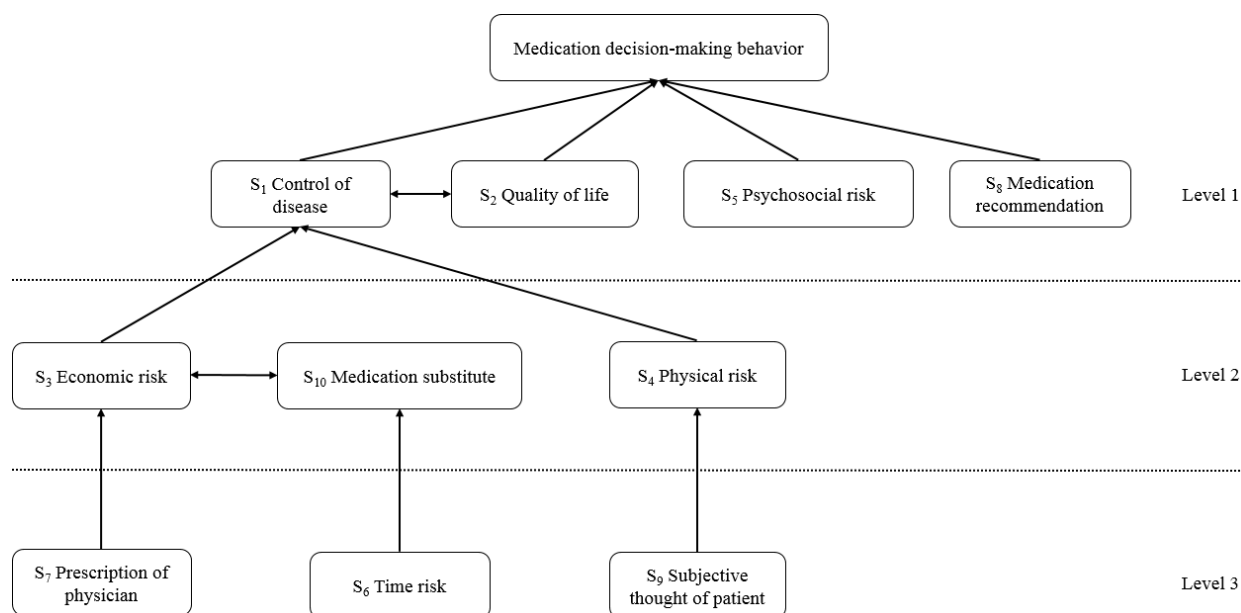


Figure 1 Interpretative structural model of factors affecting medication decision-making behaviour of patients with chronic diseases.

patients with multiple diseases are more likely associated with polypharmacy especially those with hypertension or diabetes.

On the other hand, another motivation for patients to take medications is to improve their quality of lives. The desire to lengthen the span of life and protect organs especially kidneys from the large amount of medications they used are other contributors to polypharmacy, as expressed by participants in the interviews. A number of unnecessary drug uses come from irregular ways, some even from physicians' prescriptions. However, it has been confirmed by research that polypharmacy was combined with renal impairment and exposed patients to the risk of drug-related problems.⁴² The concurrent use of multiple medications increased the risk of kidney dysfunction among older adults because it could burden the ageing kidneys to excrete multiple pharmaceutical ingredients and their metabolites.⁴³ The results of other relevant studies on the impact of polypharmacy on kidney function also indicated that every additional drug prescribed among older adults will have an independent and immediate harmful impact on their kidney function.⁴⁴ These findings suggest that some patients with chronic diseases did not have enough knowledge about drug use. Given the substantial medication burden of chronic diseases, confirmation of kidney function may be necessary to ensure properly prescribing practices in patients with chronic disease.¹³ In order to deal with this situation, medical service providers and policymakers should recognise the importance of prevention of polypharmacy in protecting older adults from kidney dysfunction and take corresponding actions.

Medication risk

Medication risk is another category emerged in this study which has an opposing effect on the polypharmacy of patients with chronic diseases. Decision-making results in medical behaviours are also accompanied by potential risks and related studies have shown that one's perception of medical risk have an impact on their health behaviours and life styles.^{26 45}

In various studies on risk perception, researchers usually referred to the specific content of risk perception as dimensions. Extant studies generally believe that risk perception is a multidimensional structure. For instance, Krewski *et al* suggest that one's risk perception is multidimensional and reflect various factors.⁴⁶ Different research questions and different indicator choices will lead to different dimensions of risk perception. As for this study, it was found through interviews that risk perception of polypharmacy in patients with chronic diseases mainly focused on four dimensions.

Patients' perception of economic risk indicates that they often have financial concerns about medication decision-making behaviour due to drug prices, their own economic conditions and medical insurance conditions. As one of the dimensions of risk perception, the level of patients' perception of economic risk will affect their

medication-taking behaviour to a certain extent. But it is worth noting that although patients with chronic diseases often stop taking certain medications for economic reasons, they tend to take other cheaper medications for alternatives. In general, with the support of medical insurance,⁴⁷ patients' perception of economic risk has no significant inhibitory effect on polypharmacy.

Another concern frequently mentioned by participants was the physical risk. However, different from the perception of economic risk, perception of physical risk often led to reduce the use of several medications, which effectively suppresses the phenomenon of polypharmacy. Patients' perception of physical risk is related to their own willingness to live, physician-patient trust, medication knowledge and experience. Risk perception is a critical determinant of health behaviour⁴⁵ and according to Sheeran *et al* health-related risk perception plays an important role in motivating health behaviour change.⁴⁸ The results of this study suggesting that patient education regarding medication knowledge may be worth consideration in order to control the phenomenon of polypharmacy in patients with chronic diseases. Similarly, available literature confirms that direct-to-patient educational intervention can play a preventive role in polypharmacy.⁴⁹

The other two less frequently mentioned concerns by the participants interviewed were concerns about psychology and time. Some patients with chronic diseases, especially those who possessed higher social status, may reduce the number of medications due to the concern of losing social reputation and free time caused by medications. Patients' perception of psychosocial risk is related to their own treatment attitude, the route of administration of their medications and whether their medication-taking behaviour is supported by their family members, while time risk is related to the convenience of medication purchase, the accessibility of medication pretreatment for traditional Chinese herbal medicines and whether they have enough spare time. A systematic review of patients with diabetes in the Middle East and North Africa region reached similar conclusion that factors associated with medication adherence were categorised into attitude-related, psychological feelings-related, societal-related factors and so on.⁵⁰ This provides a new idea for reducing the polypharmacy in patients with chronic diseases, but it may not be able to represent the general population.

Medication strategy

Medication strategy is the last category emerged in this study and it plays a guiding role in the specific medication-taking behaviour of patients with chronic diseases. Medication strategy refers to the patient formulating the final medication plan based on the access to medication information and other possible treatment methods. Patient's access to medication information may come to physicians, someone other than physicians or their own subjective thoughts. The combined action of the influencing factors in medication strategy ultimately determines the adherence-outcome of patients.⁵¹⁻⁵³



Most patients with chronic diseases will choose to formulate their own final medication plan based on the physician's prescription. Physicians prescribe according to their own ideas and the conditions of the hospital they are affiliated to. The influencing factors of this process include physicians' medical knowledge and clinical experience. In addition, the limitations of the hospital inventory and hospital regulation also affect this process. Inappropriate prescription was considered as one of the major challenges in the treatment of older patients.^{54–56} From the perspective of medical service providers, the most direct way to eliminate the phenomenon of polypharmacy in patients with chronic diseases is to enable physicians to prescribe more appropriate prescriptions. It was found in the interviews with physicians that physicians tend to prescribe patients immediately according to the existing medication inventory in the hospitals, but few hospitals have regulations that require the application of relevant criteria for evaluating the appropriateness of prescriptions, which is similar to the findings of Mortazavi *et al.*⁶ Studies indicate that applying relevant criteria to evaluate the appropriateness of prescriptions is an effective way to reduce inappropriate prescriptions,²⁰ which suggests that it is necessary to promote the application of relevant criteria in hospitals. Simultaneously, it was found in the interview that poor communication between physicians and patients resulted in patient's failure to accurately understand the prescriptions by physicians, which was an important promoting factor of polypharmacy in patients with chronic diseases. In agreement with this finding, Mortazavi *et al* regarded poor communication as an influential factor in the development of polypharmacy among older population.⁶ This problem indicates that strengthening communication with patients is also crucial for medical service providers.

Other patients participating in the interview may choose to take medications according to the suggestion provided by someone other than physicians due to their distrust⁵⁷ or dissatisfaction⁵⁸ with physicians. These suggestions may come from the family members, neighbours and colleagues of patients as well as other patients and drug-store clerks, which eventually reduced their medication adherence and increased the likelihood of polypharmacy.⁵⁹ The finding suggests that improved medication adherence of patients with chronic diseases are essential to reduce their polypharmacy behaviours.

We also found in the interview that some patients formulated medication plans according to their own subjective thoughts. Patients' preference for medications and specific effect of medications will affect patients' subjective thoughts and further affect patients' medication-taking behaviour. Other studies have also confirmed that patients' doubts about effectiveness of medications, self-perceived ineffectiveness of medications and preference for alternative medications were main barriers to medication adherence.^{53,60} In addition, patients frequently change the places of treatment, forming multiple prescriptions by multiple physicians is another common contributor to

polypharmacy. Similarly, Mortazavi *et al* found that lack of access to detailed records of patients' medical history, forcing physicians' prescriptions to only be based on patients' self-reports.⁶ A study in older people in Netherlands demonstrates that low continuity of healthcare is associated with a higher risk of mortality,⁶¹ emphasising the importance of a coherent patient medication information system to ensure the rationality of prescriptions by physicians and the appropriateness of medication-taking behaviour of patients with chronic diseases.

Finally, there were also a group of patients who chose or were recommended to take alternative measures other than taking medications to control chronic diseases, such as applying therapeutic equipment, taking physical exercise and controlling diet, which are collectively referred as medication substitute in this study. Most of these patients were patients with mild chronic diseases and medication treatment is not necessary for them. This finding served as an important reference to curb the phenomenon of polypharmacy since overprescribing has been regarded as a common cause of polypharmacy,²⁰ considering that medication substitute for specific patients is a feasible solution to reduce polypharmacy.

Analysis on interpretative structural model

The prescription of physician (S_7), one of the fundamental root factors, will affect the patient's willingness of control of disease (S_1) by affecting the patient's perception of the economic risk (S_3) of medication-taking behaviour, and ultimately affect the patient's medication decision-making behaviour. Patients often had economic concerns about the prescriptions issued by physicians. For instance, in the interviews, some patients complained that hospitals focused too much on their economic benefits and believed that the medications prescribed by physicians were too expensive, which increased the patients' perception of the economic risk of their medication-taking behaviour, further discouraged the patient's willingness to control their diseases through medications and had an impact on the patients' medication adherence, which is consistent with the results of other relevant research.^{62,63} Another root factor is the patient's perception of the time risk (S_6), which affects the patient's willingness of control of disease (S_1) by affecting the possible medication substitute (S_{10}) and the patient's perception of the economic risk (S_3) of medication-taking behaviour, and ultimately affect the patient's medication decision-making behaviour. It was found in this study and other related studies that patients may find other medication substitutes because they think it takes too much time to take medications.⁶⁴ Further, appropriate medication substitutes will increase patients' perception of the economic risk of their medication-taking behaviour, and then reduce their willingness to control the disease through medications. The last root factor, subjective thought of patient (S_9) will affect the patient's willingness of control of disease (S_1) by affecting the patient's perception of the physical risk (S_4) of medication-taking

behaviour, and ultimately affect the patient's medication decision-making behaviour. Specifically, all participants in the interviews mentioned that medications may have side effects. Patients' subjective concerns about the side effects of medications increased patients' perception of the physical risk of their medication-taking behaviour, and also reduced their willingness to control diseases through medications. Similar results have been found in other studies on medication adherence.^{65–67}

It is worth noting that patient's willingness to control diseases (S_1) and desire to improve the quality of life (S_2) have mutual effects, both of which belong to the medication benefit. For patients with chronic diseases, controlling diseases can improve the quality of life, and to improve the quality of life also means the control of diseases, the two complement each other. There are also interactions between the patient's perception of the economic risk (S_3) of medication-taking behaviour and the possible medication substitute (S_{10}), suggesting that patients will make decision on medication substitutes according to their perceived economic risk of their medication-taking behaviour. The existence of appropriate medication substitutes will in turn affect their perception of the economic risk of their medication-taking behaviour. In addition, the two influencing factors in the first level, the patient's perception of the psychosocial risk (S_5) of medication-taking behaviour and the medication recommendation (S_8) provided by others, are relatively isolated from other influencing factors, indicating that they lack interactions with other influencing factors and are not closely related to other influencing factors in the interpretative structural model, although they can directly affect the final medication decision-making behaviour of patients with chronic diseases.

Limitations

All participants of the interview were born in China and this study was conducted in the context of the Chinese culture and health system, the findings of this study may not reflect the perspectives of patients and physicians from culturally diverse backgrounds. In addition, due to the long time required for in-depth interview and the sensitivity of the study subject, data could not be collected from those who declined participation and certain experiences may not be reported by participants in the interview. It is possible that the findings of the study are not transferable to other patients.

Conclusion

At present, the phenomenon of polypharmacy among patients with chronic diseases in China is prevalent. The causes of the medication decision-making behaviour of patients are complex, involving multiple influencing factors and different from each other in different populations. The focus of this study was to identify the influencing factors of the medication-taking behaviour in patients with chronic diseases, according to which, analyse the motivation of patients to take multiple medications, that

is, polypharmacy. Based on the results of this study, the influencing factors of the medication-taking behaviour can be ultimately clustered into three aspects: medication benefit, medication risk and medication strategy. As to medication risk, the specific risks perceived by patients can be divided into four specific dimensions: economic risk, physical risk, psychosocial risk and time risk. All these influencing factors constitute the source of motivation for patients with chronic diseases to take multiple medications.

Tackling the challenge of polypharmacy, further safety measures should be proposed based on such issues. For instance, to strengthen the education of medication knowledge among patients with chronic diseases, making patients perceive the potential risks of polypharmacy and stop taking multiple medications. In terms of medical service providers, corresponding regulations should be formulated, including the application of relevant criteria for evaluating the appropriateness of prescriptions to reduce misprescribing, and the improvement of the continuity of treatment for patients with chronic diseases to reduce overprescribing and so on.

Twitter Da Feng @fengda

Acknowledgements The authors would like to express their gratitude to all institutions involved in this study and participants who shared their experience.

Contributors All authors contributed to the design of this study. YL, JW and DF collected data. YL, RW, RH and YC performed the statistical analyses. YL wrote the original draft and created graphs. RW, RH, YC, JW and DF revised the manuscript.

Funding This work was funded by the National Natural Science Foundation of China (71804052).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the Ethics Committee of the Tongji Medical College of Huazhong University of Science and Technology (2017S319).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data that support the findings of this study are available from the first author, YL, upon reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Yuxin Liu <http://orcid.org/0000-0002-6243-5005>

Ruoxi Wang <http://orcid.org/0000-0002-9695-0582>

Jia Wang <http://orcid.org/0000-0001-7160-5662>

Da Feng <http://orcid.org/0000-0003-4392-760X>



REFERENCES

- 1 Salive ME. Multimorbidity in older adults. *Epidemiol Rev* 2013;35:75–83.
- 2 Zhang R, Lu Y, Shi L, et al. Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data. *BMJ Open* 2019;9:e24268.
- 3 Valderas JM, Starfield B, Sibbald B, et al. Defining comorbidity: implications for understanding health and health services. *Ann Fam Med* 2009;7:357–63.
- 4 Liu X-L, Willis K, Wu C-JJ, et al. Preparing Chinese patients with comorbid heart disease and diabetes for home management: a mixed methods study. *BMJ Open* 2019;9:e29816.
- 5 Hung WW, Ross JS, Boockvar KS, et al. Recent trends in chronic disease, impairment and disability among older adults in the United States. *BMC Geriatr* 2011;11:47.
- 6 Mortazavi SS, Shati M, Malakouti SK, et al. Physicians' role in the development of inappropriate polypharmacy among older adults in Iran: a qualitative study. *BMJ Open* 2019;9:e24128.
- 7 Stewart RB. Polypharmacy in the elderly: a fait accompli? *DICP* 1990;24:321–3.
- 8 De las Cuevas C, Sanz EJ, Cuevas C. Polypharmacy in psychiatric practice in the Canary Islands. *BMC Psychiatry* 2004;4:18.
- 9 Rollason V, Vogt N. Reduction of polypharmacy in the elderly: a systematic review of the role of the pharmacist. *Drugs Aging* 2003;20:817–32.
- 10 Haider SI, Johnell K, Thorslund M, et al. Analysis of the association between polypharmacy and socioeconomic position among elderly aged > or =77 years in Sweden. *Clin Ther* 2008;30:419–27.
- 11 Mastromarino V, Casenghi M, Testa M, et al. Polypharmacy in heart failure patients. *Curr Heart Fail Rep* 2014;11:212–9.
- 12 Mortazavi SS, Shati M, Keshkar A, et al. Defining polypharmacy in the elderly: a systematic review protocol. *BMJ Open* 2016;6:e10989.
- 13 Ballew SH, Chen Y, Daya NR, et al. Frailty, kidney function, and polypharmacy: the atherosclerosis risk in communities (ARIC) study. *Am J Kidney Dis* 2017;69:228–36.
- 14 Formica M, Politano P, Marazzi F, et al. Acute kidney injury and chronic kidney disease in the elderly and polypharmacy. *Blood Purif* 2018;46:332–6.
- 15 Milton JC, Hill-Smith I, Jackson SHD. Prescribing for older people. *BMJ* 2008;336:606–9.
- 16 Caughey GE, Roughead EE, Pratt N, et al. Increased risk of hip fracture in the elderly associated with prochlorperazine: is a prescribing cascade contributing? *Pharmacoepidemiol Drug Saf* 2010;19:977–82.
- 17 Caughey GE, Roughead EE, Vitry AI, et al. Comorbidity in the elderly with diabetes: identification of areas of potential treatment conflicts. *Diabetes Res Clin Pract* 2010;87:385–93.
- 18 Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf* 2014;13:57–65.
- 19 Santibáñez-Beltrán S, Villarreal-Ríos E, Galicia-Rodríguez L. [Economic cost of polypharmacy in the elderly in primary health care]. *Rev Med Inst Mex Seguro Soc* 2013;51:192–9.
- 20 O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. *Drugs Aging* 2012;29:437–52.
- 21 Mortazavi SS, Shati M, Khankeh HR, et al. Self-medication among the elderly in Iran: a content analysis study. *BMC Geriatr* 2017;17:198.
- 22 Taylor-Gooby P, Zinn JO. Current directions in risk research: new developments in psychology and sociology. *Risk Anal* 2006;26:397–411.
- 23 Fisher JD, Fisher WA. Changing AIDS-risk behavior. *Psychol Bull* 1992;111:455–74.
- 24 Rosenstock IM, Strecher VJ, Becker MH. Social learning theory and the health belief model. *Health Educ Q* 1988;15:175–83.
- 25 Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev* 1977;84:191–215.
- 26 Scollan-Koliopoulos M, Walker EA, Bleich D. Perceived risk of amputation, emotions, and foot self-care among adults with type 2 diabetes. *Diabetes Educ* 2010;36:473–82.
- 27 Bradshaw C, Atkinson S, Doody O. Employing a qualitative description approach in health care research. *Glob Qual Nurs Res* 2017;4:233339361774228.
- 28 Neergaard MA, Olesen F, Andersen RS, et al. Qualitative description - the poor cousin of health research? *BMC Med Res Methodol* 2009;9:52.
- 29 Wolfswinkel JF, Furtmueller E, Wilderom CPM. Using grounded theory as a method for rigorously reviewing literature. *Europ J Inform Syst* 2013;22:45–55.
- 30 Considine J, Berry D, Sprogis SK, et al. Understanding the patient experience of early unplanned hospital readmission following acute care discharge: a qualitative descriptive study. *BMJ Open* 2020;10:e34728.
- 31 Mathiyazhagan K, Govindan K, NoorulHaq A, et al. An ISM approach for the barrier analysis in implementing green supply chain management. *J Clean Prod* 2013;47:283–97.
- 32 Zhang C, Sun L, Wen F, et al. An interpretative structural modeling based network reconfiguration strategy for power systems. *Int J Electrical Power Energy Syst* 2015;65:83–93.
- 33 Shen L, Song X, Wu Y, et al. Interpretive structural modeling based factor analysis on the implementation of emission trading system in the Chinese building sector. *J Clean Prod* 2016;127:214–27.
- 34 Dworkin SL. Sample size policy for qualitative studies using in-depth interviews. *Arch Sex Behav* 2012;41:1319–20.
- 35 Gan X, Chang R, Zuo J, et al. Barriers to the transition towards off-site construction in China: an interpretive structural modeling approach. *J Clean Prod* 2018;197:8–18.
- 36 Masnoon N, Shakib S, Kalsich-Ellett L, et al. What is polypharmacy? A systematic review of definitions. *BMC Geriatr* 2017;17:230.
- 37 Cadogan CA, Ryan C, Hughes CM. And medicine safety: when many is not too many. *Drug Safety* 2016;39:109–16.
- 38 Mizokami F, Koide Y, Noro T, et al. Polypharmacy with common diseases in hospitalized elderly patients. *Am J Geriatr Pharmacother* 2012;10:123–8.
- 39 Ferreira AR, Martins S, Fernandes L. Comorbidity and polypharmacy in elderly living in nursing homes. *Eur Psychiat* 2016;33S:S471–2.
- 40 Sørup FKH, Brunak S, Eriksson R. Association between antipsychotic drug dose and length of clinical notes: a proxy of disease severity? *BMC Med Res Methodol* 2020;20:107.
- 41 Franssen FME, Spruit MA, Wouters EFM. Determinants of polypharmacy and compliance with gold guidelines in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2011;6:493–501.
- 42 Marquito AB, Pinheiro HS, NMds F, et al. Pharmacotherapy assessment in chronic kidney disease: validation of the pair instrument for use in Brazil. *Brazil J Nephrol* 2020.
- 43 Kang H, Hong SH. Risk of kidney dysfunction from polypharmacy among older patients: a nested case-control study of the South Korean senior cohort. *Sci Rep* 2019;9:10440.
- 44 Ernst R, Fischer K, Caroline de Godoi Rezende Costa Molino, et al. polypharmacy and kidney function in community-dwelling adults age 60 years and older: a prospective observational study. *J Am Med Dir Assoc* 2020;21:254–9.
- 45 Ferrer R, Klein WM. Risk perceptions and health behavior. *Curr Opin Psychol* 2015;5:85–9.
- 46 Krewski D, Turner MC, Lemyre L, et al. Expert vs. public perception of population health risks in Canada. *J Risk Res* 2012;15:601–25.
- 47 Hu H-H, Qi Q, Yang C-H. Analysis of hospital technical efficiency in China: effect of health insurance reform. *China Economic Review* 2012;23:865–77.
- 48 Sheeran P, Harris PR, Epton T. Does heightening risk appraisals change people's intentions and behavior? A meta-analysis of experimental studies. *Psychol Bull* 2014;140:511–43.
- 49 Tannenbaum C, Martin P, Tamblyn R, et al. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the empower cluster randomized trial. *JAMA Intern Med* 2014;174:890–8.
- 50 Jaam M, Mohamed Izham Mohamed Ibrahim, nadir Kheir, Ahmed Awaisu. factors associated with medication adherence among patients with diabetes in the middle East and North Africa region: a systematic mixed studies review. *Diabetes Res Clin Pr* 2017;129:1–15.
- 51 Sofianou A, Martynenko M, Wolf MS, et al. Asthma beliefs are associated with medication adherence in older asthmatics. *J Gen Intern Med* 2013;28:67–73.
- 52 Harrold LR, Andrade SE, Briesacher BA, et al. Adherence with urate-lowering therapies for the treatment of gout. *Arthritis Res Ther* 2009;11:R46.
- 53 van Mierlo T, Fournier R, Ingham M. Targeting medication non-adherence behavior in selected autoimmune diseases: a systematic approach to digital health program development. *PLoS One* 2015;10:e129364.
- 54 Bregnhøj L, Thirstrup S, Kristensen MB, et al. Reliability of a modified medication appropriateness index in primary care. *Eur J Clin Pharmacol* 2005;61:769–73.
- 55 Fick DM, Cooper JW, Wade WE, et al. Updating the beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med* 2003;163:2716–24.
- 56 O'Mahony D, O'Sullivan D, Byrne S, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing* 2015;44:213–8.

- 57 Ennew CT, Binks MR. Impact of participative service relationships on quality, satisfaction and retention. *J Bus Res* 1999;46:121–32.
- 58 Linetzky B, Jiang D, Funnell MM, *et al.* Exploring the role of the patient-physician relationship on insulin adherence and clinical outcomes in type 2 diabetes: insights from the mosaic study. *J Diabetes* 2017;9:596–605.
- 59 Vatcharavongvan P, Puttawanchai V. Polypharmacy, medication adherence and medication management at home in elderly patients with multiple non-communicable diseases in Thai primary care. *Fmpcr* 2017;19:412–6.
- 60 Singh JA. Facilitators and barriers to adherence to urate-lowering therapy in African-Americans with gout: a qualitative study. *Arthritis Res Ther* 2014;16:R82.
- 61 Maarsingh OR, Henry Y, van de Ven PM, *et al.* Continuity of care in primary care and association with survival in older people: a 17-year prospective cohort study. *Br J Gen Pract* 2016;66:e531–9.
- 62 Heidari P, Cross W, Weller C, *et al.* Medication adherence and cost-related medication non-adherence in patients with rheumatoid arthritis: a cross-sectional study. *Int J Rheum Dis* 2019;22:555–66.
- 63 Kofłataj B, Karwat ID, Kofłataj W, *et al.* Realities of ambulatory multi-drug treatment of chronic diseases in rural areas of Lublin Province, eastern Poland - comparison of situations in 2010 and 2013. *Ann Agric Environ Med* 2015;22:530–5.
- 64 Lott R, Taylor SL, O'Neill JL, *et al.* Medication adherence among acne patients: a review. *J Cosmet Dermatol* 2010;9:160–6.
- 65 Hauber AB, Mohamed AF, Johnson FR, *et al.* Treatment preferences and medication adherence of people with type 2 diabetes using oral glucose-lowering agents. *Diabet Med* 2009;26:416–24.
- 66 Tedla YG, Bautista LE. Drug side effect symptoms and adherence to antihypertensive medication. *Am J Hypertens* 2016;29:772–9.
- 67 Dibonaventura M, Gabriel S, Dupclay L, *et al.* A patient perspective of the impact of medication side effects on adherence: results of a cross-sectional nationwide survey of patients with schizophrenia. *BMC Psychiatry* 2012;12:20.