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A systematic review of qualitative research on the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus

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ABSTRACT

Objectives To synthesise contributing factors leading to medicine-related problems (MRPs) in adult patients with cardiovascular diseases and/or diabetes mellitus from their perspectives.

Design A systematic literature review of qualitative studies regarding the contributory factors leading to MRPs, medication errors, and non-adherence, followed by a thematic synthesis of the studies.

Data sources We screened Pubmed, Embase, ISI Web of Knowledge, PsycInfo, International Pharmaceutical Abstract, and PsycExtra for qualitative studies (Interviews, focus groups, and questionnaires of a qualitative nature).

Review methods Thematic synthesis was achieved by coding and developing themes from the findings of qualitative studies.

Results The synthesis yielded 21 studies satisfied the inclusion and exclusion criteria. Three themes emerged that involved contributing factors to MRPs: patient-related factors including both socioeconomic factors (beliefs, feeling victimised, history of the condition, lack of finance, lack of knowledge/motivation/understanding, and low self-esteem) and lifestyle factors (diet, lack of exercise/time to see the doctor, obesity, smoking, and stress), medicine-related factors (belief in natural remedies, fear of medicine, lack of belief in medicines, lack of knowledge, non-adherence, and polypharmacy), and condition-related factors (lack of knowledge/understanding, fear of condition and its complications, stress, and lack of control).

Conclusions MRPs represent a major health threat, especially among adult patients with cardiovascular diseases and/or diabetes mellitus. The patients' perspectives uncovered hidden factors that could cause and/or contribute to MRPs in these groups of patients.

Article focus

▪ CVDs and DM represent a major health issue that accounts for more than half of the total death rate worldwide.

▪ The contribution of patients' beliefs and behaviours towards their medicines /conditions and its subsequent involvement in MRPs is still under-researched.

▪ An exploration of the contributory factors leading to MRPs in patients with CVDs/DM could help inform prospective interventions.

Key messages

▪ MRPs constitute a major health concern especially for adult patients with CVDs and/or DM.

▪ Whereas medicine-related factors play important role in the incidence of MRPs; other contributing factors can be involved and include: Patient-related, life-style and clinical-related factors.

▪ Identifying the contributory factors leading to MRPs could help in mitigating/preventing incidence of MRPs. Thus, data from qualitative studies must be integrated with those of quantitative nature to develop efficient and practical interventions.

Strengths and limitations of the study

▪ Timely systematic review considering the qualitative research can substantiate the previous knowledge in the literature obtained from the quantitative studies.

▪ Difficult to generalise findings due to the limited number of countries included (12 countries).

▪ Non English publications were underrepresented.

INTRODUCTION

Medicine-related problems (MRPs) emerged as a concept in the early 1990s as “the detrimental experience regarding drug therapy and which potentially or actually causes an interference with their desired outcome.”[1] MRPs affect both healthcare and economic situations and contribute to a tremendous increase in morbidity, mortality and healthcare expenditure worldwide.[2–4]

MRPs represent a major issue, particularly in chronic conditions such as cardiovascular diseases (CVDs) and diabetes mellitus (DM).[5] The aforementioned conditions are expected to be the major source of morbidity by 2020.[6, 7] In addition, these two conditions are interrelated; it has been documented that DM is a key factor that leads to CVDs as people with diabetes are three to four times more likely to have a CVD.[8, 9] Consequently, the combination of CVDs and DM, which can result in multiple complications, represents a major concern for healthcare professionals.

More specifically, patients with CVDs and/or DM are more susceptible to MRPs due to long-term use of medicines and the inevitable polypharmacy.[7, 10, 11] However, many additional factors that contribute to MRPs in patients with CVDs and/or DM have gone underreported.

Studies in the literature, which investigated risk factors contributing to MRPs in patients with CVDs/DM, were mainly quantitative; only few studies were qualitative. Quantitative studies investigating risk factors contributing to MRPs involved either direct observations or were made retrospectively using data extracted from medical records.[12–14] However, most of the studies reported old age and polypharmacy extensively; few studies reported gender, depression, education, cohabitation, and immobilisations.[15] Nonetheless, qualitative studies investigating contributory risk factors leading to MRPs have been rather limited.

Therefore, this review aims to explore and evaluate contributory factors leading to MRPs among adult patients with CVDs and/or DM from their perspectives.

METHODS

We searched the PubMed, Embase, ISI Web of Knowledge, PsycInfo, International Pharmaceutical Abstract, and PsycExtra databases for entries between January 1990 and March 2014. The search strategy evaluated articles obtained predominantly through databases. Additional articles were retrieved through the bibliography lists of published reviews, where applicable.

The search strategy combined established methodological terms for qualitative research (qualitative research, qualitative studies, nursing methodological research, narrative analysis) and the following terms: Medicine (drug/medication) related problems, medicine (drug/medication) use, diabetes mellitus, cardiovascular diseases, patients' perspectives, patients' beliefs, patients' attitudes, patients' views, patients' opinions, patients' knowledge, patients' behaviours, and contributory factors. In addition, Medical Subject Headings (MeSH) relating to MRPs, CVDs/DM, risk factors, and patients' perspectives were explored.

Study selection

We included studies that involved phone interviews, face-to-face interviews, focus groups, and open-ended questionnaires that were published in peer-reviewed journals.

The inclusion criteria involved studies focusing on the patients' perspectives on the use of medicines and MRPs and involved adult patients with CVDs and/or DM.

On the other hand, the exclusion criteria flagged studies that were quantitative in nature, studies with closed-ended questionnaires, and studies focusing on conditions other than CVD/DM.

Initially, one reviewer (AA) conducted the search and did screening for the titles. At this stage, studies with irrelevant titles were excluded. Then, the

abstracts of the remaining studies were evaluated independently for inclusion by two reviewers (MG and ZA). Any disagreements that were encountered were resolved via a discussion. No language limits were applied and non-English studies were translated into English.

Data synthesis and analysis

We used the systematic review approach to extract data from relevant articles.[16] For data synthesis, we adopted the thematic analysis approach,[17] which is able to extract concepts and hypotheses from multiple qualitative studies. Based on the extracted results, we developed textual summaries and tables. We were then able to identify emerging themes from the textual summaries. Subsequently, we agreed upon the final list of themes through discussions and consensus. Finally, we coded the full list of papers for the presence or absence of themes. The codes were tabulated afterwards by country in order to inspect similarities and differences across countries.

Since our approach was qualitative, the presence of a theme in more than one paper did not indicate its importance in the studied population.[18] However, a theme appearing in more than one paper did denote to a degree its validity. Thus, the number of studies within a specific theme was reported in this review.

Quality of synthesis assessment

The quality of papers was assessed using the checklist developed by Dixon-Woods et al. (2004).[16] This assessment was based mainly on clarity, consideration of ethical issues, and transferability of the sample, data, and analysis across different settings. Furthermore, the critical appraisal skills programme criteria[19] were used to rank the papers based on 10 questions that fulfilled the clarity, methods, and results of the studies. Consequently, studies were grouped into low (one star: 0 to 3 points), medium (two stars: 4 to 7 points), and high quality (three stars: 8 to 10 points). Low-quality studies were not excluded, but caution was taken when interpreting their results.

RESULTS

A total of 21 studies (including 836 participants) from 12 countries met the inclusion criteria (Table 1) and were conducted in the following countries: Australia,[20] Brazil,[21] Cameroon,[22] Canada,[23] Croatia,[24] Ireland,[25] Malaysia,[26, 27] South Africa,[28] Spain,[29] Taiwan,[30] the United Kingdom,[7, 31–36] and the United States.[37–39] The majority of the studies investigated DMT2 (*n* = 15); fewer studies investigated CVDs. Thus, only two studies investigated hypertension (HTN), one investigated heart failure, and one studied CVDs in general. The remaining two studies investigated DM/HTN and DM/HTN/stroke, respectively. Eight studies used focus groups, 12 used interviews, and one study used a mixture of these methods. The review covered areas related to patients, conditions, and medicines.

Table 1l **Characteristics of the included studies**

Study	Country	Study type	Patients' diagnosis	Method of analysis	Study population	Study settings	Study aims	Study quality
Al-Qazaz et al 2011	Malaysia	Semi-structured interviews	DMT2	Content analysis	12 diabetic patients, with at least one year of diabetes and a prescription of oral hypoglycemic	Universiti Sains Malaysia (USM) Health Clinic	To explore diabetic patients' experience and knowledge about diabetes and its medication and to understand the factors contributing to medication	**

							adherence in Malaysian population.	
Brown et al 2007	UK	One-to-one interviews	DMT2	Thematic analysis	17 African–Caribbean diabetes patients with age above 18 years; 13 first generation immigrants and four second generation immigrants	Inner city Nottingham	To gain an understanding of how health beliefs influence the way African–Caribbean people with diabetes manage their illness.	***
Choudhury et al 2009	UK	Structured interview	DMT2	Thematic analysis	14 invited individuals, Bangladeshi (four males and 10 females), in the age range of 26 to 67 years, with DMT2 (had it since six months - 27 years) and were recruited either in Swansea or Birmingham. Interviews were made in either	Participants from local communities in Swansea and Birmingham were invited for the interview	To examine the understanding and beliefs of people with diabetes from the Bangladeshi community living in the UK.	**

					English or in Sylheti as the researcher was bilingual			
Coronado et al 2004	USA	Focus groups	DMT2	Matrix analysis by Morgan and Krueger	42 Individuals (14 men and 28 women) in six focus groups, who had diabetes, had a family history of diabetes, or knew someone who had diabetes.	Fred Hutchinson Cancer Research Center's project office in Sunnyside, Yakima village and Skagit Valley Community College and at the Catholic church in Burlington	To investigate the perceptions about the causes of and treatments for DMT2	*
Cottrell et al 2013	Australia	Structured interview	HF	Repertory grid technique	92 patients (older than 18 years) with heart failure	Heart Failure Service outpatient clinic, Royal Brisbane and Women's Hospital in Brisbane, Australia	To elicit individuals' beliefs about their heart failure treatment and to investigate whether generated constructs were different between adherent and nonadherent patients.	*

Gascon et al 2004	Spain	Focus groups with open ended questions	HTN	Thematic analysis	Seven focus groups of 44 patients (24 men and 20 women), diagnosed with hypertension, between the ages of 18 and 80 years, being treated with antihypertensives for 3 months, being non-compliant and having sufficiently good physical and mental health to participate.	Two primary healthcare centres	To identify factors related to non-compliance with the treatment of patients with hypertension.	**
Gordon et al 2007	UK	Face-to-face interviews	CVD	Thematic analysis	98 patients (41 males and 57 females) in the age range of 32 – 89 years.	Home interviews of patients recruited from five general surgeries and pharmacy interviews at four community pharmacies	To examine medication-related problems from the perspective of patients with a chronic condition and to identify how they may be supported in managing their medication.	**

Grace et al 2008	UK	Focus groups	DMT2	Thematic analysis	17 focus groups of adult diabetic patients	Tower Hamlets, a socioeconomically deprived London borough	To understand lay beliefs and attitudes, religious teachings, and professional perceptions in relation to diabetes prevention in the Bangladeshi community.	***
Heymann et al 2012	UK	Focus groups	DM and HTN	Thematic analysis	10 focus groups of 86 (42 males and 44 females) patients with hypertension in three age ranges: 41-50, 51-60, 61-70 years (six groups); and patients with hypertension and DM in the age ranges: 51-60, 61-70 years (a total of four groups).	UK	To explore beliefs and perceptions regarding hypertension and gain an understanding of barriers to treatment among patients with and without DM.	***
Hu et al 2013	USA	Focus groups	DMT2	Content analysis	Five focus groups of 73 Hispanic immigrants; 18 years or older	free health clinic in central North Carolina	To explore perceived barriers among Hispanic immigrants with	**

							diabetes and their family members.	
Jolles et al 2013	Canada	Semi-structured interviews	HTN	Thematic analysis	26 Patients, in the age range of 26 - 85 years and 62% females, able to speak, read and write English; diagnosed with hypertension by a healthcare provider, and currently taking an antihypertensive medication.	Two hypertension clinics at the University of Alberta in Edmonton	To understand hypertensive patients' perspectives regarding blood pressure and hypertension treatment.	**
Kiawi et al 2006	Cameroon	In-depth interviews, semi-structured	DMT2, HTN and stroke	Content analysis	15 interviews of 62 patients (27 women and five men), selection criteria included they had lived at least six months in the community, were nominated by other community members, and	Four urban health districts, one from each of the main ecological areas of Cameroon.	To investigate of lay knowledge, attitudes, and behaviors relating to diabetes and its main risk factors of urban Cameroonians.	***

					were age above 15 years.			
Lai et al 2005	Taiwan	In-depth interviews	DMT2	Thematic analysis	22 diabetic patients (12 males and 10 females), in the age range of 44 - 80 years, with a duration of illness more than one year.	Rural Taiwan community	To investigate Chinese diabetic patients' perceptions about their illness and treatment strategies to facilitate patient-centred, culture-sensitive clinical skills.	**
Lawton et al. 2006	UK	In-depth interviews with open-ended approach	DMT2	Thematic analysis	31 patients (23 Pakistani and eight Indian), aged 18 years and over, and diagnosed with DMT2	General Practices in Edinburgh	Patients' perception and practical considerations	**
Mohd Ali and Jussof 2009	Malaysia	In-depth open-ended interviews	DMT2	Thematic analysis	18 patients (9 males and 9 females) in the age of 15-75 years, and 13 healthcare professionals (nine doctors, three pharmacists and	Endocrinology clinic of a teaching hospital in Kuala Lumpur	To explore the perspectives and experiences of Malay patients in managing Type 2 diabetes as a chronic illness and provide recommendatio	***

					one diabetic nurse educator).		ns that aim to enhance adherence to treatment and help patients to improve their self-management skills.	
Mshunqane et al 2012	South Africa	Patient focus groups (n = 10) and healthcare professional focus groups (n = 8) and in-depth interviews. The questions were open-ended	DMT2	Thematic analysis	Patients who had been diagnosed with type 2 diabetes for at least one year, who were between 30 and 65 years of age	Dr George Mukhari Hospital outpatients' diabetes clinic	To determine the knowledge that patients with type 2 diabetes have about the management of their disease, as well as the perceptions of the health care team about the services given to patients.	***
Peel et al 2004	UK	In-depth interviews	DMT2	Thematic analysis	40 newly diagnosed DMT2 patients in the age range of 21 – 77 years	Across the Lothian region in Scotland	To explore the patients' emotional reactions about their DMT2 diagnosis, and their views about information provision at the time of	**

							diagnosis.	
Peres et al 2007	Brazil	Interviews	DMT2	Content analysis	24 diabetic females, age between 25 and 76 years old, literate, with eight years of schooling, from Ribeirão Preto, who perform household activities.	Nursing Education Center for Adults and Elderly - CEEAI, University of São Paulo	Identify the difficulties patients encounter when controlling diabetes	**
Rustveld et al 2009	USA	Focus groups	DMT2	Thematic analysis	34 patients in six focus groups (three in English and three in Spanish), older than 18 years and with DMT2	Three Harris County Hospital District (HCHD) community health centers in Houston, Texas	To elicit attitudes, attributions, and self-efficacy related to diabetes self-care in both English- and Spanish-speaking Hispanic men.	**
Smith et al 2003	Ireland	Focus groups	DMT2	Thematic analysis	25 patients from three general practices, having DM for at least one year	Patients were invited to participate in the focus group	To explore the views and health beliefs of patients with Type 2 diabetes who had experienced	**

							a new structured diabetes shared care service.	
Vinter-Repalust et al 2004	Croatia	Focus groups	DMT2	Thematic analysis	Seven focus groups of 49 patients (22 males and 27 females), in the age range of 44 - 83 years, ambulatory patients with the diagnosis of DMT2, with differences not only in age and sex, but also in the method of treatment of diabetes as well.	Zagreb Medical School	To explore type 2 diabetic patients' attitudes, thoughts, and fears connected with their illness; their expectations of the health care system; and the problems they encountered while adhering to the therapeutic regimen.	***

Narrative synthesis

The main findings of the review showed that contributory factors to MRPs involved three themes: patient-related (socioeconomic and lifestyle), medicine-related, and condition-related factors. Table 2 lists the studies that reported or discussed each theme.

Table 2l **Themes and subthemes emerging from the studies**

Theme/ Sub-theme	Countries, studies
Patient related factors (socioeconomic)	
Belief	UK (Brown et al 2007, Grace et al 2008, Lawton et al 2006)
Family history of condition	UK (Grace et al 2008, Lawton et al 2006), USA (Coronado et al 2004)
Feeling victimised	South Africa (Mshunqane et al 2012), Croatia (Vinter-Repalust et al 2004), Ireland (Smith et al 2002
Lack of finance	Ireland (Smith et al 2002), South Africa (Mshunqane et al 2012), Croatia (Vinter-Repalust et al 2004), USA (Hu et al 2013)
Lack of knowledge	Croatia (Vinter-Repalust et al 2004)
Lack of motivation	Croatia (Vinter-Repalust et al 2004)
Lack of information/ understanding from doctors	UK (Brown et al 2007, Choudhury et al 2009)
Low self-esteem	Croatia (Vinter-Repalust et al 2004), USA (Rustveld et al 2009)
Patient related factors (life-style)	
Decrease alcohol intake	Canada (Jolles et al 2013),
Decrease caffeine intake	Canada (Jolles et al 2013), South Africa (Mshunqane et al 2012)
Diet	Australia (Cotrell et al 2013), Brazil (Peres et al 2007), Canada (Jolles et al 2013), Croatia (Vinter-Repalust et al 2004), Ireland (Smith et al 2002), UK (Brown et al 2007, Choudhury et al 2009, Grace et al 2008, Heymann et al 2012, Lawton et al 2006), USA (Coronado et al 2004, Hu et al 2013, Rustveld et al 2009), South Africa (Mshunqane et al 2012), Taiwan (Lai et al 2005)
Lack of exercise	Brazil (Peres et al 2007), Canada (Jolles et al 2013), UK (Brown et al 2007, Choudhury et al 2009, Grace et al 2008, Heymann et al 2012, Lawton et al 2006), South Africa (Mshunqane et al 2012), USA (Coronado et al 2004, Hu et al 2013, Rustveld et al 2009)

Lack of time to see doctor	Malaysia (Al-Qazaz et al 2011)
Obesity	Brazil (Peres et al 2007), South Africa (Mshunqane et al 2012), UK (Brown et al 2007), USA (Coronado et al 2004)
Smoking	Canada (Jolles et al 2013), UK (Heymann et al 2012)
Stress	Ireland (Smith et al 2002), UK (Brown et al, 2007, Grace et al 2008, Heymann et al 2012), USA (Coronado et al 2004)
Medicine related factors	
Belief in natural remedies as alternative to medicines	Spain (Gascon et al 2004), UK (Brown et al 2007), USA (Coronado et al 2004)
Difficulty/ refusal to take medicine	Brazil (Peres et al 2007), Croatia (Vinter-Repalust et al 2004)
Fear of being stuck with medicines all life	Spain (Gascon et al 2004), UK (Gordon et al 2007)
Fear of side effects	Ireland (Smith et al 2002), Malaysia (Al-Qazaz et al 2011), UK (Heymann et al 2012), Spain (Gascon et al 2004), Taiwan (Lai et al 2005)
Fear of the chemical nature of medicines	Taiwan (Lai et al 2005), UK (Brown et al 2007)
Forgetfullness	Brazil (Peres et al 2007), Malaysia (Al-Qazaz et al 2011, Mohd Ali and Jusoff 2009), Spain (Gascon et al 2004)
Lack of belief in medicines	Australia (Cotrell et al 2013)
Lack of knowledge about medicines mechanism of actions	Canada (Jolles et al 2013), Spain (Gascon et al 2004), UK (Gordon et al 2007)
Non-adherence	Canada (Jolles et al 2013), Croatia (Vinter-Repalust et al 2004), Taiwan (Lai et al 2005), UK (Gordon et al 2007), USA (Hu et al 2013, Rustveld et al 2009)
Polypharmacy	Brazil (Peres et al 2007),
Condition related factors	
Lack of control over condition	Brazil (Peres et al 2007), Ireland (Smith et al 2002)
Lack of knowledge/ understanding of condition	Australia (Cotrell et al 2013), Cameroon (Kiawi et al 2006), Canada (Jolles et al 2013), Malaysia (Al-Qazaz et al 2011, Mohd Ali and Jusoff 2009), Spain (Gascon et al 2004), UK (Brown et al 2007, Choudhury et al 2009, Heymann et al 2012, Peele et al 2004), USA (Coronado et al 2004)
Fear of condition, its causes and complications	South Africa (Mshunqane et al 2012), UK (Choudhury et al 2009, Lawton et al 2006), USA (Coronado et al 2004)
Stress from condition	Croatia (Vinter-Repalust et al 2004)

Patient-related factors

Socioeconomic-related factors

Patients from six countries reported socioeconomic factors leading to MRPs in both DM and CVDs, including: beliefs, family history of the condition, poor finances, relationships with healthcare professionals (lack of communication and not enough education), inadequate knowledge, and low self-esteem (Table 2).

Beliefs regarding CVDs/DM were reported as a problem in three studies from the United Kingdom.[31, 33, 35] Patients perceived that DM was given by God and higher powers had control over their condition. One patient reported:

"God has given me this disease of sugar. Whatever happens, it happens because God wants it to happen."

Moreover, a family history of DM was reported in three studies from the United Kingdom[33 40] and the United States.[37]

In addition, poor finances were reported by patients in four studies from Ireland,[25] South Africa,[28] Croatia,[24] and the United States.[38] A lack of necessary finances prevents patients from buying the appropriate food (for their diet)[28] and going to doctors.[25]

Consequently, the financial situation implicated the relationship of the patients with the healthcare professionals. Patients have reported that they were not getting value for their money from healthcare providers.[25] For instance, one patient reported:

" I don't mind paying when I'm sick, but it's very expensive to pay the GP when I'm only getting a check-up with the nurse."

Thus, the patients felt victimised by healthcare professionals[24, 25, 28] and reported a lack of communication with healthcare professionals.[17] They

described doctors as either too busy to see them[25, 26] or not giving enough information about diagnosis and medicines.[31, 32, 36] Other patients reported having been belittled by doctors.[24] In another study, patients accounted for the lack of communication with healthcare professionals by language barriers.[32]

Subsequently, patients reported a lack of knowledge as a major cause for DMT2.[24] This situation led to the lack of motivation about their disease and affected the intake of medicines. Patients asserted the need for further education and training about their condition.

A lack of knowledge resulted in the patients' low-self esteem towards their condition.[24, 39] Hence, patients felt unaccepted socially, less comfortable with their colleagues, and less worthy for being diabetic.[24, 39]

Lifestyle-related factors

Lifestyle-factors were reported in studies from 11 countries and included: diet (excessive alcohol/caffeine intake), lack of exercise, lack of time to see the doctor, obesity, smoking, and stress.

Diet was a major issue stated in 16 studies (Table 2). In this respect, patients had different behaviours towards their diet. For instance, one group of patients admitted the importance of a healthy diet, yet could not control their diets.[21, 30–32] Thus, one participant reported:[21]

"Regarding the diet, I try to fight so as not to eat certain foods, but sometimes I can't help myself."

In this respect, patients appreciated the importance of a healthy diet in controlling DM,[31] yet overestimated its importance to be beyond medicines.[30] They were also aware that a poor diet, including excess alcohol[23] and caffeine intake,[23, 28] exacerbated their conditions. Another group of patients misunderstood the concept of a healthy diet. They believed that eating bitter foods could control DM[32] or applied portion sizes to their

diets.[39] In the latter case, patients had difficulty eating smaller portions and/or even changing their favourite foods. On other occasions, patients claimed that diet quality was responsible for DM.[25]

In addition, a lack of exercise was reported in 11 studies from five countries, including Brazil,[21] Canada,[23] the United Kingdom,[31–35, 40] South Africa,[28] and the United States.[37–39] A group of patients overestimated the importance of exercise, claiming that it can cure any existing disease.[30] Patients reported difficulty exercising although they were aware of its importance.[35, 39] They justified their work, travel, stress, the weather, and lack of time as the reasons behind their decreased physical exercise.[21, 32, 33, 35, 38] A lack of time was more reported in females whose culture expected them to stay indoors after they got married.[35]

Moreover, obesity was described in four studies (Brazil,[21] South Africa,[28] the United Kingdom,[31] and the United States[41]) as a cause of DM. Patients blamed weight gain as the cause for their increase in blood glucose level and diabetic complications.[31, 37] Moreover, they attributed insulin as one of the causes of obesity.[31]

Stress emerged in five studies from three countries, including Ireland,[25] the United Kingdom,[31, 33, 34] and the United States.[41] Stress was identified as a result of changes in culture and climate, poor housing, and migration of ethnic minorities.[37] Patients considered stress to be major cause of their condition.[25, 31, 33, 34, 39, 41] For instance, one patient reported:

“In 1998, my mother died, and I was unable to go to the funeral. During these months, I developed diabetes.”

Patients also perceived that stress control could be an effective way to cure their condition[33] since stress led to a poor diet, smoking, and a lack of exercise.

Medicine-related factors

Medicine-related factors were found in 14 studies from 11 countries and included two types of factors: factors related to the use of medicines and factors related to knowledge about medicines.

Factors related to the use of medicines included medicine non-adherence and polypharmacy. Medicine non-adherence was reported in 10 studies from seven countries, including Brazil,[21] Canada,[23] Croatia,[24] Malaysia,[26, 27] Spain,[29] Taiwan,[30] the United Kingdom,[7] and the United States.[38, 39] Patients justified non-adherence to medicines as difficulty following the treatment regimen,[24] depression and stress,[39] forgetfulness in taking the medicines,[7, 21, 26, 27, 29] a lack of routine in taking the medicines,[23] changes in medicine routines,[23] and the inconvenience of taking insulin. For instance, patients complained that oral hypoglycemics are more convenient to take than insulin:[29]

"I prefer pills more than insulin. You know, swallowing a pill causes no pain. And when I know I will eat more I just take another pill or an extra half."

Furthermore, intentional non-adherence was reported in some studies where patients changed their insulin doses depending on their food regimen.[29] In another scenario, patients stopped taking their medicines when they exercised, acting on the assumption that exercise reduces blood sugar level. Thus, patients changed the dose/regimen of their medicines to fit with their daily activities.[7]

Poylpharmacy was reported among patients with DMT2 in two studies from Brazil[21] and Canada.[27] Polypharmacy caused inconvenience in taking medicines:[21]

"Medication: this has been my biggest problem in this current phase. I take medication for blood pressure, circulation, diabetes, vitamins. I used to mix up the time of each, but today, thanks to orientation, I'm overcoming this

stage."

Factors relating to knowledge about medicines included lack of knowledge about how the medicines worked, fear of the chemical nature of medicines and their side effects, and a lack of belief in medicine.

The lack of knowledge about how medicines worked was described in three studies in Canada,[23] the United Kingdom,[7] and Spain.[29] Patients could not identify most of their medicines apart from the diuretics, which they called "water pills."[23] Moreover, patients could not understand how their medicines worked, even when they read the patient information leaflet.[29]

This lack of knowledge created fear in patients regarding the chemical nature of medicines, the side effects of medicines, and being obliged to take medicines all of their lives.[7, 25, 26, 29–31, 34] For instance, patients referred to oral hypoglycemic agents and insulin as "pharmaceutical toxins."[30]

Additionally, patients were afraid of the side effects and complications of medicines. They attributed various side effects to medicines, including hypoglycemia and gastrointestinal disturbances to insulin,[31] kidney failure to oral hypoglycemic agents,[30] and nausea/vomiting to antihypertensive agents.[29] In the last case, a patient reported:

"I don't like them (medicines); they have lots of side effects. They can make you sick… I think that I might get worse instead of better."

These fears promoted a lack of belief in medicines among patients.[20] Subsequently, patients started to believe in natural remedies as an alternative to medicines.[29, 31, 41] They referred to natural therapies as "*a cure*" that should be used alongside traditional medicines.[41] In another scenario, patients believed that natural therapies were superior to medicines.[31] In this respect, natural therapies reported for curing DM included natural drinks

(composed of minerals and water);[41] and plant products (such as aloe vera, arnica, cactus, silk cottonwood tree, tree spinach, and violet water).[31]

Condition-related factors

Condition (clinical)-related factors were reported from 11 countries as a major theme. Factors included a lack of knowledge/understanding of the condition, fear of the condition and its complications, stress from the condition, and a lack of control over the condition.

Lack of knowledge/understanding of the condition (CVDs/DM) emerged as a major theme in 11 studies from seven countries, including Australia,[20] Cameroon,[22] Canada,[23] Malaysia,[26, 27] Spain,[29] the United Kingdom,[31, 32, 34, 36] and the United States.[41]

For CVDs, patients expressed a lack of knowledge about their heart failure, hypertension, and stroke. Patients with heart failure did not know enough about their disease symptoms.[20] Moreover, hypertensive patients did not understand the nature of their disease,[27, 29] struggled to define their condition,[23] and considered it an underlying risk factor to myocardial infarction rather than a disease.[34] Patients justified their lack of knowledge by citing short consultations with physicians, not obtaining enough information from physicians, and obtaining information from non-medical sources such as television and magazines. For instance, one patient reported:

"Anything I know about blood pressure I've read in books, the doctor tells me absolutely nothing . . . High blood pressure: factors related to compliance with treatment 127. I want him to tell me where high blood pressure comes from."

Similarly, patients with DM lacked knowledge about the disease and misunderstood its causes and complications.[22, 24, 26, 28, 31, 32, 35] Regarding the DM condition and causes, patients' perceptions of DM were influenced by other people's accounts and experiences.[31] Patients viewed the condition as an illness that took away their health and strength[35] and

changed their lifestyle.[24] They could not differentiate between DMT1 and DMT2,[26] considered high sugar intake to be the cause of DM, and perceived DM to be sexually and genetically transmitted.[22, 32] Moreover, patients believed that diabetes was not dangerous if it did not require insulin.[31] Patients were only aware of the microvascular complications (such as foot disease) of DM.[25] Moreover, they were aware of the disease's signs and symptoms (such as dry mouth, tiredness, dizziness, irritation, blurred vision, micturition, and extreme thirst) only after they encountered them.[27, 41]

The lack of knowledge about the condition created fear in the patients' minds of the disease itself[41] and they could not accept the disease easily.[24, 32] One patient reported:[41]

"Diabetes is a disease that kills you little by little."

Diseases additionally resulted in stress about the condition that was particularly observed in patients with multiple comorbidities.[35] For instance, diabetic patients who had asthma as a comorbidity could not exercise due to asthma symptoms, such as shortness of breath and swollen feet and joints:

"They tell you to exercise…
but I can't move around a lot because I have
a problem with my leg (arthritis). If I walk a little,
then it swells up."

As a result, patients were not able to control their condition,[21, 25] which led to frustration, depression, and anxiety.

DISCUSSION

To our knowledge, this review is the first systematic analysis of the perspectives of adult patients with CVDs/DM on contributory factors leading to MRPs. We explored the patients' knowledge, beliefs, and behaviours towards

medicines. The majority of studies evaluated patients with DM; only a few studies evaluated patients with CVDs. The four themes emerging from this review include: socioeconomic-, lifestyle-, clinical-, and medicine-related factors.

Patient-related factors

Socioeconomic-related factors

Socioeconomic factors (genetic, cultural behaviour, and financial situations) affected the patients' perceptions of disease and the medicines contributing to MRPs. Patients perceived genetic factors and religious beliefs to be the cause of their DM.[18, 20] Patients from both Christian and Muslim backgrounds named God as the cause for their DM. These attitudes were confirmed by other studies that showed that religious values contributed to MRPs.[42, 43] In addition, patients felt socially for their DM, which affected their self-esteem. They also blamed their financial situation for contributing to MRPs, since their finances prevented them from having the right diet and being able to afford doctors' visits. The cost of therapy has been perceived as being important, particularly with chronic conditions such as CVDs.[44] Thus, the value that the patients receive from healthcare professionals for their money was unsatisfactory. In fact, doctors' attitudes towards the patients played an important role in the patients being compliant with their regimens.[45] This problem was significant in ethnic minorities where a lack of communication between doctors and patients lead to misunderstanding.[42] Patients confirmed the need for further information and training, emphasising the importance of getting information from healthcare professionals.

Lifestyle-related factors

Lifestyle factors were perceived as a vital component for the control of conditions (CVDs/DM). Patients felt that they needed to adjust their diet, engage in physical activity, and manage their moods to cope with conditions. In relation to diet, they either did not understand the concept of a healthy diet or they had difficulty managing a good diet. Thus, some patients assumed that a healthy diet meant eating less food, eating "bitter food," or eating

"natural food." Other patients overestimated the importance of diet as being more crucial than medicines. This overestimation can be attributed to the fact that the frequency of meals could serve as a reminder to take medicines.[44] In addition, patients were aware of the necessity of physical exercise but blamed the weather, work, lack of time, and stress for their not exercising.[44] Stress was a major factor that patients blamed for not taking medicines on time and eating a poor diet.

Medicine-related factors

Medicines were recognised by patients as a contributing factor to MRPs with regards to lack of knowledge about medicines, lack of belief that medicines are good, difficulty taking medicines on time, and fear of side effects. Patients reported a lack of knowledge about how the medicines worked, called them pharmaceutical toxins, and preferred herbal remedies to medicines. This point was emphasised in another study[42] that stated that the patients' lack of awareness about the use of their medicines led to MRPs. Furthermore, patients reported skipping medicines doses due to forgetfulness or they did not take their medicines on purpose (at the time of exercise). Forgetfulness in terms of taking medicines was observed more often in patients who did not have regular meals.[44] At other times, patients were scared of the side effects and complications of medicines. The medicines' side effects caused physical discomfort for patients, who started to doubt the therapy's effectiveness and skipped their medicines.[44]

Condition-related factors

Condition (clinical) factors reported by the patients revealed a lack of knowledge about the disease and its cause, a lack of control over the disease, and the existence of comorbidities with the disease.[44] Patients were accordingly not fully aware of their condition and perceived it in most cases as being a risk factor leading to other diseases. Moreover, they misidentified the causes and complications of their condition. Once the education about the condition was provided, patients felt scared and frustrated, which induced a lack of control over the disease. Moreover, the existence of comorbidities with the main condition worsened the patients' adherence to treatment and advice.

Strengths and weaknesses of the review

This review proposes a systematic and comprehensive approach to qualitative studies of contributory factors to MRPs of adult patients with CVDs/DM. We adopted a thematic synthesis approach to eligible studies regarding the treatment experiences from patients' perspectives. The studies involved 836 participants. However, despite the diversity of the participants and different contexts in the studies, we were able to develop themes that indicated an overlap among the studies.

We used recognised methods from the literature regarding patients' experiences/perspectives in order to synthesise and develop analytical themes.[17, 46] We included the details of each study in relation to the aims, participants, settings, and methods applied. We rated the studies' qualities based on methods from the literature. In this respect, we found that studies with the highest ratings contributed most to the final analytical themes.

One limitation of the review is that it was restricted to the experiences of the patients involved in the studies. Moreover, studies of non-English speaking individuals and people seeking palliative care were underrepresented. Thus, the review was extracted from studies in 12 countries only. Therefore, the generalisability of the findings of this review to patients from different countries (other than the 12 aforementioned countries) may be difficult. However, the analytical themes developed offer a high level of conceptual thinking that can be applied across different contexts.

Implications of the research

This review examined the contribution of patients' perceptions, behaviours, and beliefs in understanding different aspects of underlying risk factors that may lead to MRPs. Syntheses of the qualitative research on such risk factors should complement the findings from quantitative research. Having a systematic review when planning new qualitative research may help to avoid unintentional examination of questions that have already been extensively researched. Finally, the findings of this study on patients' perspectives could

better inform the development of future screening tools and interventions for avoiding MRPs. Additionally, our results may also increase researchers' knowledge of generic issues in this field, even when attempting to target a specific ethnic or cultural group.

Implication towards practices

Patients' perspectives about medicine use and factors affecting their treatment regimen are often different from the medical viewpoint. Worldwide, people with CVD and/or DM widely perceive that their conditions are principally stress-related conditions and fear addiction or dependence on medicines, which leads to non-adherence to required treatments. These misconceptions and fears commonly cause people to reduce or stop treatment. If we are to be successful at minimising and preventing MRPs, incorporating patients' perspectives as well as considering medical records are paramount. An increased understanding between doctors and their patients must play a part in future strategies for reducing MRPs in patients with CVDs and/or DM.

CONCLUSIONS

This thematic synthesis of qualitative studies on patients' perspectives of the potential risk factors of MRPs shows that underlying factors that may lead to MRPs require further in-depth research. Factors influencing patients' success in treatment included patient-related (socioeconomic and lifestyle), medicine-related (fear of medicine, non-adherence, and polypharmacy), and condition-related factors (fear of condition and its complications). In summary, more qualitative research should be conducted on patients with CVDs and/or DM to understand and address issues related to the treatment regimens and subsequently reduce the cost of undesired hospital admissions resulting from MRPs.

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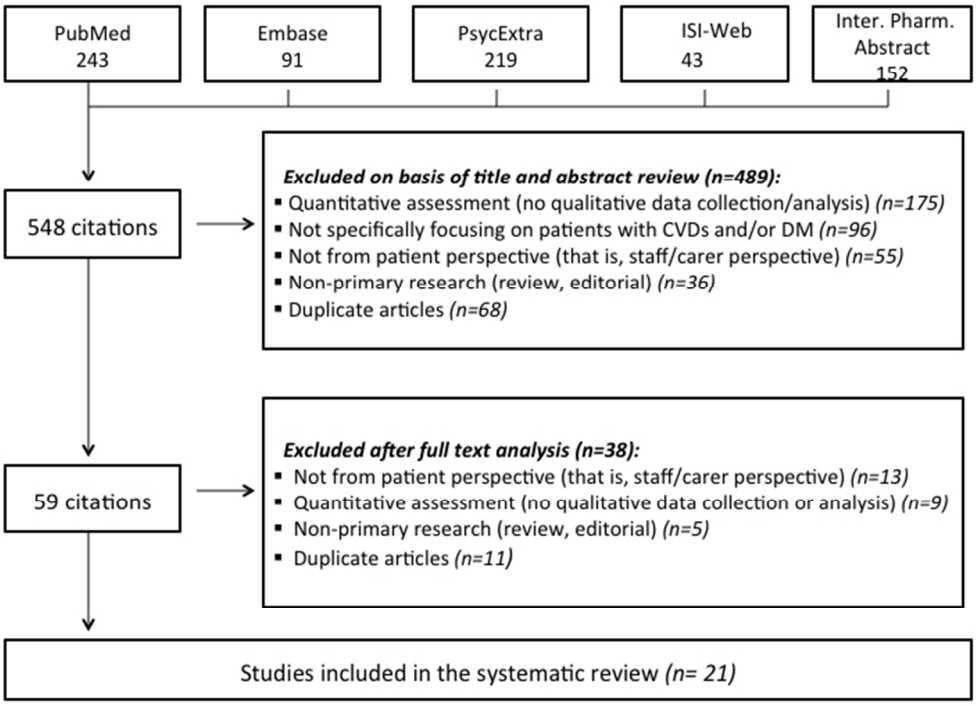
Figure legend

Figure 1 Data extraction and study selection process.



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A systematic review of qualitative research on the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus

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A systematic review of qualitative research on the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus

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ABSTRACT

Objectives To synthesise contributing factors leading to medicine-related problems (MRPs) in adult patients with cardiovascular diseases and/or diabetes mellitus from their perspectives.

Design A systematic literature review of qualitative studies regarding the contributory factors leading to MRPs, medication errors, and non-adherence, followed by a thematic synthesis of the studies.

Data sources We screened Pubmed, Embase, ISI Web of Knowledge, PsycInfo, International Pharmaceutical Abstract, and PsycExtra for qualitative studies (Interviews, focus groups, and questionnaires of a qualitative nature).

Review methods Thematic synthesis was achieved by coding and developing themes from the findings of qualitative studies.

Results The synthesis yielded 21 studies which satisfied the inclusion and exclusion criteria. Three themes emerged that involved contributing factors to MRPs: patient-related factors including both socioeconomic factors (beliefs, feeling victimised, history of the condition, lack of finance, lack of motivation, and low self-esteem) and lifestyle factors (diet, lack of exercise/time to see the doctor, obesity, smoking, and stress), medicine-related factors (belief in natural remedies, fear of medicine, lack of belief in medicines, lack of knowledge, non-adherence, and polypharmacy), and condition-related factors (lack of knowledge/understanding, fear of condition and its complications, and lack of control).

Conclusions MRPs represent a major health threat, especially among adult patients with cardiovascular diseases and/or diabetes mellitus. The patients' perspectives uncovered hidden factors that could cause and/or contribute to MRPs in these groups of patients.

Article focus

- CVDs and DM represent a major health issue that accounts for more than half of the total death rate worldwide.
- The contribution of patients' beliefs and behaviours towards their medicines /conditions and its subsequent involvement in MRPs is still under-researched.
- An exploration of the contributory factors leading to MRPs in patients with CVDs/DM could help inform prospective interventions.

Key messages

- MRPs constitute a major health concern especially for adult patients with CVDs and/or DM.
- Whereas medicine-related factors play important role in the incidence of MRPs; other contributing factors can be involved and include: Patient-related, life-style and clinical-related factors.
- Identifying the contributory factors leading to MRPs could help in mitigating/preventing incidence of MRPs. Thus, data from qualitative studies must be integrated with those of quantitative nature to develop efficient and practical interventions.

Strengths and limitations of the study

- To our knowledge, it is the first systematic review conducted on qualitative research regarding the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus.
- The study underatook a comprehensive systematic review with thematic synthesis approach .
- Despite using studies from 12 countries, the analytical themes developed from the review comprised a high level of conceptual thinking which could be applied across different studies.
- The review was restricted to the experiences of patients with 12 countries which could limit the generalisability of the findings.
- The qualitative studies (n = 21) in the literature were limited, so further qualitative studies are needed to assess the contributory factors leading to medicine-related problems.

INTRODUCTION

Medicine-related problems (MRPs) emerged as a concept in the early 1990s as “the detrimental experience regarding drug therapy and which potentially or actually causes an interference with their desired outcome.”[1] MRPs affect both healthcare and economic situations and contribute to a tremendous increase in morbidity, mortality and healthcare expenditure worldwide.[2-4]

MRPs represent a major issue, particularly in chronic conditions such as cardiovascular diseases (CVDs) and diabetes mellitus (DM).[5] The aforementioned conditions are expected to be the major source of morbidity by 2020.[6 7] In addition, these two conditions are interrelated; it has been documented that DM is a key factor that leads to CVDs as people with diabetes are three to four times more likely to have a CVD.[8 9] Consequently, the combination of CVDs and DM, which can result in multiple complications, represents a major concern for healthcare professionals.

More specifically, patients with CVDs and/or DM are more susceptible to MRPs due to long-term use of medicines and the inevitable polypharmacy.[7 10 11] However, many additional factors that contribute to MRPs in patients with CVDs and/or DM have gone underreported.

Studies in the literature, which investigated risk factors contributing to MRPs in patients with CVDs/DM, were mainly quantitative; only few studies were qualitative. Quantitative studies investigating risk factors contributing to MRPs involved either direct observations or were made retrospectively using data extracted from medical records.[12-15] However, most of the studies reported old age and polypharmacy extensively; few studies reported gender, depression, education, cohabitation, and immobilisations.[16] Nonetheless, qualitative studies investigating contributory risk factors leading to MRPs have been rather limited.

Therefore, this review aims to explore and evaluate contributory factors leading to MRPs among adult patients with CVDs and/or DM from their perspectives.

METHODS

We searched the PubMed, Embase, ISI Web of Knowledge, PsycInfo, International Pharmaceutical Abstract, and PsycExtra databases for entries between January 1990 and March 2014. The search strategy evaluated articles obtained predominantly through databases. Additional articles were retrieved through the bibliography lists of published reviews, where applicable.

The search strategy combined established methodological terms for qualitative research (qualitative research, qualitative studies, nursing methodological research, narrative analysis) and the following terms: Medicine (drug/medication) related problems, medicine (drug/medication) use, diabetes mellitus, cardiovascular diseases, patients' perspectives, patients' beliefs, patients' attitudes, patients' views, patients' opinions, patients' knowledge, patients' behaviours, and contributory factors. In addition, Medical Subject Headings (MeSH) relating to MRPs, CVDs/DM, risk factors, and patients' perspectives were explored.

Study selection

We included studies that utilised phone interviews, face-to-face interviews, focus groups, and open-ended questionnaires that were published in peer-reviewed journals.

The inclusion criteria involved studies focusing on the patients' perspectives on the use of medicines and MRPs and were conducted on adult patients with CVDs and/or DM.

On the other hand, the exclusion criteria flagged studies that were quantitative in nature, studies with closed-ended questionnaires, and studies focusing on conditions other than CVD/DM.

Initially, one reviewer (AA) conducted the search and did screening for the titles. At this stage, studies with irrelevant titles were excluded. Then, the

abstracts of the remaining studies were evaluated independently for inclusion by two reviewers (MG and ZA). Any disagreements that were encountered were resolved via a discussion. No language limits were applied. However, the search results only generated English studies. Figure 1 demonstrate the details of the data extraction process.

Data synthesis and analysis

In order to extract data from articles, we adopted the systematic review approach for qualitative research by Dixon-Woods et al.[17] This allowed the emergence of broad concepts. Then, data was synthesised by utilising the thematic analysis approach,[18] which enables extraction of concepts and hypotheses from multiple qualitative studies.

Based on the extracted results, we developed textual summaries and tables. From the textual summaries and tables, we identified emerging themes which described the meaning and content of the included studies. We then inspected similarities and differences across the textual summaries in order to avoid contradiction and reduce the developed number of themes. Subsequently, we agreed on the final list of themes through discussion and consensus.

Finally, we coded the full list of papers for the presence or absence of themes. The codes were tabulated afterwards by country in order to inspect similarities and differences across countries.

Since our approach was qualitative, the presence of a theme in more than one paper did not indicate its importance in the studied population.[19] However, a theme appearing in more than one paper did denote to a degree its validity. Thus, the number of studies within a specific theme was reported in this review.

Quality of synthesis assessment

The quality of papers was assessed using the checklist developed by Dixon-Woods et al. (2004).[17] This assessment was based mainly on clarity,

consideration of ethical issues, and transferability of the sample, data, and analysis across different settings. Furthermore, the critical appraisal skills programme criteria[20] were used to rank the papers based on 10 questions that fulfilled the clarity, methods, and results of the studies. Consequently, studies were grouped into low (one star: 0 to 3 points), medium (two stars: 4 to 7 points), and high quality (three stars: 8 to 10 points). Low-quality studies were not excluded, but caution was taken when interpreting their results.

RESULTS

A total of 21 studies (including 836 participants) from 12 countries met the inclusion criteria (Table 1) and were conducted in the following countries: Australia,[21] Brazil,[22] Cameroon,[23] Canada,[24] Croatia,[25] Ireland,[26] Malaysia,[27 28] South Africa,[29] Spain,[30] Taiwan,[31] the United Kingdom,[7 32-37] and the United States.[38-40] The majority of the studies investigated type 2 DM (*n* = 15); fewer studies investigated CVDs. Thus, only two studies investigated hypertension (HTN), one investigated heart failure, and one studied CVDs in general. The remaining two studies investigated DM/HTN and DM/HTN/stroke, respectively. Eight studies used focus groups, 12 used interviews, and one study used a mixture of these methods. The review covered areas related to patients, conditions, and medicines.

Table 1l **Characteristics of the included studies**

Study	Country	Study type	Patients' diagnosis	Method of analysis	Study population	Study settings	Study aims	Study quality
Al-Qazaz et al 2011[27]	Malaysia	Semi-structured interviews	Type 2 DM	Content analysis	12 diabetic patients, with at least one year of diabetes and a prescription of oral hypoglycemic	Universiti Sains Malaysia (USM) Health Clinic	To explore diabetic patients' experience and knowledge about diabetes and its medication and to understand the factors contributing to medication adherence in	**

							Malaysian population.	
Brown et al 2007[32]	UK	One-to-one interviews	Type 2 DM	Thematic analysis	17 African–Caribbean diabetes patients with age above 18 years; 13 first generation immigrants and four second generation immigrants	Inner city Nottingham	To gain an understanding of how health beliefs influence the way African–Caribbean people with diabetes manage their illness.	***
Choudhury et al 2009[33]	UK	Structured interview	Type 2 DM	Thematic analysis	14 invited individuals, Bangladeshi (four males and 10 females), in the age range of 26 to 67 years, with type 2 DM (had it since six months - 27 years) and were recruited either in Swansea or Birmingham.	Participants from local communities in Swansea and Birmingham were invited for the interview	To examine the understanding and beliefs of people with diabetes from the Bangladeshi community living in the UK.	**

					Interviews were made in either English or in Sylheti as the researcher was bilingual			
Coronado et al 2004[38]	USA	Focus groups	Type 2 DM	Matrix analysis by Morgan and Krueger	42 Individuals (14 men and 28 women) in six focus groups, who had diabetes, had a family history of diabetes, or knew someone who had diabetes.	Fred Hutchinson Cancer Research Center's project office in Sunnyside, Yakima village and Skagit Valley Community College and at the Catholic church in Burlington	To investigate the perceptions about the causes of and treatments for type 2 DM	*
Cottrell et al 2013[21]	Australia	Structured interview	HF	Repertory grid technique	92 patients (older than 18 years) with heart failure	Heart Failure Service outpatient clinic, Royal Brisbane and Women's Hospital in Brisbane, Australia	To elicit individuals' beliefs about their heart failure treatment and to investigate whether generated constructs were different between adherent and nonadherent patients.	*

Gascon et al 2004[30]	Spain	Focus groups with open ended questions	HTN	Thematic analysis	Seven focus groups of 44 patients (24 men and 20 women), diagnosed with hypertension, between the ages of 18 and 80 years, being treated with antihypertensives for 3 months, being non-compliant and having sufficiently good physical and mental health to participate.	Two primary healthcare centres	To identify factors related to non-compliance with the treatment of patients with hypertension.	**
Gordon et al 2007[7]	UK	Face-to-face interviews	CVD	Thematic analysis	98 patients (41 males and 57 females) in the age range of 32 – 89 years.	Home interviews of patients recruited from five general surgeries and pharmacy interviews at four community pharmacies	To examine medication-related problems from the perspective of patients with a chronic condition and to identify how they may be supported in managing their medication.	**

Grace et al 2008[34]	UK	Focus groups	Type 2 DM	Thematic analysis	17 focus groups of adult diabetic patients	Tower Hamlets, a socioeconomically deprived London borough	To understand lay beliefs and attitudes, religious teachings, and professional perceptions in relation to diabetes prevention in the Bangladeshi community.	***
Heymann et al 2012[35]	UK	Focus groups	DM and HTN	Thematic analysis	10 focus groups of 86 (42 males and 44 females) patients with hypertension in three age ranges: 41-50, 51-60, 61-70 years (six groups); and patients with hypertension and DM in the age ranges: 51-60, 61-70 years (a total of four groups).	UK	To explore beliefs and perceptions regarding hypertension and gain an understanding of barriers to treatment among patients with and without DM.	***
Hu et al 2013[39]	USA	Focus groups	Type 2 DM	Content analysis	Five focus groups of 73 Hispanic immigrants; 18	free health clinic in central North Carolina	To explore perceived barriers among Hispanic	**

					years or older		immigrants with diabetes and their family members.	
Jolles et al 2013[24]	Canada	Semi-structured interviews	HTN	Thematic analysis	26 Patients, in the age range of 26 - 85 years and 62% females, able to speak, read and write English; diagnosed with hypertension by a healthcare provider, and currently taking an antihypertensive medication.	Two hypertension clinics at the University of Alberta in Edmonton	To understand hypertensive patients' perspectives regarding blood pressure and hypertension treatment.	**
Kiawi et al 2006[23]	Cameroon	In-depth interviews, semi-structured	Type 2 DM, HTN and stroke	Content analysis	15 interviews of 62 patients (27 women and five men), selection criteria included they had lived at least six months in the community, were nominated by other	Four urban health districts, one from each of the main ecological areas of Cameroon.	To investigate of lay knowledge, attitudes, and behaviors relating to diabetes and its main risk factors of urban Cameroonians.	***

					community members, and were age above 15 years.			
Lai et al 2005[31]	Taiwan	In-depth interviews	Type 2 DM	Thematic analysis	22 diabetic patients (12 males and 10 females), in the age range of 44 - 80 years, with a duration of illness more than one year.	Rural Taiwan community	To investigate Chinese diabetic patients' perceptions about their illness and treatment strategies to facilitate patient-centred, culture-sensitive clinical skills.	**
Lawton et al. 2006[36]	UK	In-depth interviews with open-ended approach	Type 2 DM	Thematic analysis	31 patients (23 Pakistani and eight Indian), aged 18 years and over, and diagnosed with type 2 DM	General Practices in Edinburgh	Patients' perception and practical considerations	**
Mohd Ali and Jussoff 2009[28]	Malaysia	In-depth open-ended interviews	Type 2 DM	Thematic analysis	18 patients (9 males and 9 females) in the age of 15-75 years, and 13 healthcare professionals (nine doctors, three	Endocrinology clinic of a teaching hospital in Kuala Lumpur	To explore the perspectives and experiences of Malay patients in managing type 2 DM as a chronic illness and provide	***

					pharmacists and one diabetic nurse educator).		recommendations that aim to enhance adherence to treatment and help patients to improve their self-management skills.	
Mshunqane et al 2012[29]	South Africa	Patient focus groups (n = 10) and healthcare professional focus groups (n = 8) and in-depth interviews. The questions were open-ended	Type 2 DM	Thematic analysis	Patients who had been diagnosed with type 2 diabetes for at least one year, who were between 30 and 65 years of age	Dr George Mukhari Hospital outpatients' diabetes clinic	To determine the knowledge that patients with type 2 DM have about the management of their disease, as well as the perceptions of the health care team about the services given to patients.	***
Peel et al 2004[37]	UK	In-depth interviews	Type 2 DM	Thematic analysis	40 newly diagnosed TYPE 2 DIABETES MELLITUS patients in the age range of 21 – 77 years	Across the Lothian region in Scotland	To explore the patients' emotional reactions about their type 2 DM diagnosis, and their views about information provision at the time of	**

							diagnosis.	
Peres et al 2007[22]	Brazil	Interviews	Type 2 DM	Content analysis	24 diabetic females, age between 25 and 76 years old, literate, with eight years of schooling, from Ribeirão Preto, who perform household activities.	Nursing Education Center for Adults and Elderly - CEEAI, University of São Paulo	Identify the difficulties patients encounter when controlling diabetes	**
Rustveld et al 2009[40]	USA	Focus groups	Type 2 DM	Thematic analysis	34 patients in six focus groups (three in English and three in Spanish), older than 18 years and with type 2 DM	Three Harris County Hospital District (HCHD) community health centers in Houston, Texas	To elicit attitudes, attributions, and self-efficacy related to diabetes self-care in both English- and Spanish-speaking Hispanic men.	**
Smith et al 2003[26]	Ireland	Focus groups	Type 2 DM	Thematic analysis	25 patients from three general practices, having DM for at least one year	Patients were invited to participate in the focus group	To explore the views and health beliefs of patients with type 2 DM who had experienced	**

							a new structured diabetes shared care service.	
Vinter-Repalust et al 2004[25]	Croatia	Focus groups	Type 2 DM	Thematic analysis	Seven focus groups of 49 patients (22 males and 27 females), in the age range of 44 - 83 years, ambulatory patients with the diagnosis of type 2 DM, with differences not only in age and sex, but also in the method of treatment of diabetes as well.	Zagreb Medical School	To explore type 2 diabetic patients' attitudes, thoughts, and fears connected with their illness; their expectations of the health care system; and the problems they encountered while adhering to the therapeutic regimen.	***

Narrative synthesis

The main findings of the review showed that contributory factors to MRPs involved three themes: patient-related (socioeconomic and lifestyle), medicine-related, and condition-related factors. Table 2 lists the studies that reported or discussed each theme.

Table 2| **Themes and subthemes emerging from the studies**

Theme/ Sub-theme	Countries, studies
Patient related factors (socioeconomic)	
Belief	UK (Brown et al 2007[32], Grace et al 2008[34], Lawton et al 2006[36])
Family history of condition	UK (Grace et al 2008[34], Lawton et al 2006[36]), USA (Coronado et al 2004[38])
Feeling victimised	South Africa (Mshunqane et al 2012[29]), Croatia (Vinter-Repalust et al 2004[25]), Ireland (Smith et al 2002[26])
Lack of finance	Ireland (Smith et al 2002[26]), South Africa (Mshunqane et al 2012[29]), Croatia (Vinter-Repalust et al 2004[25]), USA (Hu et al 2013[39])
Lack of knowledge	Croatia (Vinter-Repalust et al 2004[25])
Lack of motivation	Croatia (Vinter-Repalust et al 2004[25])
Lack of information/ understanding from doctors	UK (Brown et al 2007[32], Choudhury et al 2009[33])
Low self-esteem	Croatia (Vinter-Repalust et al 2004[25]), USA (Rustveld et al 2009[40])
Patient related factors (life-style)	
Decrease alcohol intake	Canada (Jolles et al 2013[24]),
Decrease caffeine intake	Canada (Jolles et al 2013[24]), South Africa (Mshunqane et al 2012[29])
Diet	Australia (Cotrell et al 2013[21]), Brazil (Peres et al 2007[22]), Canada (Jolles et al 2013[24]), Croatia (Vinter-Repalust et al 2004[25]), Ireland (Smith et al 2002[26]), UK (Brown et al 2007[32], Choudhury et al 2009[33], Grace et al 2008[34], Heymann et al 2012[35], Lawton et al 2006[36]), USA (Coronado et al 2004[38], Hu et al 2013[39], Rustveld et al 2009[40]), South Africa (Mshunqane et al 2012[29]), Taiwan (Lai et al 2005[31])
Lack of exercise	Brazil (Peres et al 2007[22]), Canada (Jolles et al 2013[24]), UK (Brown et al 2007[32], Choudhury et al 2009[33], Grace et al 2008[34], Heymann et al 2012[35], Lawton et al 2006[36]), South Africa (Mshunqane et al 2012[29]), USA (Coronado et al 2004[38], Hu et al 2013[39], Rustveld et al 2009[40])
Lack of time to see doctor	Malaysia (Al-Qazaz et al 2011[27])

Obesity	Brazil (Peres et al 2007[22]), South Africa (Mshunqane et al 2012[29]), UK (Brown et al 2007[32]), USA (Coronado et al 2004[38])
Smoking	Canada (Jolles et al 2013[24]), UK (Heymann et al 2012[35])
Stress	Ireland (Smith et al 2002[26]), UK (Brown et al, 2007[32], Grace et al 2008[34], Heymann et al 2012[35]), USA (Coronado et al 2004[38])
Medicine related factors	
Belief in natural remedies as alternative to medicines	Spain (Gascon et al 2004[30]), UK (Brown et al 2007[32]), USA (Coronado et al 2004[38])
Difficulty/ refusal to take medicine	Brazil (Peres et al 2007[22]), Croatia (Vinter-Repalust et al 2004[25])
Fear of being stuck with medicines all life	Spain (Gascon et al 2004[30]), UK (Gordon et al 2007[7])
Fear of side effects	Ireland (Smith et al 2002[26]), Malaysia (Al-Qazaz et al 2011[27]), UK (Heymann et al 2012[35]), Spain (Gascon et al 2004[30]), Taiwan (Lai et al 2005[31])
Fear of the chemical nature of medicines	Taiwan (Lai et al 2005[31]), UK (Brown et al 2007[32])
Forgetfullness	Brazil (Peres et al 2007[22]), Malaysia (Al-Qazaz et al 2011[27], Mohd Ali and Jusoff 2009[28]), Spain (Gascon et al 2004[30])
Lack of belief in medicines	Australia (Cotrell et al 2013[21])
Lack of knowledge about medicines mechanism of actions	Canada (Jolles et al 2013[24]), Spain (Gascon et al 2004[30]), UK (Gordon et al 2007[7])
Non-adherence	Canada (Jolles et al 2013[24]), Croatia (Vinter-Repalust et al 2004[25]), Taiwan (Lai et al 2005[31]), UK (Gordon et al 2007[7]), USA (Hu et al 2013[39], Rustveld et al 2009[40])
Polypharmacy	Brazil (Peres et al 2007[22])
Condition related factors	
Lack of control over condition	Brazil (Peres et al 2007[22]), Ireland (Smith et al 2002[26])
Lack of knowledge/ understanding of condition	Australia (Cotrell et al 2013[21]), Cameroon (Kiawi et al 2006[23]), Canada (Jolles et al 2013[24]), Malaysia (Al-Qazaz et al 2011[27], Mohd Ali and Jusoff 2009[28]), Spain (Gascon et al 2004[30]), UK (Brown et al 2007[32], Choudhury et al 2009[33], Heymann et al 2012[35], Peele et al 2004[37]), USA (Coronado et al 2004[38])
Fear of condition, its causes and complications	South Africa (Mshunqane et al 2012[29]), UK (Choudhury et al 2009[33], Lawton et al 2006[36]), USA (Coronado et al 2004[38])
Stress from condition	Croatia (Vinter-Repalust et al 2004[25])

Patient-related factors

Socioeconomic-related factors

Patients from six countries reported socioeconomic factors leading to MRPs in both DM and CVDs, including: beliefs, family history of the condition, poor finances, relationships with healthcare professionals (lack of communication and not enough education), inadequate knowledge, and low self-esteem (Table 2).

Beliefs regarding CVDs/DM were reported as a problem in three studies from the United Kingdom.[32 34 36] Patients perceived that DM was given by God and higher powers had control over their condition. One patient reported:

> *"God has given me this disease of sugar. Whatever happens, it happens because God wants it to happen."*

Moreover, a family history of DM was reported in three studies from the United Kingdom[34 36] and the United States.[38]

In addition, poor finances were reported by patients in four studies from Ireland,[26] South Africa,[29] Croatia,[25] and the United States.[39] A lack of necessary finances prevents patients from buying the appropriate food (for their diet)[29] and going to doctors.[26]

Consequently, the financial situation implicated the relationship of the patients with the healthcare professionals. Patients have reported that they were not getting value for their money from healthcare providers.[26] For instance, one patient reported:

> *" I don't mind paying when I'm sick, but it's very expensive to pay the GP when I'm only getting a check-up with the nurse."*

Thus, the patients felt victimised by healthcare professionals[25 26 29] and reported a lack of communication with healthcare professionals.[18] They

described doctors as either too busy to see them[26 27] or not giving enough information about diagnosis and medicines.[32 33 37] Other patients reported having been belittled by doctors.[25] In another study, patients accounted for the lack of communication with healthcare professionals by language barriers.[33]

Subsequently, patients reported a lack of knowledge as a major cause for type 2 DM.[25] This situation led to the lack of motivation about their disease and affected the intake of medicines. Patients asserted the need for further education and training about their condition.

A lack of knowledge resulted in the patients' low-self esteem towards their condition.[25 40] Hence, patients felt unaccepted socially, less comfortable with their colleagues, and less worthy for being diabetic.[25 40]

Lifestyle-related factors

Lifestyle-factors were reported in studies from 11 countries and included: diet (excessive alcohol/caffeine intake), lack of exercise, lack of time to see the doctor, obesity, smoking, and stress.

Diet was a major issue stated in 16 studies (Table 2). In this respect, patients had different behaviours towards their diet. For instance, one group of patients admitted the importance of a healthy diet, yet could not control their diets.[22 31-33] Thus, one participant reported:[22]

"Regarding the diet, I try to fight so as not to eat certain foods, but sometimes I can't help myself."

In this respect, patients appreciated the importance of a healthy diet in controlling DM,[32] yet overestimated its importance to be beyond medicines.[31] They were also aware that a poor diet, including excess alcohol[24] and caffeine intake,[24 29] exacerbated their conditions. Another group of patients misunderstood the concept of a healthy diet. They believed that eating bitter foods could control DM[33] or applied portion sizes to their

diets.[40] In the latter case, patients had difficulty eating smaller portions and/or even changing their favourite foods. On other occasions, patients claimed that diet quality was responsible for DM.[26]

In addition, a lack of exercise was reported in 11 studies from five countries, including Brazil,[22] Canada,[24] the United Kingdom,[32-36] South Africa,[29] and the United States.[38-40] A group of patients overestimated the importance of exercise, claiming that it can cure any existing disease.[31] Patients reported difficulty exercising although they were aware of its importance.[36 40] They justified their work, travel, stress, the weather, and lack of time as the reasons behind their decreased physical exercise.[22 33 34 36 39] A lack of time was more reported in females whose culture expected them to stay indoors after they got married.[36]

Moreover, obesity was described in four studies (Brazil, [22] South Africa,[29] the United Kingdom,[32] and the United States[38]) as a cause of DM. Patients blamed weight gain as the cause for their increase in blood glucose level and diabetic complications.[32 38] Moreover, they attributed insulin as one of the causes of obesity.[32]

Stress emerged in five studies from three countries, including Ireland,[26] the United Kingdom,[32 34 35] and the United States.[38] Stress was identified as a result of changes in culture and climate, poor housing, and migration of ethnic minorities.[38] Patients considered stress to be major cause of their condition.[26 32 34 35 38 40] For instance, one patient reported:

"In 1998, my mother died, and I was unable to go to the funeral. During these months, I developed diabetes."

Patients also perceived that stress control could be an effective way to cure their condition[34] since stress led to a poor diet, smoking, and a lack of exercise.

Medicine-related factors

Medicine-related factors were found in 14 studies from 11 countries and included two types of factors: factors related to the use of medicines and factors related to knowledge about medicines.

Factors related to the use of medicines included medicine non-adherence and polypharmacy. Medicine non-adherence was reported in 10 studies from seven countries, including Brazil,[22] Canada,[24] Croatia,[25] Malaysia,[27 28] Spain,[30] Taiwan,[31] the United Kingdom,[7] and the United States.[39 40] Patients justified non-adherence to medicines as difficulty following the treatment regimen,[25] depression and stress,[40] forgetfulness in taking the medicines,[7 22 27 28 30] a lack of routine in taking the medicines,[24] changes in medicine routines,[24] and the inconvenience of taking insulin. For instance, patients complained that oral hypoglycemics are more convenient to take than insulin:[30]

"I prefer pills more than insulin. You know, swallowing a pill causes no pain. And when I know I will eat more I just take another pill or an extra half."

Furthermore, intentional non-adherence was reported in some studies where patients changed their insulin doses depending on their food regimen.[30] In another scenario, patients stopped taking their medicines when they exercised, acting on the assumption that exercise reduces blood sugar level. Thus, patients changed the dose/regimen of their medicines to fit with their daily activities.[7]

Poylpharmacy was reported among patients with type 2 DM in two studies from Brazil[22] and Canada.[28] Polypharmacy caused inconvenience in taking medicines:[22]

"Medication: this has been my biggest problem in this current phase. I take medication for blood pressure, circulation, diabetes, vitamins. I used to mix up the time of each, but today, thanks to orientation, I'm overcoming this stage."

Factors relating to knowledge about medicines included lack of knowledge about how the medicines worked, fear of the chemical nature of medicines and their side effects, and a lack of belief in medicine.

The lack of knowledge about how medicines worked was described in three studies in Canada,[24] the United Kingdom,[7] and Spain.[30] Patients could not identify most of their medicines apart from the diuretics, which they called "water pills."[24] Moreover, patients could not understand how their medicines worked, even when they read the patient information leaflet.[30]

This lack of knowledge created fear in patients regarding the chemical nature of medicines, the side effects of medicines, and being obliged to take medicines all of their lives.[7 26 27 30-32 35] For instance, patients referred to oral hypoglycemic agents and insulin as "pharmaceutical toxins."[31]

Additionally, patients were afraid of the side effects and complications of medicines. They attributed various side effects to medicines, including hypoglycemia and gastrointestinal disturbances to insulin,[32] kidney failure to oral hypoglycemic agents,[31] and nausea/vomiting to antihypertensive agents.[30] In the last case, a patient reported:

"I don't like them (medicines); they have lots of side effects. They can make you sick… I think that I might get worse instead of better."

These fears promoted a lack of belief in medicines among patients.[21] Subsequently, patients started to believe in natural remedies as an alternative to medicines.[30 32 38] They referred to natural therapies as "*a cure*" that should be used alongside traditional medicines.[38] In another scenario, patients believed that natural therapies were superior to medicines.[32] In this respect, natural therapies reported for curing DM included natural drinks (composed of minerals and water);[38] and plant products (such as aloe vera, arnica, cactus, silk cottonwood tree, tree spinach, and violet water).[32]

Condition-related factors

Condition (clinical)-related factors were reported from 11 countries as a major theme. Factors included a lack of knowledge/understanding of the condition, fear of the condition and its complications, stress from the condition, and a lack of control over the condition.

Lack of knowledge/understanding of the condition (CVDs/DM) emerged as a major theme in 11 studies from seven countries, including Australia,[21] Cameroon,[23] Canada,[24] Malaysia,[27 28] Spain,[30] the United Kingdom,[32 33 35 37] and the United States.[38]

For CVDs, patients expressed a lack of knowledge about their heart failure, hypertension, and stroke. Patients with heart failure did not know enough about their disease symptoms.[21] Moreover, hypertensive patients did not understand the nature of their disease,[28 30] struggled to define their condition,[24] and considered it an underlying risk factor to myocardial infarction rather than a disease.[35] Patients justified their lack of knowledge by citing short consultations with physicians, not obtaining enough information from physicians, and obtaining information from non-medical sources such as television and magazines. For instance, one patient reported:

"Anything I know about blood pressure I've read in books, the doctor tells me absolutely nothing . . . High blood pressure: factors related to compliance with treatment 127. I want him to tell me where high blood pressure comes from."

Similarly, patients with DM lacked knowledge about the disease and misunderstood its causes and complications.[23 25 27 29 32 33 36] Regarding the DM condition and causes, patients' perceptions of DM were influenced by other people's accounts and experiences.[32] Patients viewed the condition as an illness that took away their health and strength[36] and changed their lifestyle.[25] They could not differentiate between DMT1 and type 2 DM,[27] considered high sugar intake to be the cause of DM, and

perceived DM to be sexually and genetically transmitted.[23 33] Moreover, patients believed that diabetes was not dangerous if it did not require insulin.[32] Patients were only aware of the microvascular complications (such as foot disease) of DM.[26] Moreover, they were aware of the disease's signs and symptoms (such as dry mouth, tiredness, dizziness, irritation, blurred vision, micturition, and extreme thirst) only after they encountered them.[28 38]

The lack of knowledge about the condition created fear in the patients' minds of the disease itself[38] and they could not accept the disease easily.[25 33] One patient reported:[38]

"Diabetes is a disease that kills you little by little."

Diseases additionally resulted in stress about the condition that was particularly observed in patients with multiple comorbidities.[36] For instance, diabetic patients who had asthma as a comorbidity could not exercise due to asthma symptoms, such as shortness of breath and swollen feet and joints:

"They tell you to exercise…
but I can't move around a lot because I have
a problem with my leg (arthritis). If I walk a little,
then it swells up."

As a result, patients were not able to control their condition,[22 26] which led to frustration, depression, and anxiety.

DISCUSSION

To our knowledge, this review is the first systematic analysis of the perspectives of adult patients with CVDs/DM on contributory factors leading to MRPs. We explored the patients' knowledge, beliefs, and behaviours towards medicines. The majority of studies evaluated patients with DM; only a few

studies evaluated patients with CVDs. The three themes emerging from this review included: patient- (socioeconomic- and lifestyle-), clinical-, and medicine-related factors.

Patient-related factors

Socioeconomic-related factors

Socioeconomic factors (genetic, cultural behaviour, and financial situations) affected the patients' perceptions of disease and the medicines contributing to MRPs. Patients perceived genetic factors and religious beliefs to be the cause of their DM.[19 21] Patients from both Christian and Muslim backgrounds named God as the cause for their DM. These attitudes were confirmed by other studies that showed that religious values contributed to MRPs.[41 42] In addition, patients felt socially for their DM, which affected their self-esteem. They also blamed their financial situation for contributing to MRPs, since their finances prevented them from having the right diet and being able to afford doctors' visits. The cost of therapy has been perceived as being important, particularly with chronic conditions such as CVDs.[43] Thus, the value that the patients receive from healthcare professionals for their money was unsatisfactory. In fact, doctors' attitudes towards the patients played an important role in the patients being compliant with their regimens.[44] This problem was significant in ethnic minorities where a lack of communication between doctors and patients lead to misunderstanding.[41] Patients confirmed the need for further information and training, emphasising the importance of getting information from healthcare professionals.

Lifestyle-related factors

Lifestyle factors were perceived as a vital component for the control of conditions (CVDs/DM). Patients felt that they needed to adjust their diet, engage in physical activity, and manage their moods to cope with conditions. In relation to diet, they either did not understand the concept of a healthy diet or they had difficulty managing a good diet. Thus, some patients assumed that a healthy diet meant eating less food, eating "bitter food," or eating "natural food." Other patients overestimated the importance of diet as being more crucial than medicines. This overestimation can be attributed to the fact

that the frequency of meals could serve as a reminder to take medicines.[43] In addition, patients were aware of the necessity of physical exercise but blamed the weather, work, lack of time, and stress for their not exercising.[43] Stress was a major factor that patients blamed for not taking medicines on time and eating a poor diet.

Medicine-related factors

Medicines were recognised by patients as a contributing factor to MRPs with regards to lack of knowledge about medicines, lack of belief that medicines are good, difficulty taking medicines on time, and fear of side effects. Patients reported a lack of knowledge about how the medicines worked, called them pharmaceutical toxins, and preferred herbal remedies to medicines. This point was emphasised in another study[41] that stated that the patients' lack of awareness about the use of their medicines led to MRPs. Furthermore, patients reported skipping medicines doses due to forgetfulness or they did not take their medicines on purpose (at the time of exercise). Forgetfulness in terms of taking medicines was observed more often in patients who did not have regular meals.[43] At other times, patients were scared of the side effects and complications of medicines. The medicines' side effects caused physical discomfort for patients, who started to doubt the therapy's effectiveness and skipped their medicines.[43]

Condition-related factors

Condition (clinical) factors reported by the patients revealed a lack of knowledge about the disease and its cause, a lack of control over the disease, and the existence of comorbidities with the disease.[43] Patients were accordingly not fully aware of their condition and perceived it in most cases as being a risk factor leading to other diseases. Moreover, they misidentified the causes and complications of their condition. Once the education about the condition was provided, patients felt scared and frustrated, which induced a lack of control over the disease. Moreover, the existence of comorbidities with the main condition worsened the patients' adherence to treatment and advice.

Strengths and weaknesses of the review

This review proposes a systematic and comprehensive approach to qualitative studies of contributory factors to MRPs of adult patients with CVDs/DM. We adopted a thematic synthesis approach to eligible studies regarding the treatment experiences from patients' perspectives. The studies involved 836 participants. However, despite the diversity of the participants and different contexts in the studies, we were able to develop themes that indicated an overlap among the studies.

We used recognised methods from the literature regarding patients' experiences/perspectives in order to synthesise and develop analytical themes.[18 45] We included the details of each study in relation to the aims, participants, settings, and methods applied. We rated the studies' qualities based on methods from the literature. In this respect, we found that studies with the highest ratings contributed most to the final analytical themes.

One limitation of the review is that it was restricted to the experiences of the patients involved in the studies. Moreover, perspectives and beliefs of non-English speaking patients and those seeking palliative care were not integrated in this review due to lack of studies representing them. Thus, the review was extracted from studies in 12 countries only. Therefore, the generalisability of the findings of this review to patients from different countries (other than the 12 aforementioned countries) may be difficult. However, the analytical themes developed offer a high level of conceptual thinking that can be applied across different contexts.

Implications of the research

This review examined the contribution of patients' perceptions, behaviours, and beliefs in understanding different aspects of underlying risk factors that may lead to MRPs. Syntheses of the qualitative research on such risk factors should complement the findings from quantitative research. Having a systematic review when planning new qualitative research may help to avoid unintentional examination of questions that have already been extensively researched. Finally, the findings of this study on patients' perspectives could

better inform the development of future screening tools and interventions for avoiding MRPs. Additionally, our results may also increase researchers' knowledge of generic issues in this field, even when attempting to target a specific ethnic or cultural group.

Implication towards practices

Patients' perspectives about medicine use and factors affecting their treatment regimen are often different from the medical viewpoint. Worldwide, people with CVD and/or DM widely perceive that their conditions are principally stress-related conditions and fear addiction or dependence on medicines, which leads to non-adherence to required treatments. These misconceptions and fears commonly cause people to reduce or stop treatment. If we are to be successful at minimising and preventing MRPs, incorporating patients' perspectives as well as considering medical records are paramount. An increased understanding between doctors and their patients must play a part in future strategies for reducing MRPs in patients with CVDs and/or DM.

CONCLUSIONS

This thematic synthesis of qualitative studies on patients' perspectives of the potential risk factors of MRPs shows that underlying factors that may lead to MRPs require further in-depth research. Factors influencing patients' success in treatment included patient-related (socioeconomic and lifestyle), medicine-related (fear of medicine, non-adherence, and polypharmacy), and condition-related factors (fear of condition and its complications). In summary, more qualitative research should be conducted on patients with CVDs and/or DM to understand and address issues related to the treatment regimens and subsequently reduce the cost of undesired hospital admissions resulting from MRPs.

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Figure legend

Figure 1 Data extraction and study selection process.

A systematic review of qualitative research on the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus

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ABSTRACT

Objectives To synthesise contributing factors leading to medicine-related problems (MRPs) in adult patients with cardiovascular diseases and/or diabetes mellitus from their perspectives.

Design A systematic literature review of qualitative studies regarding the contributory factors leading to MRPs, medication errors, and non-adherence, followed by a thematic synthesis of the studies.

Data sources We screened Pubmed, Embase, ISI Web of Knowledge, PsycInfo, International Pharmaceutical Abstract, and PsycExtra for qualitative studies (Interviews, focus groups, and questionnaires of a qualitative nature).

Review methods Thematic synthesis was achieved by coding and developing themes from the findings of qualitative studies.

Results The synthesis yielded 21 studies which satisfied the inclusion and exclusion criteria. Three themes emerged that involved contributing factors to MRPs: patient-related factors including both socioeconomic factors (beliefs, feeling victimised, history of the condition, lack of finance, lack of motivation, and low self-esteem) and lifestyle factors (diet, lack of exercise/time to see the doctor, obesity, smoking, and stress), medicine-related factors (belief in natural remedies, fear of medicine, lack of belief in medicines, lack of knowledge, non-adherence, and polypharmacy), and condition-related factors (lack of knowledge/understanding, fear of condition and its complications, and lack of control).

Conclusions MRPs represent a major health threat, especially among adult patients with cardiovascular diseases and/or diabetes mellitus. The patients' perspectives uncovered hidden factors that could cause and/or contribute to MRPs in these groups of patients.

Article focus

- CVDs and DM represent a major health issue that accounts for more than half of the total death rate worldwide.
- The contribution of patients' beliefs and behaviours towards their medicines /conditions and its subsequent involvement in MRPs is still under-researched.
- An exploration of the contributory factors leading to MRPs in patients with CVDs/DM could help inform prospective interventions.

Key messages

- MRPs constitute a major health concern especially for adult patients with CVDs and/or DM.
- Whereas medicine-related factors play important role in the incidence of MRPs; other contributing factors can be involved and include: Patient-related, life-style and clinical-related factors.
- Identifying the contributory factors leading to MRPs could help in mitigating/preventing incidence of MRPs. Thus, data from qualitative studies must be integrated with those of quantitative nature to develop efficient and practical interventions.

Strengths and limitations of the study

- To our knowledge, it is the first systematic review conducted on qualitative research regarding the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus.
- The study underatook a comprehensive systematic review with thematic synthesis approach .
- Despite using studies from 12 countries, the analytical themes developed from the review comprised a high level of conceptual thinking which could be applied across different studies.
- The review was restricted to the experiences of patients with 12 countries which could limit the generalisability of the findings.
- The qualitative studies (n = 21) in the literature were limited, so further qualitative studies are needed to assess the contributory factors leading to medicine-related problems.

Contributors AA participated in protocol development, literature searching, data extraction, data analysis, and manuscript preparation. MG participated in protocol development, data analysis, literature searching, data extraction, and manuscript preparation. HA participated in protocol development, data analysis, and manuscript preparation. ZA participated in protocol development, literature searching, data extraction, and manuscript preparation. All authors have read and approved the final manuscript.

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INTRODUCTION

Medicine-related problems (MRPs) emerged as a concept in the early 1990s as “the detrimental experience regarding drug therapy and which potentially or actually causes an interference with their desired outcome.”[1] MRPs affect both healthcare and economic situations and contribute to a tremendous increase in morbidity, mortality and healthcare expenditure worldwide.[2-4]

MRPs represent a major issue, particularly in chronic conditions such as cardiovascular diseases (CVDs) and diabetes mellitus (DM).[5] The aforementioned conditions are expected to be the major source of morbidity by 2020.[6 7] In addition, these two conditions are interrelated; it has been documented that DM is a key factor that leads to CVDs as people with diabetes are three to four times more likely to have a CVD.[8 9] Consequently, the combination of CVDs and DM, which can result in multiple complications, represents a major concern for healthcare professionals.

More specifically, patients with CVDs and/or DM are more susceptible to MRPs due to long-term use of medicines and the inevitable polypharmacy.[7 10 11] However, many additional factors that contribute to MRPs in patients with CVDs and/or DM have gone underreported.

Studies in the literature, which investigated risk factors contributing to MRPs in patients with CVDs/DM, were mainly quantitative; only few studies were qualitative. Quantitative studies investigating risk factors contributing to MRPs involved either direct observations or were made retrospectively using data extracted from medical records.[12-15] However, most of the studies reported old age and polypharmacy extensively; few studies reported gender, depression, education, cohabitation, and immobilisations.[16] Nonetheless, qualitative studies investigating contributory risk factors leading to MRPs have been rather limited.

Therefore, this review aims to explore and evaluate contributory factors leading to MRPs among adult patients with CVDs and/or DM from their perspectives.

METHODS

We searched the PubMed, Embase, ISI Web of Knowledge, PsycInfo, International Pharmaceutical Abstract, and PsycExtra databases for entries between January 1990 and March 2014. The search strategy evaluated articles obtained predominantly through databases. Additional articles were retrieved through the bibliography lists of published reviews, where applicable.

The search strategy combined established methodological terms for qualitative research (qualitative research, qualitative studies, nursing methodological research, narrative analysis) and the following terms: Medicine (drug/medication) related problems, medicine (drug/medication) use, diabetes mellitus, cardiovascular diseases, patients' perspectives, patients' beliefs, patients' attitudes, patients' views, patients' opinions, patients' knowledge, patients' behaviours, and contributory factors. In addition, Medical Subject Headings (MeSH) relating to MRPs, CVDs/DM, risk factors, and patients' perspectives were explored.

Study selection

We included studies that utilised phone interviews, face-to-face interviews, focus groups, and open-ended questionnaires that were published in peer-reviewed journals.

The inclusion criteria involved studies focusing on the patients' perspectives on the use of medicines and MRPs and were conducted on adult patients with CVDs and/or DM.

On the other hand, the exclusion criteria flagged studies that were quantitative in nature, studies with closed-ended questionnaires, and studies focusing on conditions other than CVD/DM.

Initially, one reviewer (AA) conducted the search and did screening for the titles. At this stage, studies with irrelevant titles were excluded. Then, the

abstracts of the remaining studies were evaluated independently for inclusion by two reviewers (MG and ZA). Any disagreements that were encountered were resolved via a discussion. No language limits were applied. However, the search results only generated English studies. Figure 1 demonstrate the details of the data extraction process.

Data synthesis and analysis

In order to extract data from articles, we adopted the systematic review approach for qualitative research by Dixon-Woods et al.[17] This allowed the emergence of broad concepts. Then, data was synthesised by utilising the thematic analysis approach,[18] which enables extraction of concepts and hypotheses from multiple qualitative studies.

Based on the extracted results, we developed textual summaries and tables. From the textual summaries and tables, we identified emerging themes which described the meaning and content of the included studies. We then inspected similarities and differences across the textual summaries in order to avoid contradiction and reduce the developed number of themes. Subsequently, we agreed on the final list of themes through discussion and consensus.

Finally, we coded the full list of papers for the presence or absence of themes. The codes were tabulated afterwards by country in order to inspect similarities and differences across countries.

Since our approach was qualitative, the presence of a theme in more than one paper did not indicate its importance in the studied population.[19] However, a theme appearing in more than one paper did denote to a degree its validity. Thus, the number of studies within a specific theme was reported in this review.

Quality of synthesis assessment

The quality of papers was assessed using the checklist developed by Dixon-Woods et al. (2004).[17] This assessment was based mainly on clarity,

consideration of ethical issues, and transferability of the sample, data, and analysis across different settings. Furthermore, the critical appraisal skills programme criteria[20] were used to rank the papers based on 10 questions that fulfilled the clarity, methods, and results of the studies. Consequently, studies were grouped into low (one star: 0 to 3 points), medium (two stars: 4 to 7 points), and high quality (three stars: 8 to 10 points). Low-quality studies were not excluded, but caution was taken when interpreting their results.

RESULTS

A total of 21 studies (including 836 participants) from 12 countries met the inclusion criteria (Table 1) and were conducted in the following countries: Australia,[21] Brazil,[22] Cameroon,[23] Canada,[24] Croatia,[25] Ireland,[26] Malaysia,[27 28] South Africa,[29] Spain,[30] Taiwan,[31] the United Kingdom,[7 32-37] and the United States.[38-40] The majority of the studies investigated type 2 DM (*n* = 15); fewer studies investigated CVDs. Thus, only two studies investigated hypertension (HTN), one investigated heart failure, and one studied CVDs in general. The remaining two studies investigated DM/HTN and DM/HTN/stroke, respectively. Eight studies used focus groups, 12 used interviews, and one study used a mixture of these methods. The review covered areas related to patients, conditions, and medicines.

Table 1l **Characteristics of the included studies**

Study	Country	Study type	Patients' diagnosis	Method of analysis	Study population	Study settings	Study aims	Study quality
Al-Qazaz et al 2011[27]	Malaysia	Semi-structured interviews	Type 2 DM	Content analysis	12 diabetic patients, with at least one year of diabetes and a prescription of oral hypoglycemic	Universiti Sains Malaysia (USM) Health Clinic	To explore diabetic patients' experience and knowledge about diabetes and its medication and to understand the factors contributing to medication adherence in	**

							Malaysian population.	
Brown et al 2007[32]	UK	One-to-one interviews	Type 2 DM	Thematic analysis	17 African–Caribbean diabetes patients with age above 18 years; 13 first generation immigrants and four second generation immigrants	Inner city Nottingham	To gain an understanding of how health beliefs influence the way African–Caribbean people with diabetes manage their illness.	***
Choudhury et al 2009[33]	UK	Structured interview	Type 2 DM	Thematic analysis	14 invited individuals, Bangladeshi (four males and 10 females), in the age range of 26 to 67 years, with type 2 DM (had it since six months - 27 years) and were recruited either in Swansea or Birmingham.	Participants from local communities in Swansea and Birmingham were invited for the interview	To examine the understanding and beliefs of people with diabetes from the Bangladeshi community living in the UK.	**

					Interviews were made in either English or in Sylheti as the researcher was bilingual			
Coronado et al 2004[38]	USA	Focus groups	Type 2 DM	Matrix analysis by Morgan and Krueger	42 Individuals (14 men and 28 women) in six focus groups, who had diabetes, had a family history of diabetes, or knew someone who had diabetes.	Fred Hutchinson Cancer Research Center's project office in Sunnyside, Yakima village and Skagit Valley Community College and at the Catholic church in Burlington	To investigate the perceptions about the causes of and treatments for type 2 DM	*
Cottrell et al 2013[21]	Australia	Structured interview	HF	Repertory grid technique	92 patients (older than 18 years) with heart failure	Heart Failure Service outpatient clinic, Royal Brisbane and Women's Hospital in Brisbane, Australia	To elicit individuals' beliefs about their heart failure treatment and to investigate whether generated constructs were different between adherent and nonadherent patients.	*

Gascon et al 2004[30]	Spain	Focus groups with open ended questions	HTN	Thematic analysis	Seven focus groups of 44 patients (24 men and 20 women), diagnosed with hypertension, between the ages of 18 and 80 years, being treated with antihypertensives for 3 months, being non-compliant and having sufficiently good physical and mental health to participate.	Two primary healthcare centres	To identify factors related to non-compliance with the treatment of patients with hypertension.	**
Gordon et al 2007[7]	UK	Face-to-face interviews	CVD	Thematic analysis	98 patients (41 males and 57 females) in the age range of 32 – 89 years.	Home interviews of patients recruited from five general surgeries and pharmacy interviews at four community pharmacies	To examine medication-related problems from the perspective of patients with a chronic condition and to identify how they may be supported in managing their medication.	**

Grace et al 2008[34]	UK	Focus groups	Type 2 DM	Thematic analysis	17 focus groups of adult diabetic patients	Tower Hamlets, a socioeconomically deprived London borough	To understand lay beliefs and attitudes, religious teachings, and professional perceptions in relation to diabetes prevention in the Bangladeshi community.	***
Heymann et al 2012[35]	UK	Focus groups	DM and HTN	Thematic analysis	10 focus groups of 86 (42 males and 44 females) patients with hypertension in three age ranges: 41-50, 51-60, 61-70 years (six groups); and patients with hypertension and DM in the age ranges: 51-60, 61-70 years (a total of four groups).	UK	To explore beliefs and perceptions regarding hypertension and gain an understanding of barriers to treatment among patients with and without DM.	***
Hu et al 2013[39]	USA	Focus groups	Type 2 DM	Content analysis	Five focus groups of 73 Hispanic immigrants; 18	free health clinic in central North Carolina	To explore perceived barriers among Hispanic	**

					years or older		immigrants with diabetes and their family members.	
Jolles et al 2013[24]	Canada	Semi-structured interviews	HTN	Thematic analysis	26 Patients, in the age range of 26 - 85 years and 62% females, able to speak, read and write English; diagnosed with hypertension by a healthcare provider, and currently taking an antihypertensive medication.	Two hypertension clinics at the University of Alberta in Edmonton	To understand hypertensive patients' perspectives regarding blood pressure and hypertension treatment.	**
Kiawi et al 2006[23]	Cameroon	In-depth interviews, semi-structured	Type 2 DM, HTN and stroke	Content analysis	15 interviews of 62 patients (27 women and five men), selection criteria included they had lived at least six months in the community, were nominated by other	Four urban health districts, one from each of the main ecological areas of Cameroon.	To investigate of lay knowledge, attitudes, and behaviors relating to diabetes and its main risk factors of urban Cameroonians.	***

					community members, and were age above 15 years.			
Lai et al 2005[31]	Taiwan	In-depth interviews	Type 2 DM	Thematic analysis	22 diabetic patients (12 males and 10 females), in the age range of 44 - 80 years, with a duration of illness more than one year.	Rural Taiwan community	To investigate Chinese diabetic patients' perceptions about their illness and treatment strategies to facilitate patient-centred, culture-sensitive clinical skills.	**
Lawton et al. 2006[36]	UK	In-depth interviews with open-ended approach	Type 2 DM	Thematic analysis	31 patients (23 Pakistani and eight Indian), aged 18 years and over, and diagnosed with type 2 DM	General Practices in Edinburgh	Patients' perception and practical considerations	**
Mohd Ali and Jussoff 2009[28]	Malaysia	In-depth open-ended interviews	Type 2 DM	Thematic analysis	18 patients (9 males and 9 females) in the age of 15-75 years, and 13 healthcare professionals (nine doctors, three	Endocrinology clinic of a teaching hospital in Kuala Lumpur	To explore the perspectives and experiences of Malay patients in managing type 2 DM as a chronic illness and provide	***

					pharmacists and one diabetic nurse educator).		recommendations that aim to enhance adherence to treatment and help patients to improve their self-management skills.	
Mshunqane et al 2012[29]	South Africa	Patient focus groups (n = 10) and healthcare professional focus groups (n = 8) and in-depth interviews. The questions were open-ended	Type 2 DM	Thematic analysis	Patients who had been diagnosed with type 2 diabetes for at least one year, who were between 30 and 65 years of age	Dr George Mukhari Hospital outpatients' diabetes clinic	To determine the knowledge that patients with type 2 DM have about the management of their disease, as well as the perceptions of the health care team about the services given to patients.	***
Peel et al 2004[37]	UK	In-depth interviews	Type 2 DM	Thematic analysis	40 newly diagnosed TYPE 2 DIABETES MELLITUS patients in the age range of 21 – 77 years	Across the Lothian region in Scotland	To explore the patients' emotional reactions about their type 2 DM diagnosis, and their views about information provision at the time of	**

							diagnosis.	
Peres et al 2007[22]	Brazil	Interviews	Type 2 DM	Content analysis	24 diabetic females, age between 25 and 76 years old, literate, with eight years of schooling, from Ribeirão Preto, who perform household activities.	Nursing Education Center for Adults and Elderly - CEEAI, University of São Paulo	Identify the difficulties patients encounter when controlling diabetes	**
Rustveld et al 2009[40]	USA	Focus groups	Type 2 DM	Thematic analysis	34 patients in six focus groups (three in English and three in Spanish), older than 18 years and with type 2 DM	Three Harris County Hospital District (HCHD) community health centers in Houston, Texas	To elicit attitudes, attributions, and self-efficacy related to diabetes self-care in both English- and Spanish-speaking Hispanic men.	**
Smith et al 2003[26]	Ireland	Focus groups	Type 2 DM	Thematic analysis	25 patients from three general practices, having DM for at least one year	Patients were invited to participate in the focus group	To explore the views and health beliefs of patients with type 2 DM who had experienced	**

							a new structured diabetes shared care service.	
Vinter-Repalust et al 2004[25]	Croatia	Focus groups	Type 2 DM	Thematic analysis	Seven focus groups of 49 patients (22 males and 27 females), in the age range of 44 - 83 years, ambulatory patients with the diagnosis of type 2 DM, with differences not only in age and sex, but also in the method of treatment of diabetes as well.	Zagreb Medical School	To explore type 2 diabetic patients' attitudes, thoughts, and fears connected with their illness; their expectations of the health care system; and the problems they encountered while adhering to the therapeutic regimen.	***

Narrative synthesis

The main findings of the review showed that contributory factors to MRPs involved three themes: patient-related (socioeconomic and lifestyle), medicine-related, and condition-related factors. Table 2 lists the studies that reported or discussed each theme.

Table 2| **Themes and subthemes emerging from the studies**

Theme/ Sub-theme	Countries, studies
Patient related factors (socioeconomic)	
Belief	UK (Brown et al 2007[32], Grace et al 2008[34], Lawton et al 2006[36])
Family history of condition	UK (Grace et al 2008[34], Lawton et al 2006[36]), USA (Coronado et al 2004[38])
Feeling victimised	South Africa (Mshunqane et al 2012[29]), Croatia (Vinter-Repalust et al 2004[25]), Ireland (Smith et al 2002[26])
Lack of finance	Ireland (Smith et al 2002[26]), South Africa (Mshunqane et al 2012[29]), Croatia (Vinter-Repalust et al 2004[25]), USA (Hu et al 2013[39])
Lack of knowledge	Croatia (Vinter-Repalust et al 2004[25])
Lack of motivation	Croatia (Vinter-Repalust et al 2004[25])
Lack of information/ understanding from doctors	UK (Brown et al 2007[32], Choudhury et al 2009[33])
Low self-esteem	Croatia (Vinter-Repalust et al 2004[25]), USA (Rustveld et al 2009[40])
Patient related factors (life-style)	
Decrease alcohol intake	Canada (Jolles et al 2013[24]),
Decrease caffeine intake	Canada (Jolles et al 2013[24]), South Africa (Mshunqane et al 2012[29])
Diet	Australia (Cotrell et al 2013[21]), Brazil (Peres et al 2007[22]), Canada (Jolles et al 2013[24]), Croatia (Vinter-Repalust et al 2004[25]), Ireland (Smith et al 2002[26]), UK (Brown et al 2007[32], Choudhury et al 2009[33], Grace et al 2008[34], Heymann et al 2012[35], Lawton et al 2006[36]), USA (Coronado et al 2004[38], Hu et al 2013[39], Rustveld et al 2009[40]), South Africa (Mshunqane et al 2012[29]), Taiwan (Lai et al 2005[31])
Lack of exercise	Brazil (Peres et al 2007[22]), Canada (Jolles et al 2013[24]), UK (Brown et al 2007[32], Choudhury et al 2009[33], Grace et al 2008[34], Heymann et al 2012[35], Lawton et al 2006[36]), South Africa (Mshunqane et al 2012[29]), USA (Coronado et al 2004[38], Hu et al 2013[39], Rustveld et al 2009[40])
Lack of time to see doctor	Malaysia (Al-Qazaz et al 2011[27])

Obesity	Brazil (Peres et al 2007[22]), South Africa (Mshunqane et al 2012[29]), UK (Brown et al 2007[32]), USA (Coronado et al 2004[38])
Smoking	Canada (Jolles et al 2013[24]), UK (Heymann et al 2012[35])
Stress	Ireland (Smith et al 2002[26]), UK (Brown et al, 2007[32], Grace et al 2008[34], Heymann et al 2012[35]), USA (Coronado et al 2004[38])
Medicine related factors	
Belief in natural remedies as alternative to medicines	Spain (Gascon et al 2004[30]), UK (Brown et al 2007[32]), USA (Coronado et al 2004[38])
Difficulty/ refusal to take medicine	Brazil (Peres et al 2007[22]), Croatia (Vinter-Repalust et al 2004[25])
Fear of being stuck with medicines all life	Spain (Gascon et al 2004[30]), UK (Gordon et al 2007[7])
Fear of side effects	Ireland (Smith et al 2002[26]), Malaysia (Al-Qazaz et al 2011[27]), UK (Heymann et al 2012[35]), Spain (Gascon et al 2004[30]), Taiwan (Lai et al 2005[31])
Fear of the chemical nature of medicines	Taiwan (Lai et al 2005[31]), UK (Brown et al 2007[32])
Forgetfullness	Brazil (Peres et al 2007[22]), Malaysia (Al-Qazaz et al 2011[27], Mohd Ali and Jusoff 2009[28]), Spain (Gascon et al 2004[30])
Lack of belief in medicines	Australia (Cotrell et al 2013[21])
Lack of knowledge about medicines mechanism of actions	Canada (Jolles et al 2013[24]), Spain (Gascon et al 2004[30]), UK (Gordon et al 2007[7])
Non-adherence	Canada (Jolles et al 2013[24]), Croatia (Vinter-Repalust et al 2004[25]), Taiwan (Lai et al 2005[31]), UK (Gordon et al 2007[7]), USA (Hu et al 2013[39], Rustveld et al 2009[40])
Polypharmacy	Brazil (Peres et al 2007[22])
Condition related factors	
Lack of control over condition	Brazil (Peres et al 2007[22]), Ireland (Smith et al 2002[26])
Lack of knowledge/ understanding of condition	Australia (Cotrell et al 2013[21]), Cameroon (Kiawi et al 2006[23]), Canada (Jolles et al 2013[24]), Malaysia (Al-Qazaz et al 2011[27], Mohd Ali and Jusoff 2009[28]), Spain (Gascon et al 2004[30]), UK (Brown et al 2007[32], Choudhury et al 2009[33], Heymann et al 2012[35], Peele et al 2004[37]), USA (Coronado et al 2004[38])
Fear of condition, its causes and complications	South Africa (Mshunqane et al 2012[29]), UK (Choudhury et al 2009[33], Lawton et al 2006[36]), USA (Coronado et al 2004[38])
Stress from condition	Croatia (Vinter-Repalust et al 2004[25])

Patient-related factors

Socioeconomic-related factors

Patients from six countries reported socioeconomic factors leading to MRPs in both DM and CVDs, including: beliefs, family history of the condition, poor finances, relationships with healthcare professionals (lack of communication and not enough education), inadequate knowledge, and low self-esteem (Table 2).

Beliefs regarding CVDs/DM were reported as a problem in three studies from the United Kingdom.[32 34 36] Patients perceived that DM was given by God and higher powers had control over their condition. One patient reported:

"God has given me this disease of sugar. Whatever happens, it happens because God wants it to happen."

Moreover, a family history of DM was reported in three studies from the United Kingdom[34 36] and the United States.[38]

In addition, poor finances were reported by patients in four studies from Ireland,[26] South Africa,[29] Croatia,[25] and the United States.[39] A lack of necessary finances prevents patients from buying the appropriate food (for their diet)[29] and going to doctors.[26]

Consequently, the financial situation implicated the relationship of the patients with the healthcare professionals. Patients have reported that they were not getting value for their money from healthcare providers.[26] For instance, one patient reported:

" I don't mind paying when I'm sick, but it's very expensive to pay the GP when I'm only getting a check-up with the nurse."

Thus, the patients felt victimised by healthcare professionals[25 26 29] and reported a lack of communication with healthcare professionals.[18] They

described doctors as either too busy to see them[26 27] or not giving enough information about diagnosis and medicines.[32 33 37] Other patients reported having been belittled by doctors.[25] In another study, patients accounted for the lack of communication with healthcare professionals by language barriers.[33]

Subsequently, patients reported a lack of knowledge as a major cause for type 2 DM.[25] This situation led to the lack of motivation about their disease and affected the intake of medicines. Patients asserted the need for further education and training about their condition.

A lack of knowledge resulted in the patients' low-self esteem towards their condition.[25 40] Hence, patients felt unaccepted socially, less comfortable with their colleagues, and less worthy for being diabetic.[25 40]

Lifestyle-related factors

Lifestyle-factors were reported in studies from 11 countries and included: diet (excessive alcohol/caffeine intake), lack of exercise, lack of time to see the doctor, obesity, smoking, and stress.

Diet was a major issue stated in 16 studies (Table 2). In this respect, patients had different behaviours towards their diet. For instance, one group of patients admitted the importance of a healthy diet, yet could not control their diets.[22 31-33] Thus, one participant reported:[22]

"Regarding the diet, I try to fight so as not to eat certain foods, but sometimes I can't help myself."

In this respect, patients appreciated the importance of a healthy diet in controlling DM,[32] yet overestimated its importance to be beyond medicines.[31] They were also aware that a poor diet, including excess alcohol[24] and caffeine intake,[24 29] exacerbated their conditions. Another group of patients misunderstood the concept of a healthy diet. They believed that eating bitter foods could control DM[33] or applied portion sizes to their

diets.[40] In the latter case, patients had difficulty eating smaller portions and/or even changing their favourite foods. On other occasions, patients claimed that diet quality was responsible for DM.[26]

In addition, a lack of exercise was reported in 11 studies from five countries, including Brazil,[22] Canada,[24] the United Kingdom,[32-36] South Africa,[29] and the United States.[38-40] A group of patients overestimated the importance of exercise, claiming that it can cure any existing disease.[31] Patients reported difficulty exercising although they were aware of its importance.[36 40] They justified their work, travel, stress, the weather, and lack of time as the reasons behind their decreased physical exercise.[22 33 34 36 39] A lack of time was more reported in females whose culture expected them to stay indoors after they got married.[36]

Moreover, obesity was described in four studies (Brazil, [22] South Africa,[29] the United Kingdom,[32] and the United States[38]) as a cause of DM. Patients blamed weight gain as the cause for their increase in blood glucose level and diabetic complications.[32 38] Moreover, they attributed insulin as one of the causes of obesity.[32]

Stress emerged in five studies from three countries, including Ireland,[26] the United Kingdom,[32 34 35] and the United States.[38] Stress was identified as a result of changes in culture and climate, poor housing, and migration of ethnic minorities.[38] Patients considered stress to be major cause of their condition.[26 32 34 35 38 40] For instance, one patient reported:

"In 1998, my mother died, and I was unable to go to the funeral. During these months, I developed diabetes."

Patients also perceived that stress control could be an effective way to cure their condition[34] since stress led to a poor diet, smoking, and a lack of exercise.

Medicine-related factors

Medicine-related factors were found in 14 studies from 11 countries and included two types of factors: factors related to the use of medicines and factors related to knowledge about medicines.

Factors related to the use of medicines included medicine non-adherence and polypharmacy. Medicine non-adherence was reported in 10 studies from seven countries, including Brazil,[22] Canada,[24] Croatia,[25] Malaysia,[27 28] Spain,[30] Taiwan,[31] the United Kingdom,[7] and the United States.[39 40] Patients justified non-adherence to medicines as difficulty following the treatment regimen,[25] depression and stress,[40] forgetfulness in taking the medicines,[7 22 27 28 30] a lack of routine in taking the medicines,[24] changes in medicine routines,[24] and the inconvenience of taking insulin. For instance, patients complained that oral hypoglycemics are more convenient to take than insulin:[30]

"I prefer pills more than insulin. You know, swallowing a pill causes no pain. And when I know I will eat more I just take another pill or an extra half."

Furthermore, intentional non-adherence was reported in some studies where patients changed their insulin doses depending on their food regimen.[30] In another scenario, patients stopped taking their medicines when they exercised, acting on the assumption that exercise reduces blood sugar level. Thus, patients changed the dose/regimen of their medicines to fit with their daily activities.[7]

Poylpharmacy was reported among patients with type 2 DM in two studies from Brazil[22] and Canada.[28] Polypharmacy caused inconvenience in taking medicines:[22]

"Medication: this has been my biggest problem in this current phase. I take medication for blood pressure, circulation, diabetes, vitamins. I used to mix up the time of each, but today, thanks to orientation, I'm overcoming this stage."

Factors relating to knowledge about medicines included lack of knowledge about how the medicines worked, fear of the chemical nature of medicines and their side effects, and a lack of belief in medicine.

The lack of knowledge about how medicines worked was described in three studies in Canada,[24] the United Kingdom,[7] and Spain.[30] Patients could not identify most of their medicines apart from the diuretics, which they called "water pills."[24] Moreover, patients could not understand how their medicines worked, even when they read the patient information leaflet.[30]

This lack of knowledge created fear in patients regarding the chemical nature of medicines, the side effects of medicines, and being obliged to take medicines all of their lives.[7 26 27 30-32 35] For instance, patients referred to oral hypoglycemic agents and insulin as "pharmaceutical toxins."[31]

Additionally, patients were afraid of the side effects and complications of medicines. They attributed various side effects to medicines, including hypoglycemia and gastrointestinal disturbances to insulin,[32] kidney failure to oral hypoglycemic agents,[31] and nausea/vomiting to antihypertensive agents.[30] In the last case, a patient reported:

> *"I don't like them (medicines); they have lots of side effects. They can make you sick… I think that I might get worse instead of better."*

These fears promoted a lack of belief in medicines among patients.[21] Subsequently, patients started to believe in natural remedies as an alternative to medicines.[30 32 38] They referred to natural therapies as "*a cure*" that should be used alongside traditional medicines.[38] In another scenario, patients believed that natural therapies were superior to medicines.[32] In this respect, natural therapies reported for curing DM included natural drinks (composed of minerals and water);[38] and plant products (such as aloe vera, arnica, cactus, silk cottonwood tree, tree spinach, and violet water).[32]

Condition-related factors

Condition (clinical)-related factors were reported from 11 countries as a major theme. Factors included a lack of knowledge/understanding of the condition, fear of the condition and its complications, stress from the condition, and a lack of control over the condition.

Lack of knowledge/understanding of the condition (CVDs/DM) emerged as a major theme in 11 studies from seven countries, including Australia,[21] Cameroon,[23] Canada,[24] Malaysia,[27 28] Spain,[30] the United Kingdom,[32 33 35 37] and the United States.[38]

For CVDs, patients expressed a lack of knowledge about their heart failure, hypertension, and stroke. Patients with heart failure did not know enough about their disease symptoms.[21] Moreover, hypertensive patients did not understand the nature of their disease,[28 30] struggled to define their condition,[24] and considered it an underlying risk factor to myocardial infarction rather than a disease.[35] Patients justified their lack of knowledge by citing short consultations with physicians, not obtaining enough information from physicians, and obtaining information from non-medical sources such as television and magazines. For instance, one patient reported:

"Anything I know about blood pressure I've read in books, the doctor tells me absolutely nothing . . . High blood pressure: factors related to compliance with treatment 127. I want him to tell me where high blood pressure comes from."

Similarly, patients with DM lacked knowledge about the disease and misunderstood its causes and complications.[23 25 27 29 32 33 36] Regarding the DM condition and causes, patients' perceptions of DM were influenced by other people's accounts and experiences.[32] Patients viewed the condition as an illness that took away their health and strength[36] and changed their lifestyle.[25] They could not differentiate between DMT1 and type 2 DM,[27] considered high sugar intake to be the cause of DM, and

perceived DM to be sexually and genetically transmitted.[23 33] Moreover, patients believed that diabetes was not dangerous if it did not require insulin.[32] Patients were only aware of the microvascular complications (such as foot disease) of DM.[26] Moreover, they were aware of the disease's signs and symptoms (such as dry mouth, tiredness, dizziness, irritation, blurred vision, micturition, and extreme thirst) only after they encountered them.[28 38]

The lack of knowledge about the condition created fear in the patients' minds of the disease itself[38] and they could not accept the disease easily.[25 33] One patient reported:[38]

"Diabetes is a disease that kills you little by little."

Diseases additionally resulted in stress about the condition that was particularly observed in patients with multiple comorbidities.[36] For instance, diabetic patients who had asthma as a comorbidity could not exercise due to asthma symptoms, such as shortness of breath and swollen feet and joints:

"They tell you to exercise…
but I can't move around a lot because I have
a problem with my leg (arthritis). If I walk a little,
then it swells up."

As a result, patients were not able to control their condition,[22 26] which led to frustration, depression, and anxiety.

DISCUSSION

To our knowledge, this review is the first systematic analysis of the perspectives of adult patients with CVDs/DM on contributory factors leading to MRPs. We explored the patients' knowledge, beliefs, and behaviours towards medicines. The majority of studies evaluated patients with DM; only a few

studies evaluated patients with CVDs. The three themes emerging from this review included: patient- (socioeconomic- and lifestyle-), clinical-, and medicine-related factors.

Patient-related factors

Socioeconomic-related factors

Socioeconomic factors (genetic, cultural behaviour, and financial situations) affected the patients' perceptions of disease and the medicines contributing to MRPs. Patients perceived genetic factors and religious beliefs to be the cause of their DM.[19 21] Patients from both Christian and Muslim backgrounds named God as the cause for their DM. These attitudes were confirmed by other studies that showed that religious values contributed to MRPs.[41 42] In addition, patients felt socially for their DM, which affected their self-esteem. They also blamed their financial situation for contributing to MRPs, since their finances prevented them from having the right diet and being able to afford doctors' visits. The cost of therapy has been perceived as being important, particularly with chronic conditions such as CVDs.[43] Thus, the value that the patients receive from healthcare professionals for their money was unsatisfactory. In fact, doctors' attitudes towards the patients played an important role in the patients being compliant with their regimens.[44] This problem was significant in ethnic minorities where a lack of communication between doctors and patients lead to misunderstanding.[41] Patients confirmed the need for further information and training, emphasising the importance of getting information from healthcare professionals.

Lifestyle-related factors

Lifestyle factors were perceived as a vital component for the control of conditions (CVDs/DM). Patients felt that they needed to adjust their diet, engage in physical activity, and manage their moods to cope with conditions. In relation to diet, they either did not understand the concept of a healthy diet or they had difficulty managing a good diet. Thus, some patients assumed that a healthy diet meant eating less food, eating "bitter food," or eating "natural food." Other patients overestimated the importance of diet as being more crucial than medicines. This overestimation can be attributed to the fact

that the frequency of meals could serve as a reminder to take medicines.[43] In addition, patients were aware of the necessity of physical exercise but blamed the weather, work, lack of time, and stress for their not exercising.[43] Stress was a major factor that patients blamed for not taking medicines on time and eating a poor diet.

Medicine-related factors

Medicines were recognised by patients as a contributing factor to MRPs with regards to lack of knowledge about medicines, lack of belief that medicines are good, difficulty taking medicines on time, and fear of side effects. Patients reported a lack of knowledge about how the medicines worked, called them pharmaceutical toxins, and preferred herbal remedies to medicines. This point was emphasised in another study[41] that stated that the patients' lack of awareness about the use of their medicines led to MRPs. Furthermore, patients reported skipping medicines doses due to forgetfulness or they did not take their medicines on purpose (at the time of exercise). Forgetfulness in terms of taking medicines was observed more often in patients who did not have regular meals.[43] At other times, patients were scared of the side effects and complications of medicines. The medicines' side effects caused physical discomfort for patients, who started to doubt the therapy's effectiveness and skipped their medicines.[43]

Condition-related factors

Condition (clinical) factors reported by the patients revealed a lack of knowledge about the disease and its cause, a lack of control over the disease, and the existence of comorbidities with the disease.[43] Patients were accordingly not fully aware of their condition and perceived it in most cases as being a risk factor leading to other diseases. Moreover, they misidentified the causes and complications of their condition. Once the education about the condition was provided, patients felt scared and frustrated, which induced a lack of control over the disease. Moreover, the existence of comorbidities with the main condition worsened the patients' adherence to treatment and advice.

Strengths and weaknesses of the review

This review proposes a systematic and comprehensive approach to qualitative studies of contributory factors to MRPs of adult patients with CVDs/DM. We adopted a thematic synthesis approach to eligible studies regarding the treatment experiences from patients' perspectives. The studies involved 836 participants. However, despite the diversity of the participants and different contexts in the studies, we were able to develop themes that indicated an overlap among the studies.

We used recognised methods from the literature regarding patients' experiences/perspectives in order to synthesise and develop analytical themes.[18 45] We included the details of each study in relation to the aims, participants, settings, and methods applied. We rated the studies' qualities based on methods from the literature. In this respect, we found that studies with the highest ratings contributed most to the final analytical themes.

One limitation of the review is that it was restricted to the experiences of the patients involved in the studies. Moreover, perspectives and beliefs of non-English speaking patients and those seeking palliative care were not integrated in this review due to lack of studies representing them. Thus, the review was extracted from studies in 12 countries only. Therefore, the generalisability of the findings of this review to patients from different countries (other than the 12 aforementioned countries) may be difficult. However, the analytical themes developed offer a high level of conceptual thinking that can be applied across different contexts.

Implications of the research

This review examined the contribution of patients' perceptions, behaviours, and beliefs in understanding different aspects of underlying risk factors that may lead to MRPs. Syntheses of the qualitative research on such risk factors should complement the findings from quantitative research. Having a systematic review when planning new qualitative research may help to avoid unintentional examination of questions that have already been extensively researched. Finally, the findings of this study on patients' perspectives could

better inform the development of future screening tools and interventions for avoiding MRPs. Additionally, our results may also increase researchers' knowledge of generic issues in this field, even when attempting to target a specific ethnic or cultural group.

Implication towards practices

Patients' perspectives about medicine use and factors affecting their treatment regimen are often different from the medical viewpoint. Worldwide, people with CVD and/or DM widely perceive that their conditions are principally stress-related conditions and fear addiction or dependence on medicines, which leads to non-adherence to required treatments. These misconceptions and fears commonly cause people to reduce or stop treatment. If we are to be successful at minimising and preventing MRPs, incorporating patients' perspectives as well as considering medical records are paramount. An increased understanding between doctors and their patients must play a part in future strategies for reducing MRPs in patients with CVDs and/or DM.

CONCLUSIONS

This thematic synthesis of qualitative studies on patients' perspectives of the potential risk factors of MRPs shows that underlying factors that may lead to MRPs require further in-depth research. Factors influencing patients' success in treatment included patient-related (socioeconomic and lifestyle), medicine-related (fear of medicine, non-adherence, and polypharmacy), and condition-related factors (fear of condition and its complications). In summary, more qualitative research should be conducted on patients with CVDs and/or DM to understand and address issues related to the treatment regimens and subsequently reduce the cost of undesired hospital admissions resulting from MRPs.

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Figure legend

Figure 1 Data extraction and study selection process.

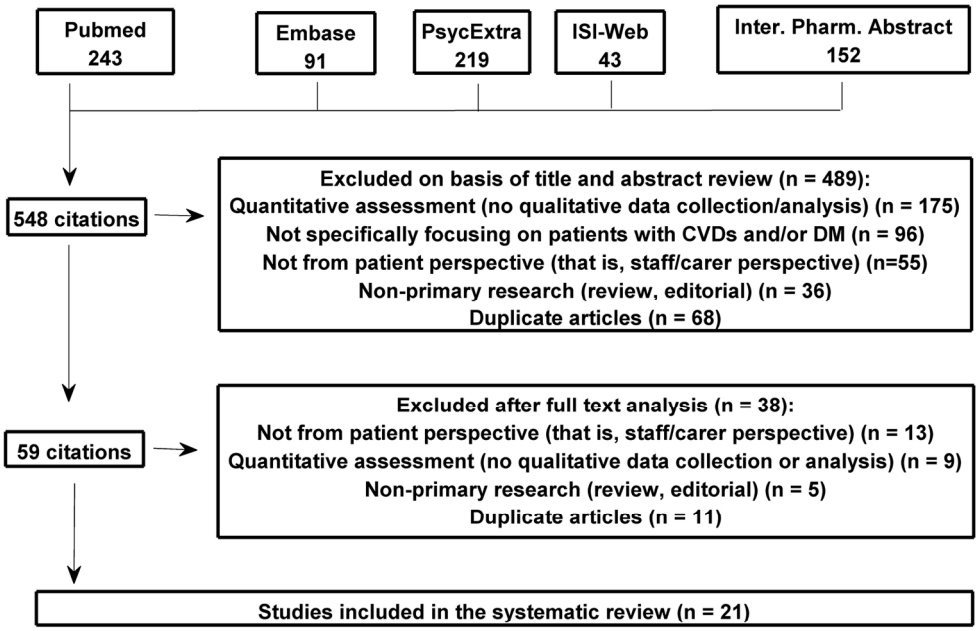

Figure 1
152x114mm (300 x 300 DPI)