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REVIEW

Medication adherence in the older adults with chronic multimorbidity: a systematic review of qualitative studies on patient's experience

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Key summary points

Aim To investigate potential factors associated with medication adherence in the older and chronic population through a PRISMA systematic review of qualitative studies on patients' experience.

Findings The main barriers and facilitators of non-adherence were found to be patients' beliefs about polypharmacy and drug prioritization, patient's experience and capabilities, prescriber-patient relationship, health literacy, treatment characteristics and complexity, family and social support.

Message The present findings, derived from two well-established theoretical frameworks (ABC Taxonomy, Three Factor model) and stemming from the patient's narratives, may provide healthcare professionals with practical information to enhance medication adherence in clinical practice.

Abstract

Purpose Medication non-adherence represents a socially relevant challenge, particularly when interlinked to multiple chronic diseases and polypharmacy. Non-adherence rates affect treatment efficacy and increase health care costs. The aim of the study was to identify factors influencing medication adherence in the older adults through a systematic review of qualitative studies on patients' experience.

Methods Two electronic databases were searched for qualitative studies on medication adherence in chronic diseases (hypertension, heart disease, COPD, asthma) involving people aged 65+. The systematic review was performed according to the PRISMA statement guidelines, employing theoretical frameworks of the ABC Taxonomy of patient adherence and Three Factor model of determinants of behaviour.

Results The initial database search identified 1234 records, of which 39 studies were considered eligible. Most of the studies focused on hypertension and were conducted in English-speaking countries. According to the ABC Taxonomy, Persistence and Implementation were the most often considered phases. Considering the Three Factor model, the most often reported themes were Information and Strategies upon being adherent. Stemming from the review findings and the patients' narratives, a new integrated model was proposed. It reports the patient's decisional flowchart describing barriers and facilitators (personal, social and environmental) to adherence.

Conclusion Medication adherence is a complex and multifaceted process. The implementation of theoretical frameworks along with a patient-centred perspective may provide clinicians with useful suggestions for clinical practice, enhancing the patient's ability to adhere.

Keywords Adherence · Medication · Chronicity · Multimorbidity · Older adults

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Introduction

Due to scientific, medical and technological advancements, the growth and aging of the global population has been a continuous process during the last decades. In 2017, people aged 60 or more reached 962 Mio. In 2050, this rapidly changing scenario will result in a large-scale demographic boost: 2.1 billion of individuals with 60 or more years compared to 2.0 billion of persons at ages 10–24, with a faster growth of the number of older people in developing countries [1]. This global aging process puts new challenges to be tackled worldwide by healthcare systems.

On this regard, multimorbidity is a scenario which tends to become more prevalent with age and requires tailored and multi-target treatments [2]. Less than the 10% of the older adults are not prescribed medications, whereas the 50% need to take 5 or more drugs, and the 10%—10 or more drugs [3, 4]. When it comes to medications, proper adherence to medical plans represents a fundamental prerequisite for assuring safety and effectiveness [5, 6]. Considering the negative consequences in terms of economic burden and quality of life worsening [7, 8], non-adherence to medical prescriptions is, indeed, socially relevant. Rates of medication adherence among the older adults vary according to the kind of treatment and to geographical locations but are often far from being optimal [9–11].

Given the recognized complexity of the patients' behaviour when it comes to execute the treatment, different conceptualizations of the adherence process have been proposed to efficaciously address all its facets. On this regard, the ABC Taxonomy defines adherence to medications as a stadial process constituted by three phases: (1) Initiation: focusing on the binary action of taking the first dose of a prescribed medication; (2) Implementation: dealing with drug assumption and, specifically, with the extent to which the patient's medication-taking matches the prescribed dosing regimen; (3) Discontinuation/persistence: underlying the interruption of the prescribed drug assumption [12, 13]. Another helpful theorization to explain variation in patient adherence is the Three-factor model, also called Information–Motivation–Strategy (IMS) Model [14], which pays attention to three dimensions useful when intervening on adherence: (1) Information: intended as the "know how" necessary to adhere and gained by patient-prescriber relation; (2) Motivation: related to support the behaviour to commit to the treatment encompassing all cognitive, social, cultural, normative and contextual factors; (3) Strategy: including workable plans for the disease management in order to overcome practical barriers.

Furthermore, factors influencing adherence to medication are proved to be diverse and interrelated, ranging from social aspects (e.g. patient-prescriber relations, social support or stigma) to treatment characteristics (e.g. complexity of dosage, multiple prescriptions) and patients' beliefs and characteristics (e.g. concerns about medications, cognitive impairment) [5, 15]. Up to now, adherence models may not be structured enough to address the complex and evolving needs which characterize the older population. A patient-centred and holistic approach is needed to face the ever-growing healthcare challenges of the future [16]. Qualitative research on factors related to adherence may be helpful to this scope.

The aim of our systematic review was to identify barriers and facilitators of medication adherence perceived by the older adults by analysing qualitative studies on this topic. The ABC Taxonomy and the Three Factor model were applied as theoretical frameworks to guide the content analysis.

Methods

A systematic review of the qualitative studies on older patient's perspective on medication adherence was performed, according to the latest updates of the PRISMA (preferred reporting items for systematic reviews and meta-analyses) statements and guidelines [17]. Scopus and Pubmed were used for the search. The following search string was adopted: (adherence OR compliance) AND qualitative AND chronic disease (this last one eventually and alternatively replaced with the words hypertension, heart disease, COPD, asthma).

The systematic review was registered on the PROSPERO database (PROSPERO 2017 CRD42017068424).

Inclusion and exclusion criteria

Qualitative research articles on medication adherence in chronic diseases were considered eligible. Inclusion criteria were: articles published in peer-reviewed journals from 2000 to October 2017, English language, focused on patients' perspective, patients aged 65 or more. Exclusion criteria were: quantitative studies, behavioural adherence, healthcare professionals' perspective, medication adherence only marginally reported, studies with less than 10 patients, patients aged < 65 or > 18 years without any other information on age composition. Reviews, book chapters, editorials and grey literature were not considered eligible, as well as studies based only or extensively on telephone interviews.

Articles descriptive analysis

The identified articles were organized into a synoptic table and main descriptive areas were selected: geographic region, nation and corresponding Human Development Index (HDI) value [18]; methodology; disease/s; sample ethnicity; sample

size; mean age or, where not precisely specified, age range of studied subjects.

Articles content analysis within the framework of the ABC Taxonomy and the Three Factor model

Regarding the ABC Taxonomy [12, 13] and the Three Factor model [14], the presence of each model sub-concept (Initiation, Implementation, Persistence/Discontinuation for the ABC Taxonomy; Information, Motivation, Strategy for the Three Factor model) both in the interviewers' questions and in the answers given by the patients, was identified through a qualitative methodology (MM and ST, final supervision by AG).

The information retrieved was organized as follows: interviewer/inquiry themes (representing the researcher theoretical approach while asking upon adherence to medication) and patient/response themes (representing patients' replies, considerations or remarks). The word "inquiry" is referred to structured, semi-structured, qualitative interviews, focus groups topics or other methodologies used to collect qualitative data. The interviewer/inquiry themes were thus retraced by analysing lists of questions asked (when present), brief interview summaries or focus groups topics. With the word "response" we referred to the patient's answers to such inquiries (transcribed verbatim and cited or simply reported and synthesized through bullet points).

The reviewers (MM, ST), marked whether the meaningful concept considered was present or not, and if so, whether it was enclosed in the interviewer's questions, in the patient's answers or in both of the two. Being a qualitative approach, ad-hoc guidelines were developed for each model sub-concept, to strengthen the accuracy of the process.

Concerning the ABC Taxonomy, ad hoc guidelines were detailed as follows. Initiation: connected to beliefs and attitudes belonging to the first commitment to therapy, such as the start of drug taking or refusal behaviours towards a specific class of treatments (medicine prioritisation). Interviewers' questions or patients' answers following the rationale: "when you started to take drugs…", or "I decided not to take those meds because", retracing the "timing" aspect since the start, or showing avoidance towards the physician prescription, were considered matching the Initiation phase. Implementation: interviewers or patients asking or talking about schedules, posology, memory, barriers, facilitators, ICT technologies and every aspect related to practical solutions (e.g. "I usually leave the pill box right on the table, so I can see it"/"How do you usually take your meds?"), were considered satisfactory criteria to account the presence of the Implementation phase. Persistence/Discontinuation: the ABC Taxonomy considers these two sub-concepts jointly, hence the attribution process proceeded accordingly: every question/answer regarding interrupting behaviours (e.g. I stopped taking my meds because…/Why did you discontinue your treatment?) or, on the contrary, related to the willingness to keep following prescription (e.g. "I kept on taking my heart pills, I was feeling so much better") were considered matching the Persistence/discontinuation dimension.

Similarly, the Three Factor model sub-contents were retraced thusly: Information: inquiries or answers focused on the importance of awareness and disease-knowledge, such as side effects, future implications, risk factors, non-adherence consequences, prevention and the mediator role of the physician in providing advice while facing the new treatment (i.e. information plus relation) were considered (e.g. "Have you received adequate information regarding your treatment?"/"Are you aware of the risks of non-treated hypertension?/"I felt like the GP was too busy to answer my questions"). Motivation: interviewers or patients asking/talking about personal attitudes towards personal performances of health promotion behaviours, as well as social motivation, social support for enactment for health promotion behaviours, was considered (e.g. Why do you take your medicine as prescribed?/I felt like I had to, because I needed to take care of myself"). Strategy: the focus of the analysis was oriented on the medication administration, ranging from the agenda management (e.g. "how do you manage time and schedules of your drugs?") to the operational instruments and activities (i.e. pill box, ICTs, mobile application e.g. "I usually set an alarm on my smartphone to remember it").

Finally, the main themes (main areas of intervention) were identified.

Discussions regarding additional issues and emerging themes were reviewed by all the authors as the analysis progressed, with a continuous feedback and feedforward procedure until a stabilized procedure was coded. After stabilizing it, all the articles were read following the agreed matrix of data synthesis and every reviewer proceeded independently in putting the check symbols in the spreadsheet. Two reviewers (MM, ST) performed the ABC Taxonomy and Three Factor themes attribution, then a revision of the first attribution was performed in pair, accounting the degree of agreement ad highlighting the most critical papers. The same procedure was accomplished with the third reviewer attribution (AG), to consolidate the matching attribution and discuss the most critical outputs. For each sub-concept, in case of uncertainty or disagreement, a triangulation between the three reviewers was performed. Then a final supervision was finalized by PK, MK-M, LM and EC.

Results

1234 papers were identified from the search string performed; after duplicates removal, title, abstract and text reading, 39 research articles were considered eligible [20, 20–57] (Table 1, Fig. 1). Of a note was the high heterogeneity of methodologies used for data collection and analysis. In particular, the format of reporting varied widely from paper to paper: some studies reported bullet points with just the main topics explored, whereas others reported the entire interview protocol. Similar observations are addressed to variables such as age composition and sample ethnicity reporting, which varied widely from study to study (Table 2).

It is worth noticing that the majority of analysed studies were conducted in the English-speaking countries (Table 3). Furthermore, an interesting portion of the qualitative studies focused on specific sub-populations (veterans, African American citizens, frail populations, developing countries, etc.) [20, 23, 32, 34, 37, 44–46, 54, 57].

With regard to the methodology adopted, semi-structured interviews were the most preferred to collect patients' narratives (58.9%), followed by a combination between a semi-structured interview and focus groups (15.4%), focus group exclusively (12.8%), a combination between structured interviews and focus groups (7.7%) and, finally, by structured interviews alone (2.6%). One single paper reported a "qualitative" interview which was not further defined.

With regard to the diseases, articles dealing with two or more conditions were broken down into separate conditions, in order to analyse the single frequency of appearance. As a result, the cumulative frequency listed in Table 2 exceeds the total number of articles included in the review. To the contrary, articles regarding "chronic morbidities" (without specifying which ones) or articles including several and heterogenous medical conditions (more than 10), were collected in the category "multiple chronic conditions" (Table 2). Overall, hypertension was the most often studied condition, being the focus of 48.7% of the analysed papers.

Similar exercise performed for ethnicity, and the related frequency of occurrence was calculated (Table 2). The most often included ethnicities were the African American/Black (20.5%) and the Caucasian (12.8%) ones. Interestingly, 46.1% of the studies did not specify the ethnicity in the study description. Regarding the sample size, most of the studies involved a small number of participants, with only the 10.2% dealing with more than 50 patients.

From the patient's narratives different barriers and facilitators of non-adherence emerged, which were grouped into the following areas: [A] Patient's beliefs and concerns about treatment; [B] Patients' beliefs about polypharmacy and drug prioritization; [C] Patient's experience and capabilities; [D] Prescriber-patient relationship; [E] Health literacy; [F] Treatment characteristics and complexity; [G] Family and social support.

Content analysis findings

Results from the content analysis are displayed in Table 4. Concerning the ABC Taxonomy, the most neglected part was the Initiation phase, especially during the interviewer/inquiry phase (17.9%). Differently, during the interview/discussion section, patients referred to the Initiation phase and autonomously discussed about it (38.5%), even without an explicit request from the interviewer. Following a similar pattern, Implementation and Persistence/Discontinuation phases, despite being much more often taken into consideration if compared with Initiation (even 100% reached in the results/response phase), were much less often reported in the interview/inquiry section. Interestingly, Implementation and Persistence/Discontinuation phases shared the same percentage of occurrence in both interviewer/inquiry and patient/response sections.

Concerning the Three Factor model, Information received by the patients (referred to patients' knowledge about disease and medications), their relationship with the physician and the practical Strategies adopted to be adherent, were frequently reported, both in the interviewer/inquiry and in the patient/response sections (Table 4). To the contrary, Motivation was much less often covered topic (12.8% and 46.1% of interview/inquiry and patient/response phases, respectively).

Discussion

The qualitative studies upon medication adherence resulted to be mostly focused on occidental cultures and societies. Indeed, previous literature showed possible differences in medication adherence levels across different geographic areas [58], which are related to different incidence rates of morbidity in different populations. Thus, this aspect could generate some concerns regarding studies' comparison, preventing the possibility to generalize the results. Aware of the complexity and of the in-between differences of the potential studies' participants, it is highly suggestable to deepen the cultural aspects that may interfere with the ability to be adherent.

As for the study designs, the combination between semi-structured interviews and focus group was by far the most preferred strategy to collect patients' feedbacks in analyzed publications. Such an approach could be due to the necessity to conceive an interview protocol that can be either structured in order to cover specific topics and to collect analytical information, as well as flexible enough to allow patients to freely explore their narratives.

The high prevalence of studies focused on hypertension is probably due to the high worldwide prevalence of this

Table 1 Research articles considered eligible for the systematic review

Reference number	Geographic region	Nation of the study (HDI, ranking)	Methodology	Disease/s	Sample ethnicity	Sample size	Mean age ± SD (age range)
[33]	North America	USA (0.9, 13)	Semi-structured interview	Chronic kidney disease	White, African-American, hispanic, Asian	20	72 (55–84)
[53]	Asia	India (0.6, 130)	Semi-structured interview	Multiple chronic conditions	Asian	19	52.6 (25–78)
[48]	Southern Europe	Spain (0.9, 26)	Semi-structured interview, focus group	Multiple chronic conditions	n.d	36	65 (39–90)
[49]	Western Europe	Germany (0.9, 5)	Semi-structured interview	Rheumatoid arthritis	n.d	18	61.4 ± 12.2
[50]	Northern Europe	United Kingdom (0.9, 14)	Semi-structured interview	Parkinson disease	n.d	15	70.9 ± 8.7
[47]	South America	Brazil (0.8, 79)	Qualitative interview	Hypertension	n.d	13	(25–83)
[38]	Southern Europe	Portugal (0.8, 41)	Focus group	Multiple chronic conditions	n.d	18	≥ 65
[37]	North America	USA (0.9, 13)	Focus group	Multiple chronic conditions	White, black	50	(40–60 or older)
[35]	North America	USA (0.9, 13)	Semi-structured interview	Multiple chronic conditions	White, black, American Indian	30	30–83
[31]	Oceania	Australia (0.9, 3)	Structured interview	Diabetic kidney disease, multiple chronic conditions	n.d	23	59 ± 15.5
[30]	Oceania	Australia (0.9, 3)	Structured interview, focus group	Diabetic kidney disease	n.d	23	59.3 ± 15.5
[29]	Asia	China (0.7, 86)	Semi-structured interview	Chronic cardiovascular disease	n.d	19	71.16 ± 6.81 (65–85)
[27]	North America	USA (0.9, 13)	Semi-structured interview	Multiple chronic conditions	White, African–American	20	76 (67–90)
[28]	Northern Europe	United Kingdom (0.9, 14)	Semi-structured interview	Cardiovascular Disease	White, Black	98	67 (32–89)
[52]	North America	USA (0.9, 13)	Semi-structured interview, Focus group	Hypertension	African–American	20	54.7 ± 13.1 (25–71)
[51]	Northern Europe	United Kingdom (0.9, 14)	Semi-structured interview	Hypertension and/or diabetes mellitus	n.d	19	62.3 (44–80)
[21]	North America	USA (0.9, 13)	Semi-structured interview	Gout (+ other comorbidities not considered in the study)	African–American	35	65.1 ± 7.9
[46]	Asia	Indonesia (0.7, 116)	Semi-structured interview	Hypertension	Asian	14	69.8 ± 9.2
[45]	South America	Colombia (0.7, 90)	Semi-structured interview, Focus group	Hypertension	Hispanic	26	60 (35–82)
[44]	Africa	Nigeria (0.5, 157)	Semi-structured interview	Hypertension	Black	40	(30–90)
[42]	North America	USA (0.9, 13)	Structured interview, Focus group	Hypertension	Black, white	25	(68–82)
[43]	North America	USA (0.9, 13)	Semi-structured interview	Hypertension	n.d	48	60 ± 10.31
[39]	North America	USA (0.9, 13)	Focus group	Hypertension or Hypertension with Diabetes	n.d	86	(41–70)
[55]	North America	USA (0.9, 13)	Semi-structured interview	Hypertension	African–American	21	73.7 (57–86)

Table 1 (continued)

Reference number	Geographic region	Nation of the study (HDI, ranking)	Methodology	Disease/s	Sample ethnicity	Sample size	Mean age ± SD (age range)
[34]	North America	USA (0.9, 13)	Semi-structured interview, Focus group	Hypertension	African–American	40	57.2 ± 12.7 (21–82)
[32]	Africa	Congo (0.6, 137)	Focus group	Hypertension	Black	20	(34–74)
[24]	Northern Europe	United Kingdom (0.9, 14)	Focus group	Hypertension or Hypercholesterolaemia	n.d	92	(45–72)
[20]	North America	USA (0.9, 13)	Semi-structured interview	Hypertension	African–American	106	55.7 ± 12.8
[20]	Northern Europe	Sweden (0.9, 7)	Semi-structured interview	Hypertension	White	33	58 (35–83)
[41]	Oceania	New Zealand (0.9, 16)	Semi-structured interview	Ischaemic heart disease	New Zealand European, Maori, Asian, Others	49	(41–80; majority 61–80)
[25]	North America	Canada (0.9, 12)	Semi-structured interview	Osteoarthritis	n.d	19	67–92
[22]	Northern Europe	United Kingdom (0.9, 14)	Semi-structured interview	Coronary heart disease, hypercholesterolaemia	n.d	33	24–80
[23]	North America	USA (0.9, 13)	Semi-structured interview, Focus group	Asthma	African–American	15	33–82
[40]	Western Europe	Germany (0.9, 5)	Semi-structured interview	Rheumatoid Arthritis	n.d	22	40–70
[26]	Northern Europe	United Kingdom (0.9, 14)	Semi-structured interview	Chronic heart failure	n.d	50	67.1 (41–80)
[56]	Northern Europe	United Kingdom (0.9, 14)	Semi-structured interview	Hypertension	n.d	38	(< 50 e > 80)
[36]	Southern Europe	Greece (0.9,31)	Semi-structured interview, Focus group	Hypertension	n.d	43	Group A: 63.7 (47–79), Group B: 44.6 (40–50)
[57]	Asia	Indonesia (0.7, 116)	Semi-structured interview	Hypertension	Asian	30	65 (50–80)
[54]	Africa	Eritrea (0.4, 179)	Structured interview, Focus group	Hypertension	African	48	interviews: 61 ± 7, focus group: 53 ± 4

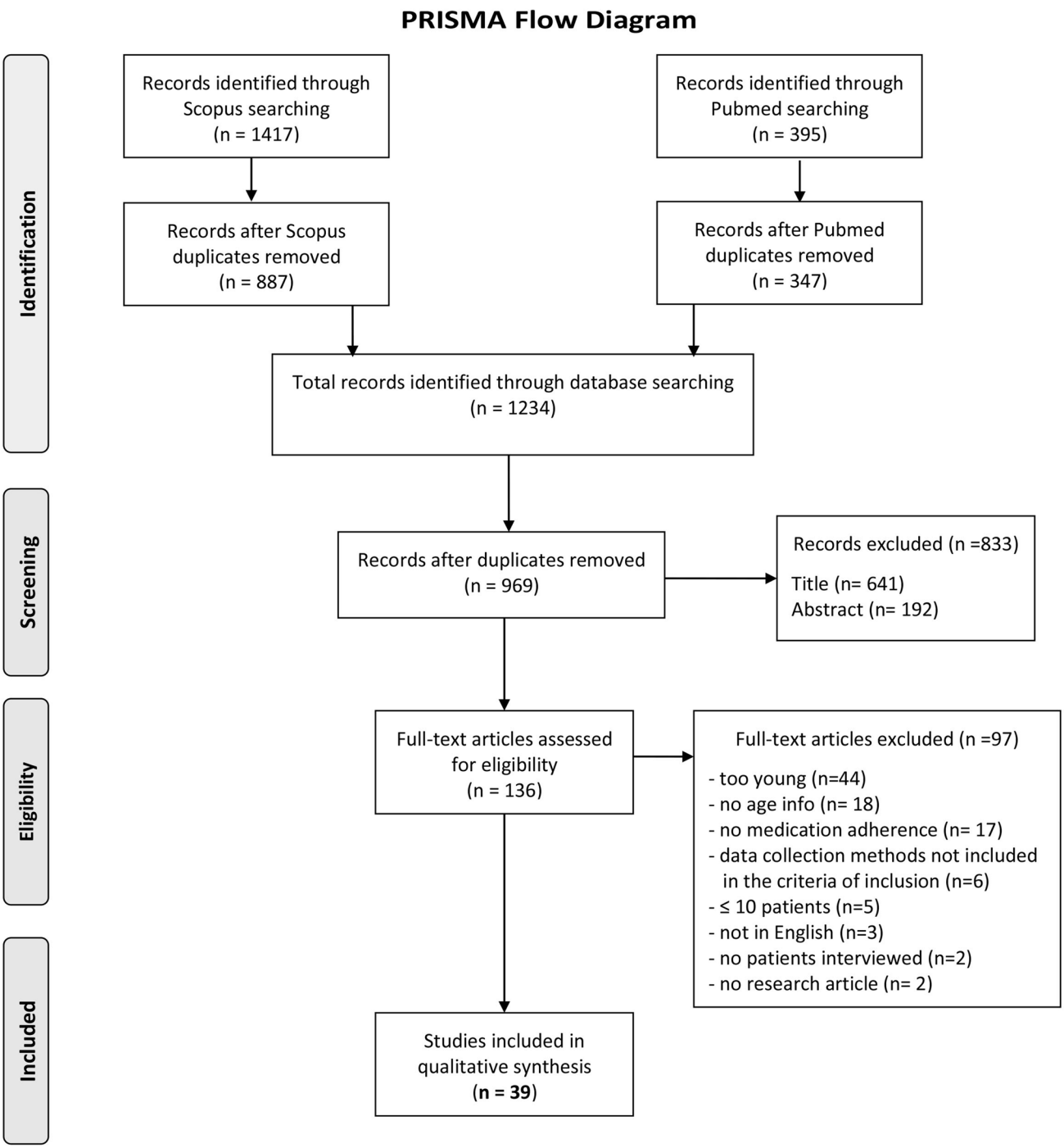

Fig. 1 PRISMA flow diagram of the systematic review

condition [59, 60], as well as to cardiovascular risks and high mortality rates connected to its undertreatment [61, 62]. Nevertheless—and most critically—hypertension is an asymptomatic disease. The non-perception of physical symptoms frequently leads to non-treatment, medication refusal or to complex adherence behavioral pattern (drug holidays, interruptions, etc.) [63–65]. Furthermore, there is an evidence that adherence level increases with higher perception of life-threatening risk [66].

Moreover, ethnicity is a relevant factor known to be related to lower adherence rates or to higher exposure to chronic diseases [66]. For instance, the African American population has shown to be more exposed to hypertension if compared with others [34, 67, 68]. Despite the lack of clear indexes of

Table 2 Frequency and percentage rates of the categories considered ($n = 39$)

Study design	*n* of papers (%)	Disease/s°	*n* of papers (%)	Sample ethnicity^	*n* of papers (%)	Sample size*	*n* of papers (%)
Semi-structured interview	23 (58.9)	Hypertension	19 (48.7)	African; African–American; Black	8 (20.5)	13–19 participants	10 (25.6)
Semi-structured interview; Focus group	6 (15.4)	Multiple chronic conditions	6 (15.4)	Caucasian	5 (12.8)	20–38 participants	17 (43.6)
Focus group	5 (12.8)	Cardiovascular disease	5 (12.8)	Asian	3 (7.7)	40–50 participants	8 (20.5)
Structured interview; Focus group	3 (7.7)	Diabetes mellitus	2 (5.1)	American–Indian	1 (2.6)	86–106 participants	4 (10.2)
Structured interview	1 (2.6)	Hypercholesterolaemia	2 (5.1)	Hispanic	1 (2.6)		
Qualitative interview	1 (2.6)	Rheumatoid arthritis	2 (5.1)	New Zealand European	1 (2.6)		
		Asthma	1 (2.6)	Maori	1 (2.6)		
		Chronic Kidney Disease	1 (2.6)	n.d.^^	18 (46.1)		
		Diabetic Kidney Disease	1 (2.6)				
		Gout	1 (2.6)				
		Osteoarthritis	1 (2.6)				
		Parkinson	1 (2.6)				
		Single condition	26 (66.7)				
		Two or more conditions	13 (33.3)				

°^Percentage rates for Disease/s and Sample Ethnicity categories obtained by subdividing co-present categories, hence reaching over the 100% of cumulative frequency. For further details see the synoptic table

*Total number of participants: 1374

^^n.d., not determined. Studies conducted in: USA ($n = 8$), United Kingdom ($n = 3$), Sweden ($n = 1$), Nigeria ($n = 1$), New Zealand ($n = 1$), Indonesia ($n = 1$), Congo ($n = 1$), Colombia ($n = 1$), Canada ($n = 1$)

adherence across different cultures, previous researches generally showed poor medication adherence in people with a lower socioeconomic status, as well as in ethnic minority groups [66]. Given the prevalence of studies with non-specified information upon ethnicity, it is suggested to further investigate the role of such a background.

Furthermore, most of the analyzed studies were focused on a small number of participants (only 10% dealt with more than 50 patients). This is likely to be due to the qualitative nature of the studies conducted, preventing the possibility to extend research protocols to a broader number of participants due to time-consuming procedures. Lastly, the studies included in this review were characterized by a relevant heterogeneity in the patient's characteristics. Such evidence suggests a possible bias of qualitative researches linked to the frequent omission of quantitative details that describe the population involved, precluding future comparisons [69].

Concerning the content analysis according to the framework of the ABC Taxonomy, only a few papers discussed the importance of the earliest phase of commitment to medical plans as expressed by the Initiation phase (e.g. medication prioritisation). This could suggest an apparent lack of interest upon the precursors of adherence [70, 71]. Interestingly, as displayed in Table 4, Implementation and Persistence phases were always retraced jointly during the content analysis of the 39 papers. In other words, whenever the Implementation phase was present, the Persistence phase followed, both in the interviewer/inquiry and in the patient/response sections. The co-presence of both concepts in the interviews' rationales and in the patients' narratives may lead to hypothesize that the difference between the two phases is mostly theoretical. In other words, such a distinction—despite being theoretically sound when it comes to analyse quantitative patterns of adherence—may result less consistent within the framework of

Table 3 Nations of the study with HDI Index and rankings (n = 39)

Nation	HDI Index, ranking	No. of papers (%)
USA	(0.9, 13)	13 (33.3)
United Kingdom	(0.9, 14)	7 (17.9)
Indonesia	(0.7, 116)	2 (5.1)
Germany	(0.9, 5)	2 (5.1)
Australia	(0.9, 3)	2 (5.1)
Nigeria	(0.5, 157)	1 (2.6)
Colombia	(0.7, 90)	1 (2.6)
Spain	(0.9, 26)	1 (2.6)
Eritrea	(0.4,179)	1 (2.6)
New Zealand	(0.9, 16)	1 (2.6)
Brazil	(0.8, 79)	1 (2.6)
Portugal	(0.8, 41)	1 (2.6)
Canada	(0.9, 12)	1 (2.6)
Sweden	(0.9, 7)	1 (2.6)
India	(0.6, 130)	1 (2.6)
Congo	(0.6, 137)	1 (2.6)
China	(0.7, 86)	1 (2.6)
Greece	(0.9, 31)	1 (2.6)

Table 4 Content analysis: frequency of appearance of ABC Taxonomy and Three Factor model sub-concepts ($n = 39$)

	Interviewer/inquiry *n* of papers (%)	Patient/response *n* of papers (%)
ABC Taxonomy		
Initiation	7 (17.9)	15 (38.5)
Implementation	34 (87.2)	39 (100.0)
Persistence/Discontinuation	34 (87.2)	39 (100.0)
Three Factor model		
Information	21 (53.8)	36 (92.3)
Motivation	5 (12.8)	18 (46.1)
Strategy	25 (64.1)	35 (89.7)

patients trying to commit to a medical prescription. Namely, the discrepancy between "what I am able to do when trying to follow at best my prescription" (Implementation) and "what I am able to do in order to keep on with such prescriptions" (Persistence) is not often clear in practical terms, leading to retrace both the phases as a whole.

As to the Three Factor model, Motivation was the most difficult dimension to be traced in the papers, being mainly an implicit cognitive-emotional driver [72], difficult to be defined [73]. Thus, motivation might have been taken for granted (both from the interviewer's and from the patient's words), as representing an implicit feature affecting different adherence patterns. Further studies are suggested on this topic in order to better define the construct and to explicitly investigate its role throughout the adherence process.

Integrated model for the betterment of daily medication adherence

In order to help medication adherence, older adults deserve a multifaceted and tailored approach, focused on both social support and multimorbidity [16, 74]. The barriers identified in this review—that is [A] Patient's beliefs and concerns about treatment; [B] Patients' beliefs about polypharmacy and drug prioritization; [C] Patient's experience and capabilities; [D] Prescriber-patient relationship; [E] Health literacy; [F] Treatment characteristics and complexity; [G] Family and social support—could potentially modulate individual difficulties and promote health-engaged attitudes. This could be particularly true in the older population characterised by frailty, various comorbidities, and related polypharmacy [75, 76].

In this regard, we integrated barriers and facilitators retraced within the framework of the ABC Taxonomy model to generate a patient's decisional flowchart, with the aim to sum up possible behavioural outcomes of the adherence process (Fig. 2).

According to this model, once the medication is prescribed, the patient enters the Initiation phase. The patients may decide not to follow the prescription (and to never do that in the future), leading to primary non-adherence [77]. Alternatively, the patient could start with two one-shot decisions: to buy (obtain) medicines and to take medicines. Modulators (environment, personal factors) may mediate the patient's decisions and actions, being barriers or facilitators, therefore affecting the quality of the Implementation/Persistence phase, leading to Discontinuation. The Discontinuation phase could be both intentional or non-intentional (e.g. forgetfulness) and it could result in two different paths: it could be only partial, that is, the patient may decide to interrupt his/her treatment for a defined period of time exclusively, causing a momentary relapse. Such a relapse will lead to another Implementation/Persistence with possible integration of new strategies. Differently, Discontinuation could also be persistent and critical, so that the patient may significantly doubt about the feasibility and desirability of the prescription received. The event will determine a cognitive-behavioral renegotiation towards the therapy, leading to face the Initiation phase once again or, in the worst case-scenario, to stop the treatment permanently (non-adherence). Differently, if the combination between environment, personal factors and the Implementation/Persistence phases is successful, a persistent, satisfactory or even better level of adherence can be reached.

Moreover, each new medication prescription leads the patient to go back over the decisional flowchart above described, readjusting totally or only in part the medication adherence. For instance, a patient may decide on the basis of different factors (e.g. previous experience, personal beliefs, external constraints) to prioritize a medicine assumption to

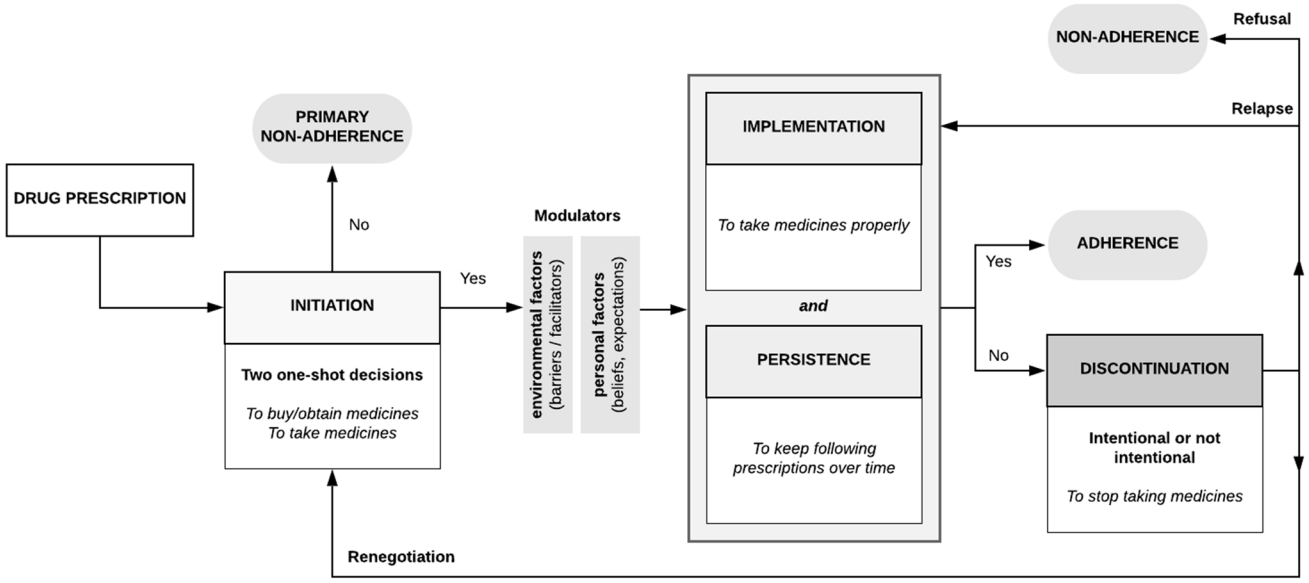

Fig. 2 Integrated adherence model stemming from the review of qualitative studies

the detriment of another, resulting to be adherent with one prescription, but not with another concomitant treatment considered less important. Bearing in mind that the older population is ever-more requested to deal with multiple medications, further studies should focus on specific issues raised by polypharmacy and adherence, as well as with the issue of medication prioritization [2, 4, 16].

Limitations and strengths

Some limitations of this study need to be detailed. First, this systematic review did not examine all nuances of adherence (e.g. behavioural adherence to diet, physical activities). Furthermore, authors considered only studies published in English language, possibly missing insights stemming from non-English researches. The exclusion of grey literature and studies based on telephone interviews deserves the same considerations. Another potentially prejudicial limitation is linked to the use of only some of the most common chronic diseases worldwide in the search strategy.

Besides these limitations and as far as our knowledge, this is the first systematic review examining qualitative studies on adherence in chronic diseases conducted through the lenses of two well established theoretical models (ABC Taxonomy and Three Factor model). The method allowed to consider the complexity and multifaceted nature of medication adherence in older adults. Moreover, the thematical analysis of the existing literature helped the authors to examine factors and phases involved in medication adherence and enabled the proposal of a new integrated model for clinical practice based both on theoretic framework and findings gained by patients' perspective.

Conclusion

Non-adherence to medications is a worldwide issue, interlinked with multiple chronic diseases and polypharmacy [11–16]. Low adherence rates have proved to determine medical complications and treatment contraindications, affecting the older population in terms of health and quality of life [2, 3, 11–16].

In the light of what stemmed from this systematic review, further researches should address the specific issues of multimorbidity and polypharmacy, as well as possible differences in beliefs and treatment management according to culture-related factors. Further investigations should also focus on the issue of medication prioritization, which often occurs in patients, yet is only infrequently reported to their healthcare professionals. The recent EMERGE guidelines, based on the ABC Taxonomy, are also highly recommended to guide and structure the methodology of future research studies on the same issue [78]. Moreover, it is suggested to specifically examine the initiation phase due to the pivotal role which it plays in the initial commitment to a prescription (e.g. medication prioritization, primary non-adherence). A better understanding of these aspects may give practical cues to health care professionals, with the aim to better understand medication adherence-related processes and to structure reliable and patient-centred interventions.

Author contributions MM, ST and AG performed the revision of the literature, providing substantial input and drafting and reviewing the manuscript. An overall supervision to the reviewing procedure (both of the literature and of the manuscript) was finalized by PK, MK-M, LM and EC. All authors gave their final approval.

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Compliance with ethical standards

Conflict of interest PK received speaker's honoraria from Aflofarm, Fresenius, Polpharma and Sandoz; and got funding from a grant from European Union's Health Programme (2014–2020) for SIMPATHY project (663082), outside this work, and The European Commission ERASMUS + Project Skills4Adherence (Grant Agreement Number: 2017-1-PL01-KA202-038672). The other authors declare no conflict of interest.

Ethical approval Ethical approval was not required as the study is based on data retrieved from already published studies.

Informed consent For a literature review, written consent is not required.

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