Medication Taking in Coronary Artery Disease: A Systematic Review and Qualitative Synthesis

Mohammed A. Rashid, MSc
Duncan Edwards, MBBS
Fiona M. Walter, MD
Jonathan Mant, MD
The Primary Care Unit, Department of Public Health and Primary Care, University of Cambridge, Strangeways Research Laboratory, Worts Causeway, Cambridge, United Kingdom

ABSTRACT

PURPOSE Despite the compelling evidence supporting cardiovascular medications in the secondary prevention of coronary artery disease, many patients discontinue treatment. In this synthesis, we sought to understand from a patient perspective the factors that promote medication persistence.

METHODS We systematically searched 7 databases (MEDLINE, Embase, Psy-cINFO, SCOPUS, CINAHL, ASSIA, and SSCI) for published qualitative research about the medication-taking experiences of patients with coronary artery disease and their partners. Articles were assessed for quality using a modified CASP (Critical Appraisal Skills Programme) checklist. Synthesis was undertaken using well-established meta-ethnographic approaches.

RESULTS We included 17 articles in the final synthesis from the United Kingdom (6), Europe (5), United States (4), China (1), and Australia (1), with a total sample size of 391 patients. Analyses suggested that some patients hold fatalistic beliefs about their disease, whereas others believe they have been cured by interventions; both can lead to failure to take medication. Patients who adapt to being a "heart patient" are positive about medication taking. Some individuals dislike taking tablets generally and are wary of long-term effects. Relationships with prescribing clinicians are of critical importance for patients, with inaccessibility and insensitive terminology negatively affecting patients' perceptions about treatments.

CONCLUSIONS Strategies to promote higher persistence of secondary prevention medications in patients with coronary artery disease need to recognize the key role of the prescribing clinician. Providing medication-specific information at the time of initiating therapy, improving the transition between secondary and primary care, and explaining the risk of disease recurrence may all help to modify patient attitudes toward drugs to prevent further cardiovascular disease.

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INTRODUCTION

Coronary artery disease remains an important cause of morbidity and mortality throughout the world. In recent years, advances in cardiovascular pharmacology and interventional cardiology have contributed to improved survival after myocardial infarction, leading to an increase in nonfatal events. Thus, although coronary artery disease incidence may be falling in many countries, the overall burden of the disease remains high, particularly in economic terms. There is a need, therefore, to refocus efforts on secondary prevention.

The secondary prevention of coronary artery disease involves the management of both lifestyle factors and physiologic parameters, often with medications. Despite the increase in prescriptions of cardiovascular medications in the last 2 decades, a large proportion of patients with coronary artery disease are still not meeting therapeutic targets, as demonstrated in the EUROASPIRE III survey (European Action on Secondary and Primary Prevention by Intervention to Reduce Events III). This situation has led to a renewed focus on whether patients continue to take medications, although such terms as compliance and concordance are increasingly

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CORRESPONDING AUTHOR
Mohammed A. Rashid, MSc
The Primary Care Unit
Department of Public Health and Primary Care
University of Cambridge
Strangeways Research Laboratory
Worts Causeway, Cambridge, CB1 8RN
mar74@medschl.cam.ac.uk

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MEDICATION TAKING IN CORONARY ARTERY DISEASE

avoided because of the associations with paternalistic clinician-patient relationships. Studies of individual cardiovascular medications, such as antiplatelet drugs, lipid-lowering drugs, and β-blockers, have all shown unfavorable outcomes when these drugs are prematurely discontinued.

Many studies have explored patients’ perspectives on lifestyle interventions, in particular, those embedded within cardiac rehabilitation programs, which continue to have suboptimal uptake and completion rates. More than 40% of the recent decline in coronary artery disease mortality has been attributed to evidence-based medications, however, and patient attitudes toward these medications have been relatively less well investigated. As the importance of partners’ influence in the holistic management of coronary artery disease is well established, their perspectives may additionally help to understand decisions about medication taking. Although qualitative research provides vital evidence about experiential phenomena, the application of findings may be limited by small sample sizes. By systematically identifying and synthesizing data from a number of studies, valuable insights may be gained about medication-taking behavior among patients with coronary artery disease, which could allow policy makers and clinicians to develop strategies to facilitate persistence.

METHODS

Meta-ethnography has been evaluated as an effective tool to synthesize qualitative studies in health research. Much as for meta-analysis in quantitative research, the goal is to provide comprehensive insight into the topic of interest, however, rather than aggregate findings, meta-ethnography seeks to interpret them and produce a new conceptual understanding.

Systematic Review

It is well established that locating qualitative research is challenging. In light of this challenge, we conducted searches across both clinical and nonclinical electronic databases (MEDLINE, Embase, PsycINFO, SCOPUS, CINAHL, ASSIA, and SSCI). The search criteria are shown in Table 1 and comprise terms in 3 groups, which were combined using Boolean logic terms “or” and “and.” In addition to database searches, we manually searched reference lists of included articles.

The search was restricted to articles published between January 1, 1990, and March 31, 2012. A unique feature of secondary prevention therapy in coronary artery disease is the initiation of several new medications simultaneously after myocardial infarction. Although research data existed for many treatments before 1990, delayed translation to clinical guidelines meant that many agents were not commonly used then.

As our synthesis aimed to explore medication taking, we excluded studies tackling lifestyle factors alone, as well as those focusing solely on interventional cardiology and surgery. In addition, studies involving predominantly healthy or high-risk individuals were excluded, as the focus was on patients with established coronary artery disease. All types of qualitative methodologies were included, as were studies from all countries and in all languages. All titles and abstracts were screened by 1 researcher (M.A.R.) and to maximize rigor, a subset were independently screened by a second researcher (D.E.), with no discrepancies in selections. Full-text articles were accessed for all selected abstracts and read by 2 reviewers (M.A.R. and D.E.) who agreed on all final inclusion decisions.

Critical Appraisal

There has been debate about the value of appraisal in qualitative syntheses, with some authors opting to judge articles exclusively on their conceptual contribution. To maintain rigor and transparency, we used a 2-step approach in this synthesis. First, all included articles were scored against a modified version of the Critical Appraisal Skills Programme (CASP) checklist to ensure any articles with poor methodology, scoring less than 50%, were excluded. Second, articles were assessed for their relevance to the synthesis using the criteria outlined by Dixon-Woods and colleagues, according to their relevance to our research question. Included articles were scored as either a key article (one providing rich data for the synthesis) or a satisfactory article (one providing some valuable data). These scores were agreed on independently by the primary researcher (M.A.R.) and at least 1 other reviewer (D.E. or F.W.) for each article.

Synthesis

Data were extracted from the included articles independently by 2 reviewers (among M.A.R., D.E., and F.M.W.). Meta-ethnography has been adapted for

| Table 1. Final Search Criteria and Search Terms |
|-----------------------------------------------|
| Sample                                       |
| Coronary artery disease                       |
| Coronary heart disease                        |
| Ischemic heart disease                        |
| Myocardial infarction                         |
| Heart attack                                  |
| Coronary artery bypass graft                  |
| Myocardial infarction                         |
| Focus                                        |
| Medications                                  |
| Medicines                                    |
| Adherence                                    |
| Compliance                                   |
| Persistence                                  |
| Concordance                                  |
| Methodology                                  |
| Qualitative                                  |
| Ethnography                                  |
| Interview                                    |
| Focus group                                  |
| Thematic analysis                            |
health research, and patient quotes about their experiences have been defined as first-order constructs and the authors’ interpretations of these constructs have been defined as second-order constructs. These second-order constructs are then used to build themes, or third-order constructs, by the synthesis team. We compiled tables for each article outlining the second-order constructs that emerged. We discussed these tables at a consensus meeting of the authors, where third-order constructs were developed and an overarching theoretical model was devised to explain the key concepts across the articles.

**RESULTS**

**Systematic Review**

Figure 1 summarizes the systematic review process using a flowchart based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidance, and Table 2 details the 17 articles included in the synthesis.

![Figure 1. Adapted PRISMA flowchart.](image)

We identified 3 articles as being from the same research group, with common funding arrangements and some common interview data, although each had a unique focus and additional primary data. To avoid overemphasizing their individual contributions, we grouped these articles together as 11a, 11b, and 11c.

**Critical Appraisal**

Articles scored between 65% and 78% on the modified CASP checklist, with a mean score of 69.5%; thus, no articles were excluded because of flawed methodology. On assigning relevance scores according to the criteria of Dixon-Woods and colleagues, we determined that 6 articles were key articles, while the remaining 11 were satisfactory. These ratings are presented in Table 2.

**Second-Order Constructs**

Second-order constructs from the 17 included articles are shown in Tables 3 through 5. During the data extraction process, it became clear that the articles could be grouped into those related to perceptions of the disease process (coronary artery disease), those related to perceptions of medications generally, and those related to relationships with clinicians. We therefore chose these subgroups to categorize the large number of constructs. Within each subgroup, second-order constructs have been arranged according to their impact on medication persistence: promotion, deterrence, or ambivalence. This classification emerged only after reviewing second-order constructs across all articles; it was not commonly used before then by authors of any of the individual articles.

**Perceptions About Coronary Artery Disease**

The first subgroup of second-order constructs relate to perceptions about coronary artery disease. As demonstrated in Table 3, most themes in this category seem to deter persistence. Articles often highlighted a fatalistic approach to disease, exemplified by one patient’s statement: “I don’t think I’ll be here much longer, the way it is going on.” In contrast, others interpreted the absence of symptoms as a challenge to the perceived need for treatment. This view was often coupled with a sense of being cured. Indeed, patients undergoing interventional procedures interpreted explanations about angiogram findings showing improvements in “blockages” to mean that they were cured. Patients who missed treatment for a few days and noticed no change to their perceived health status would begin to question their susceptibility to future events. This sense of not needing medications was therefore a manifestation of those with an excessively high (fatalistic) or low (cured) perception of their own disease susceptibility.

The need for thorough disease-specific information was also stressed, as patients did not always appreciate the link between risk factors and disease. Similarly, patients often understood myocardial infarction as
an acute event and not part of a chronic disease, with some quoting patient literature that discusses the number of weeks before they can lead a “normal life.”

Both of the articles that contributed constructs reflecting ambivalence toward medications had studied patients with a first cardiac event soon after hospital discharge, indicating a period of reflection immediately after receiving a diagnosis. Constructs relating to challenging the need for treatment were largely from patients with chronic coronary artery disease. These patterns may indicate a temporal sequence of events, as patients move from an early period of uncer-

| Table 2. Characteristics of Articles Included in the Synthesis |
|---------------------------------------------------------------|
| **Number** | **Author, Year** | **Sample Size (Setting)** | **Patients’ Age and Sex** | **Country** | **Methods** | **Relevance** | **Pharmaceutical Funding** |
|------------|------------------|---------------------------|--------------------------|-------------|-------------|--------------|---------------------------|
| 1 | Roebuck et al, 2001 | 31 (CAD; 6 wk after discharge) | Median age = 63 y (28-74 y), 21 male | United Kingdom | Interviews | SAT | No |
| 2 | Wiles and Kinmonth, 2001 | 25 (CAD; 2 and 16 wk after discharge) | Ages 34-80 y, 13 male | England | Interviews | SAT | No |
| 3 | Bergman and Berterö, 2001 | 8 (CAD; 5-8 mo after diagnosis) | Ages 49-68 y, 5 male | Sweden | Interviews | SAT | No |
| 4 | Kärner et al, 2002 | 23 (AMI; 1 y after CHD event) | Mean age = 51 y female, 57 y male; 14 male | Sweden | Interviews | SAT | No |
| 5 | Webster et al, 2002 | 35 (AMI and spouses; 2-3 wk after discharge) | Average age = 65 y, 25 male | England | Interviews | SAT | No |
| 6 | Tolmie et al, 2003 | 33 (CAD or high risk of CAD; 1-7 y after statin initiation) | Ages 24-80 y, 20 male | Scotland | Interviews | SAT | Yes |
| 7 | Kärner et al, 2004 | 25 (spouses of CHD patients; 1 y after cardiac event) | Ages 36-68 y, 8 male | Sweden | Interviews | SAT | Not mentioned |
| 8 | Attebring et al, 2005 | 20 (first AMI; median 7.5 wk after discharge) | Median age = 61.5 y (34-79 y), 12 male | Sweden | Interviews | KA | No |
| 9 | Lehane et al, 2008 | 10 (CAD; average length of treatment 2.5 y) | Ages 51-69 y, 7 male | Ireland | Interviews | KA | Yes |
| 10 | Wang et al, 2008 | 17 (first AMI; average age 18 d after discharge) | Mean age = 57 y (39-73 y), 14 male | China | Focus groups | SAT | Not mentioned |
| 11a | Decker et al, 2008 | 22 (NSTEMI with DES) | Ages 41-77 y, 13 male | United States | Interviews (telephone) | KA | Yes |
| 11b | Garavalia et al, 2009 | 40 (AMI) | Ages 44-78 y, 20 male | United States | Interviews (telephone) | KA | Yes |
| 11c | Garavalia et al, 2011 | 22 (AMI with DES) | Mean age = 53 y (45-77 y), 13 male | United States | Interviews (telephone) | KA | Yes |
| 12 | West et al, 2010 | 32 (CHD admission; 3 mo after discharge) | Aged ≥62 y, all female | United States | Interviews | SAT | No |
| 13 | White et al, 2010 | 15 (cardiac rehabilitation attendees; during program and 9 mo after it) | Aged 42-72 y, 11 male | England | Interviews | SAT | Not mentioned |
| 14 | Speechly et al, 2010 | 13 (CHD; 8 diagnosed ≥5 y, 5 diagnosed <5 y) | Aged 50-75 y, 6 male | Australia | Interviews | SAT | Yes |
| 15 | Rushworth et al, 2012 | 20 (PCI; after phase 1 cardiac rehabilitation) | Median age = 60.5 y, 15 male | Scotland | Interviews and questionnaires | KA | No |

**AMI** = acute myocardial infarction; **CAD** = coronary artery disease; **CHD** = coronary heart disease; **DES** = drug-eluting stent; **KA** = key article; **NHS** = National Health Service; **NIH** = National Institutes of Health; **NSTEMI** = non–ST-elevation myocardial infarction; **PCI** = percutaneous coronary intervention; **SAT** = satisfactory article.

* According to system of Dixon-Woods et al.24
Perceptions About Medication Taking
The largest subgroup of second-order constructs relate to perceptions about medications, shown in Table 4. Many articles highlighted a tendency to unconditionally accept treatment, as one patient commented, “There’s got to be a reason they’ve given them to me, so I’ll put them down my neck…” Individuals accepting treatment in this way were more likely to have a high regard for their prescribing clinician.32 Many individuals held a confidence that medications would reduce their likelihood of experiencing another cardiac event. Forming routines and using physical aids also promoted persistence, as did the support of family members. A number of articles also discussed the confusion individuals experienced about drug regimens. All of these articles were published after 2008 and may reflect the increasing complexity of clinical guidelines. There was particular confusion about the duration of clopidogrel therapy and a misunderstanding of the synergistic effect of dual antiplatelet therapy: “...the aspirin is less important because that is general thinning.”41 Medication inserts could cause anxiety, even when patients did not experience the adverse effects mentioned. A number of articles highlighted concerns about adverse effects affecting everyday life. This threat to identity is recognized as being central to the process of adapting to chronic disease.44

Three articles included the views of partners and contributed to a wide variety of constructs,31,33,36 and 2 of these articles raised the issue of fear of long-term harm from medications.33,36 Although partners seemed satisfied that medications were beneficial to the heart, they were concerned about harmful effects to other organs; however, the influence of partners is unlikely to be entirely negative as an article that exclusively studied partners showed that they understood the need for medications to minimize risk of future cardiac events.33 In 1 article, Chinese couples held the view that over time, medications inevitably cause “weakness,” reflecting an established concept in Chinese culture that herbal therapies are better tolerated than western alternatives.45

Relationships With Clinicians
Although many second-order constructs in the first 2 subcategories indirectly relate to interactions with clinicians,9 shared this focus as their primary focus and are shown in Table 5. The use of terms such as mild heart attack by clinicians had a lasting impact on patients,28 reducing their perceived disease severity. Patients also received conflicting information from health professionals, which challenged their general sense of security in health services. This communication breakdown was particularly problematic at the time of transfer from secondary to primary care.

Many individuals voiced a reluctance to seek medication-related information from clinicians. This reluctance often related to concerns about wasting their time; as one patient put it, “I’m sure the doctors have got far more pressing things to do than to listen to some silly...”2 The reluctance to trouble clinicians was noticeable in a Chinese cohort, wherein a high regard for physicians as professionals meant that individuals were afraid to “disrupt harmony” by challenging them.36

Patients placed great importance on the relationships they had with their prescribing clinician. Characteristics such as approachability and sensitive communication encouraged patients to negotiate management decisions jointly. The information received

| Second-Order Construct | Explanatory Notes | Articles |
|------------------------|-------------------|---------|
| **Promote persistence** | Learning to overcome anxieties and worries about medications by internalizing life changes after a cardiac event | 8, 11a |
| Adapting to the sick role | Learning to overcome anxieties and worries about medications by internalizing life changes after a cardiac event | 8, 11a |
| Understanding myocardial infarction as indicating future vulnerability | Perceived vulnerability to future myocardial infarction motivated preventive action | 2 |
| Ambivalence toward persistence | Confusion about the damage caused by cardiac event and the success of the cardiac intervention | 10, 15 |
| Uncertainty about disease and prognosis | Confusion about the damage caused by cardiac event and the success of the cardiac intervention | 10, 15 |
| **Deter persistence** | An overwhelming perceived threat of illness driven by personal experiences, family history, and anecdotal accounts | 2, 4, 5, 11a, 11b |
| Fatalistic approach to disease | An overwhelming perceived threat of illness driven by personal experiences, family history, and anecdotal accounts | 2, 4, 5, 11a, 11b |
| Absence of symptoms challenging perceived need for treatment | Lack of symptoms suggesting that one is cured, with no noticeable change if medications are missed | 4, 6, 11a, 11b, 14 |
| Level of appreciation about the link between risk factor and disease | Lacking awareness about the causes of coronary artery disease | 6, 11c, 13 |
| Understanding acute myocardial infarction as an acute event | Little feeling of future vulnerability of acute myocardial infarction, encouraged by misinterpretation of patient information literature quoting expected time to recovery | 2 |
at initiation of treatment was also important to patients, who wanted explanations individualized to them. Patients who were particularly dissatisfied with a lack of information from clinicians sought to find reassurances elsewhere, including on the Internet.  

**Third-Order Constructs**

Having considered the interpretation of individual second-order constructs, we identified several third-order constructs: forming a new identity as a “heart patient,” overcoming preexisting beliefs about medications, and the powerful influence of the clinician-patient relationship. The emergence of these third-order constructs gave a clearer insight into the entirety of patient experiences.

Figure 2 is an explanatory model describing the interplay between patients’ perceptions of medication taking and their relationships with clinicians. This model highlights the importance of having a clear understanding of patients’ experiences to inform the development of effective strategies for improving medication adherence in patients with coronary artery disease.
among various factors. In the center of the diagram is the key outcome, medication-taking behavior. The overlap with perceptions about disease and medications indicates the dynamic effect that these factors have for the individual. Although most external factors have been placed below the individual, relationships with clinicians has been placed above to indicate the important mediating role this factor may have for the others and that it may be the most modifiable of them.

The clinical importance of this model is 2-fold. The first is to help clinicians appreciate the complexity of factors contributing to medication persistence. This knowledge should prompt clinicians to explore all of these factors and recognize which of them may be important for any individual. Second, clinicians should be aware of the powerful role that they may play in shaping this behavior. This role may entail influencing how patients perceive medications and coronary artery disease, as well as balancing any strong external influences. The use of sensitive and appropriate language may encourage individuals to perceive their disease as important, but treatable.

**DISCUSSION**

Although a sizable body of evidence supports the use of medications in the secondary prevention of coronary artery disease, relatively little is known about the reasons why patients choose to persist with them or to stop taking them. In contrast, the evidence supporting cardiac rehabilitation is more contentious, yet patient experiences have been thoroughly explored in that field. In this review, we have synthesized 17 articles and produced a theoretical framework to describe these experiences, with a focus on clinical application.

Our study has strengths and limitations. We used a systematic strategy to identify studies and included a variety of databases. Data extraction and quality appraisal was performed independently by at least 2 reviewers, enhancing the rigor of the methodology. The synthesis included studies from various countries and patients from various stages of their disease. Meta-ethnography is now well established in health research and has been recognized as a key tool to make qualitative evidence accessible to policy makers.

A number of subtly different methodologies exist and may have produced alternative findings; however, the congruence of themes between articles and overlap with existing literature mean that any discrepancy is likely to be minimal. A further potential limitation is that although reviewers involved in this synthesis held various clinical and research posts, there were no social scientists on the review team; however, as all researchers had experience of both qualitative research and coronary artery disease, the absence of a social scientist is unlikely to have limited the process and indeed may have helped to maintain a focus on translating the findings to inform clinical practice.

Researchers have previously sought to synthesize qualitative data about medication-taking behavior, finding as this synthesis did, a general dislike for taking pills and a reluctance to talk to physicians. Meanwhile, a questionnaire-based study in primary care also found that those with a stronger perception of the chronicity of coronary artery disease were more likely to take medications. We are not aware of another synthesis that integrates qualitative findings about medication taking in patients with coronary artery disease.

A key message that emerges from this synthesis is the extent to which medicine-taking behavior of individuals is influenced by clinicians. Particular ways in which this information can be taken into account in clinical practice include ensuring a smooth transition between secondary and primary care to avoid conflicting information, providing an accessible route for patients to discuss medication concerns, and giving balanced information about recurrent disease risk, including the association between individual risk factors and coronary artery disease. Interventions at the policy level may include routine follow-up meetings with a primary care prescribing clinician for all patients after myocardial infarction, to establish a relationship and discuss uncertainties. A toolkit to facilitate and guide

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**Figure 2. Factors influencing medication-taking behavior in coronary artery disease.**

- Relationships with clinicians
- Perceptions about coronary artery disease
- Medication-taking behavior
- Perceptions about medications
- Preexisting health beliefs
- Socioeconomic and cultural environment
- Interactions with health system
- Influence of partner and family
this meeting may prove beneficial. In light of the potential influence of partners, their attendance at these consultations could be encouraged, although the evidence about their precise impact remains limited. As this toolkit is likely to be used in a primary care setting, a qualitative exploration of the views of general practitioners may provide additional insights for its development.

This review adds to previous work highlighting the complexity of medication-taking decisions by patients. Clinicians need to better appreciate this development, which could be incorporated into undergraduate and postgraduate medical education. Depression has been shown to increase medication discontinuation in observational studies of patients with coronary artery disease and, as this association did not emerge in our synthesis, it could be explored in further qualitative work.

In conclusion, medications play a central role in reducing cardiovascular morbidity and mortality in patients with coronary artery disease. This synthesis conceptualizes the complex decision-making processes that patients undergo when deciding whether to continue taking their medications. The often sudden nature of myocardial infarction and lack of coronary artery disease symptoms mean patients may not appreciate the severity of their disease. Alongside the adaptation to being a “heart patient,” a parallel challenge is to overcome negative beliefs about medications and tackle anxieties about actual and anticipated adverse effects. Clinicians have a unique influence on medication persistence, often unknowingly influencing patients’ thoughts through their language and lack of accessibility. By adopting a more open approach, clinicians can engage both patients and their partners in a discourse of what they think about their medications. Given the importance of coronary artery disease and the complexity of patient influences evident from this synthesis, further exploration and intervention in this area are warranted.

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Key words: coronary artery disease; heart disease; qualitative research; secondary prevention; medication; drug therapy; persistence; adherence; compliance; patient behavior

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