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Patient and Provider's perspective on barriers and facilitators for medication adherence among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A qualitative evidence synthesis

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3 **Patient and Provider's perspective on barriers and facilitators for medication adherence**
4 **among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A**
5 **qualitative evidence synthesis**
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10 **Running head:** Barriers and facilitators for medication adherence among CVD and DM
11 patients in India
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14 **Article category:** Systematic Review
15

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15 **Strengths and Limitations:**

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- This is the first review exploring factors associated with drug adherence among CVD & DM patients in India
 - Patient-related barrier was lack of knowledge about their condition, forgetfulness, stigma and stress
 - Care team-related barrier was lack of family support, risk communication and physician attitude
 - Health system-related barriers were accessibility, affordability, availability and acceptability
 - Solutions to address these barriers were peer support group, digital reminders and innovations in patient care

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41 **Abstract:**

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44 **Background:**

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46 In spite of recent technological and pharmacological advancements to treat and monitor
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48 diabetes mellitus (DM) and cardiovascular disease (CVD) patients, medication adherence is of
49
50 particular concern in countries like India. Hence, this review was done to explore the various
51
52 stakeholders' perspective on barriers and facilitators for medication adherence among CVD
53
54 and DM patients.

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57 **Methods:**

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3 A comprehensive systematic search was conducted in Medline, Cochrane library,
4 ScienceDirect and Google Scholar from January 2010 to July 2020. We used framework for
5 systems approach to healthcare delivery to conduct thematic analysis and derive relevant
6 themes, sub-themes and codes.
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10 11 12 **Results:**

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14 In total, 18 studies were included. Major barrier reported was lack of understanding about the
15 disease, complications related to non-adherence, and treatment schedule followed by
16 forgetfulness, lack of family support and risk communication. Health system-related barriers
17 such as accessibility, affordability, and acceptability were also reported by majority of the
18 studies. Creation of peer support group, digital reminder system, integration of AYUSH,
19 mental health, physiotherapy and geriatric clinics at primary healthcare level and innovations
20 in patient care were suggested to counter these barriers in medication adherence.
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30 31 **Conclusion:**

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33 Such targeted interventions should be developed to achieve better control among CVD and DM
34 patients.
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38 **Keywords:** Cardiovascular Diseases, Diabetes Mellitus, Medication Adherence, Qualitative
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INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of mortality globally and in India.^{1,2} More than a quarter (28%) of all deaths in India are attributable to CVDs with Ischemic heart disease (IHD) and stroke constituting the majority (83%).³ On the other hand, India ranks second after China in the global diabetes epidemic, with a prevalence of around 10%.⁴ Both diabetes mellitus (DM) and hypertension have long been recognized as independent risk factors for CVDs, whereas adherence to prescribed hypoglycaemic and antihypertensive drug therapies have significantly reduced the risk.⁵⁻⁷ At least half of hypertensive & DM patients stop taking their medication within a year, often without informing their provider, with further attrition over time accomplishing medication adherence a significant public health priority.⁸ Medication adherence is defined as the extent to which a person's behaviour coincides with the agreed medication regimen or health advice from a health care provider.⁹ It has three components: initiation (when the patient takes the first dose of prescribed medication), implementation (the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen), and discontinuation (when no more doses are taken after that).¹⁰ Medication adherence is of growing interest to clinicians, healthcare systems, and other stakeholders (e.g., payers). There is soaring evidence that nonadherence is often associated with lower quality of life, adverse clinical events, increased need for medical interventions, mortality, and eventually avoidable healthcare out-of-pocket expenditure.¹¹ Non-adherent hypertensive and stable coronary heart disease (CHD) patients have a five and four times higher risk of developing CHD and death when compared to adherent patients.^{12,13} Similarly, the likelihood of hospitalization is doubled among DM & hypertensive patients who are non-adherent to prescribed therapies compared with the general population. Despite recent advancements in pharmacologic treatment and technology to treat and monitor DM and CVD patients,

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3 medication adherence is of particular concern in low-and-middle-income countries (LMIC)
4 like India, where accessibility and affordability are still issues.^{3,14}
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7 Barriers to adherence can be comprehended as the patient, medication, provider, and health
8 system factors with interactions among them.^{15,16} Patient factors that influence adherence
9 include poor health literacy, cultural beliefs regarding medication effectiveness, and religious
10 healing practices.¹⁶ Low income, forgetting to take medication, and perceptions regarding pills
11 like safety concerns, convenience, and necessity add to the above list.^{15,16} Inadequate
12 knowledge about a drug and its use, not being convinced of the need for medication, fear of
13 adverse effects, and long-term treatment regimens also prompt medication discontinuation.¹⁴
14 Clinician factors cover failure to recognize nonadherence, prescription of complex and
15 multidrug regimens, ineffective communication of benefits, and excluding patients in the
16 treatment decision-making process.¹⁶ Health system factors comprise limited insurance
17 coverage, poor coordination of care between inpatient and outpatient settings, and inadequate
18 communication between prescribers (i.e., specialists and primary care clinicians). In addition,
19 the caregivers' aspect also becomes relevant in determining patients' adherence as CVD patients
20 with a caregiver are more likely to be adherent to medications.¹⁷ Hence identifying specific
21 barriers for each patient and adopting suitable techniques to overcome them is imperative to
22 improve medication adherence. Some of the facilitators successful in overcoming these barriers
23 include a personal medication counsellor in the care continuum to guide patients with
24 medication use, single-pill fixed-dose combinations, training pharmacists as coaches for drug
25 therapies, building peer groups for chronic conditions, and developing information systems in
26 the follow-up of patients.¹⁸
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53 Quantitative studies have focused on medication adherence incidence and identification of its
54 potential risk factors. They do not, however, uncover life circumstances that may influence
55 adherence from the patient perspective. The inclusion of qualitative studies in our review will
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3 provide a better understanding of the barriers and facilitators from the perspective and
4 experiences of patients, healthcare providers, and caregivers. Furthermore, this synthesis of
5 qualitative evidence aims to generate relevant and meaningful findings appropriate to the
6 individuals, develop a research plan, and eventually help make an effective policy and practices
7 in improving adherence among the patients. Therefore, the current review was done to
8 understand the perspective of various stakeholders (patients, caregivers, and healthcare
9 providers) on the barriers and facilitators for medication adherence among CVD and DM
10 patients in India. We also explored the suggestions and solutions provided by these
11 stakeholders in overcoming the reported barriers.
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25 **METHODS**

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28 This review was performed by adhering to the “enhancing transparency in reporting the
29 synthesis of qualitative research (ENTREQ)” statement.¹⁹ We registered our protocol in the
30 PROSPERO database (Registration number - CRD42020199529). We also searched
31 PROSPERO and Cochrane to ensure that no similar review protocol has been reported. We
32 also performed a preliminary search to ensure that no previous reviews of our similar topic
33 targeting the Indian population were published.
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42 **Study design**

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44 We performed an evidence synthesis of the available qualitative evidence on the barriers and
45 facilitating factors for medication adherence among CVD and DM patients. This review helped
46 synthesize the evidence of peer-reviewed articles in this field and built an organized empirical
47 research outline based on prior knowledge.
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53 ***Eligibility criteria***

54 *Study type*

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3 We have included qualitative peer-reviewed studies conducted in India for our current review.
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5 Furthermore, qualitative evidence from other mixed methods studies was screened for
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7 eligibility and included in the qualitative component was relevant to our review. In addition,
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9 we included studies using qualitative techniques for data collection such as focussed group
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11 discussion (FGD), in-depth interviews (IDI), and Key Informant Interviews (KII).
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14 *Participant type*

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16 We have included the studies reporting the barriers and facilitators of medication adherence
17
18 from patients' perspectives (CVD and DM), family members, healthcare workers (HCWs), or
19
20 health system policymakers in India. HCWs were defined as per WHO recommendation as "all
21
22 the persons involved in the actions whose primary intent is to enhance the health."²⁰
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24

25 *Outcome*

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27 The phenomenon of interest in our review was the barriers and facilitators for medication
28
29 adherence among CVD and DM patients and the suggestions and solutions to address the
30
31 barriers and improve compliance as experienced by the patients, caregivers, family members,
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33 HCWs, and other relevant stakeholders.
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36 *Exclusion criteria*

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38 We have excluded the studies not available in English, books or conference abstracts or grey
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40 literature, or editorial comments. We have also excluded the studies reporting only quantitative
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42 data such as cross-sectional surveys, case-control, cohort studies, or intervention trials.
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46 **Search strategy**

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48 We have conducted a comprehensive and systematic search in databases and search engines
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50 such as Medline, Cochrane library, ScienceDirect, and Google Scholar. A combination of
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52 medical subject heading (MeSH) and free-full text terms was used for carrying out a literature
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54 search. The detailed search strategy and search results in the databases mentioned above and
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56 search engines are provided in Supplementary File 1. In addition to this, we also checked the
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3 reference list of primary studies obtained via electronic search and included articles relevant to
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5 our review and analysis. The search was conducted in all the databases from January 2010 to
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7 July 2020 with English language restriction for publication. Furthermore, the search timeline
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9 was restricted to ensure that our work provides a broader view and identifies the emerging
10
11 issues.
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14 **Study selection process**

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16 Two investigators (YK and TR) independently performed the literature search, screened the
17
18 title and abstract of all the identified studies, and retrieved the full text for articles relevant to
19
20 our review. Further full-text screening of the retrieved articles was done again independently
21
22 by the two investigators (YK, TR) to select the studies matching the eligibility criteria of our
23
24 review. Disagreements during this process between the two investigators were resolved
25
26 through consultation with a third investigator (SR).
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30 **Data Extraction and Management**

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32 After the study selection, two investigators (YK and TR) independently extracted the relevant
33
34 data and study characteristics onto a predetermined data extraction format. Data entry was
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36 double-checked for accuracy by a third investigator (SR) by comparing the data presented in
37
38 the review and individual study reports. As a result, we have extracted the following study
39
40 characteristics: general information such as the name of the first author, the country in which
41
42 the study was done, and year of publication, in the methods section, data collection period,
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44 study design, study participants, sample size, sampling technique, and data collection
45
46 procedure. In addition, barriers, facilitators, suggestions, and solutions to medication adherence
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48 were identified systematically.
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53 **Quality assessment**

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55 Two investigators (YK and SR) independently performed the quality check using the Critical
56
57 Appraisal Skills Programme (CASP) criteria.²² This checklist has been widely used for
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3 assessing the quality of studies included in this Qualitative Evidence synthesis. This has helped
4
5 determine whether the studies included are coherent with the quality appraisal standard for
6
7 qualitative studies. This checklist consists of 10 questions concerning the study's clarity,
8
9 methodology, and results to rank the included studies. Subsequently, these studies were
10
11 stratified into high quality (three stars for studies scoring 8 to 10 points), medium quality (two
12
13 stars for studies scoring 4 to 7 points), and low rate (one star for studies scoring 0 to 3 points).
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15 We did not exclude the low-quality studies, but the interpretation of results was made with
16
17 caution. Disagreements during the quality assessment process were resolved by discussion with
18
19 the third investigator (TR).
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23 **Data Analysis**

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25 We analysed and reported the findings in separate clusters such as patients, caregivers, family
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27 members, HCWs, and policymakers to demonstrate the differences among these subgroups.
28
29 We have adopted a thematic framework analysis to analyse and synthesize the data. Thematic
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31 framework analysis has been helpful as the evidence was primarily descriptive and improved
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33 our understanding of the barriers and facilitators in medication adherence among CVD and DM
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35 patients, and helped to identify the solutions for the same. This framework synthesis has five
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37 stages of synthesizing the qualitative data.
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42 ***First stage - Familiarisation with the data:*** Primary investigator (YK) did the process of
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44 familiarisation with data by reviewing all the selected articles against the objective of our
45
46 review and found the recurrent themes across the included studies.
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50 ***The second stage - Identifying the thematic framework:*** The investigators used a
51
52 predetermined thematic framework developed using literature to guide the thematic analysis.
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54 However, we have adopted this thematic framework based on the themes emerging in our
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56 research. This final framework has provided a detailed list of facilitators and barriers for
57
58 medication adherence and also solutions to address the issue.
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3 **Third stage - Indexing:** Two independent investigators (YK and TR) have read the extracted
4 information and searched for the themes as per the predetermined thematic framework and
5 additional emerging themes. The framework underwent several revisions as and when a new
6 theme emerged. This has been performed through discussion and agreement between the entire
7 team of investigators. Next, all the studies were completely read and examined till there was
8 no new emergent theme. Coding of the data was then done as per the themes identified in our
9 analysis. Finally, each preliminary study indexing was done using the codes related to the
10 thematic framework. Whenever appropriate, sections of the studies were indexed with one or
11 more codes.
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23 **Fourth stage - Charting:** The investigators have sorted the data based on the themes and
24 presented these themes in the tabular format (chart). The rows and columns of the table indicate
25 the themes related and the studies, which enabled us to compare the study findings across
26 various themes and subthemes.
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33 **Fifth stage - Mapping and interpretation:** The investigators used these charts to define the
34 concepts identified and mapped the nature and range of phenomena. Our review explored the
35 associations between the various themes and helped in clarifying the findings. Finally, we
36 mapped and interpreted the findings in line with our objectives and emergent themes.
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42 **Patient and Public Involvement:**

43 Patients or the public were not involved in the design, or conduct, or reporting, or
44 dissemination plans of our research
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50 **Results**

51 **Study selection**

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57 A comprehensive and systematic search was done to identify the relevant studies from January
58 2010 to July 2020. In total, we identified 1187 citations, and after the removal of duplicates
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3 from multiple databases, 982 records were screened for their title and abstract and assessed for
4 eligibility. From these records, we retrieved 33 articles, and after going through the full text of
5 these articles, 18 studies were included in the review. (**Figure 1**).²²⁻³⁹

10 **Characteristics of the studies included**

11
12 Characteristics of the included studies are reported in **Table 1**. Of the 18 studies included, 9
13 (50%) were from the Southern region, followed by 7 (38%) from the Northern part of India.
14
15 The mean age of the participants ranged from 25-76 years. The typology of the studies
16 comprised of in-depth interviews (IDIs) and focussed group discussions (FGDs). The study
17 participants were primarily patients with diabetes, hypertension, or any cardiovascular diseases
18 (to explore the patient perspective), and health care workers (4 studies) providing care to them
19 (to obtain the provider perspective). The total sample size of the included studies ranged from
20 6 to 100. The majority (10 of the included studies) were done in a community setting, while
21 the rest were either facility-based or had participants from ongoing trials. Four of the included
22 studies used software for analysing the qualitative data, while the rest followed manual
23 methods. Most of the included studies (14 out of 18) had higher ratings indicating high-quality
24 evidence.

39 **Narrative synthesis**

40
41 Significant findings from the review showed that factors contributory to adherence come under
42 three themes: patient-related, family-related, and health system-related factors. The barriers,
43 facilitators, and suggestions to improve medication adherence were summarized under these
44 three themes.

51 **Barriers in medication adherence**

52
53 **Table-2** shows the thematic framework analysis related to barriers in medication adherence
54 among CVD and DM patients. All the 18 included studies have explored and reported on these
55 barriers.

Patient-related factors

A significant patient-related barrier (10 studies) reported was a lack of knowledge or understanding about the disease, its complications related to nonadherence, and the treatment schedule. The following common patient-related barrier (7 studies) was the forgetfulness to take medicine. Reasons provided for the same were the patients' busy schedule, laziness, or forgetting to take the medication while traveling out-of-station. Patients have also reported certain misconceptions about the medicines like the risk of long-term neurological illness because of medication intake, inferior quality of drugs provided in hospitals, and wrong perception about stopping the medications once the patient feels normal. Patients in some studies have reported that they practice alternate systems of medicine such as herbal medicines and avoid taking allopathic medicines leading to poorer control of their condition. Substance use such as alcohol or tobacco use, side effects related to drugs, stress, and stigma were reported to be some of the barriers by the patients in adhering to the medications.

Family-related factors

The patients and providers have reported a lack of family support as a significant contributing factor for nonadherence. For example, there was a lack of support provided by family members or caregivers in reminding the patient to take medications or accompanying the patient for a visit to healthcare facilities. In addition, the lack of social and emotional support to the patients further contributes to the nonadherence among the patients suffering from CVDs and DM. Domestic works, personal priorities, commitments, or other issues hinder the family members from providing the above-mentioned support to the patients.

Health system-related factors

In most of these studies, providers were also interviewed to understand the factors related to the health system responsible for nonadherence among CVD and DM patients. Healthcare providers and patients interviewed in almost all these studies have reported affordability,

1
2
3 accessibility, and acceptability as the major factors hindering medication adherence.
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5 Affordability is an issue with patients seeking healthcare in private facilities and patients
6
7 getting care in public healthcare facilities. Though there is no direct medical cost related to
8
9 government hospitals or primary healthcare centres, direct non-medical costs such as transport
10
11 (due to poor accessibility) and indirect costs such as loss of wages (due to inconvenient
12
13 consultation timing) were higher amongst these patients. In addition, patients have a wrong
14
15 perception that medications in public facilities are of poorer quality, making them choose
16
17 private health facilities, including those belonging to lower socioeconomic status. Lack of risk
18
19 communication, counselling, or empathy by the physicians mainly due to overburdening public
20
21 health facilities and time constraints were the other health system-related barriers reported by
22
23 the providers and patients.
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28 **Facilitators in medication adherence**

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30 Facilitators in medication adherence were also summarized using the pre-existing thematic
31
32 framework (**Table-3**). In total, ten studies have explored the facilitators in medication
33
34 adherence from the patient or providers' perspective.
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36

37 *Patient-related factors*

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39 Most of the studies (5 studies) reported fear of complications due to nonadherence and self-
40
41 perception of being healthy (once they adhere to the medications) as the significant facilitators.
42
43 In addition, having a reminder system in the form of reminder notebook, separate
44
45 pillboxes/cases/covers or personalized shelf facilitate the patients in adhering to the
46
47 medications. Some studies have also reported that integrating drug intake into daily routine
48
49 activities and peer influence acts as a good facilitator in compliance with medications.
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53 *Family-related factors*

54
55 Family support was reported as a major facilitating factor for compliance with medication.
56
57 Apart from the support, adverse experiences in the past, such as death or severe complications
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3 among the family members, instilled fear in the patients, making them more compliant to the
4
5 medications.

6 7 *Health system-related factors*

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10 Barriers reported in some of the studies, such as empathy and counselling by healthcare
11
12 providers, were considered facilitators by the other studies' patients. Another major facilitator
13
14 from the health system side is the trust that patient has on their physician and follow the advice
15
16 related to self-care and adherence effectively. Other familiar facilitators reported by the patients
17
18 and providers were the dedicated pill cover/boxes for each drug provided in the clinic, linkage
19
20 of health services with NGO for provision of counselling and generating awareness, availability
21
22 of medication, and use of polypills.
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25 26 **Suggestions to improve medication adherence**

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28 Suggestions and solutions to enhance the compliance to medication were reported in 16 out of
29
30 the 18 included studies based on either patient or provider's perspective (**Table-4**). Few
31
32 suggestions were related to patients and family members, while the majority were related to
33
34 the change in the health system.
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37 38 *Patient and family-related factors*

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40 Creating or joining a peer support group was one of the major suggestions related to the
41
42 patients. This will help by motivating the patients to be more compliant with medications and
43
44 other self-care practices. Digital reminder systems using a watch and a mobile phone can also
45
46 improve medication adherence. Related to family members, social, emotional, and financial
47
48 support to the patients has been reported as an essential suggestion by most studies.
49
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51 52 *Health system-related factors*

53
54 Innovations in patient care have been necessitated as an important factor to promote drug
55
56 adherence. This is mainly because the barriers reported by the patients were almost similar
57
58 across the studies, and the interventions followed till now don't seem to address these issues.
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3 Some of the innovations suggested were dedicated days for specific disease conditions to avoid
4 overburdening the facilities, a dedicated counselling station for drug adherence during the
5 clinic with separate human resources as the physician has time constraints during the clinic,
6 and a unique pill dispensing mechanism like colour coding, etc. In addition, information
7 Education and Communication (IEC)/Behaviour change communication (BCC) campaigns,
8 digitalizing the patient treatment record, linkage of healthcare services with NGOs or
9 community-based organizations, regular training of healthcare workers, and promotion of
10 polypill use were other common suggestions offered by the healthcare providers.
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22 **Discussion**

23 We conducted this review to integrate the qualitative evidences on barriers and facilitators for
24 medication adherence among CVD and DM patients in India. We also further explored the
25 suggestions to improve the same. The studies included in our review involved a total of 636
26 participants (534 CVD and DM patients, 102 healthcare providers). Majority of the included
27 studies were of high quality with respect to study clarity, methodology and results. We
28 summarized under three major themes: barriers, facilitators, suggestions and reported the
29 findings under the following four sub-themes: patients, care team, healthcare organization and
30 environment-related factors.
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42 *Comparison of findings with previous literature*

43 *Barriers in medication adherence*

44 Major barriers were lack of patient's understanding about the disease and its complications,
45 forgetfulness and misconception about the medications. lack of family support was seen as a
46 major barrier from both patient's and provider's perspective. In addition to these factors, stress
47 and stigma were also mentioned as an important factor for the patients to not take medicine on
48 time. We also found major health system related barriers such as lack of accessibility,
49 availability, higher cost and poor physician attitude. These findings were in line with the
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2
3 previous review conducted among South East Asian DM patients.⁴⁰ In addition, our findings
4
5 were also similar to the patients belonging to non-English speaking Hispanic, South American
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7 ethnic group, as they also had misconceptions related to therapy, lack of understanding about
8
9 their condition, stress and stigma as a factor for non-adherence.⁴¹⁻⁴³
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12 *Facilitators in medication adherence*

14 Fear of complications, self-perception of being healthy, having a reminder system were
15
16 reported as the major facilitators by patients. Physician trust, advice, empathy, counselling was
17
18 some of the provider-related facilitators in adhering to medications. Common facilitators
19
20 reported by the patients and providers were the dedicated pill cover/boxes for each drug
21
22 provided in the clinic, availability of medication and use of polypills. These findings were also
23
24 in line with the previous qualitative reviews conducted in low middle-income countries
25
26 including India.⁴¹⁻⁴³
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30 *Suggestions to improve medication adherence*

32 The solutions provided by the patients and health professionals were in line with the barriers
33
34 identified in our review. Proper physician counselling to make the patients understand about
35
36 their own condition, complications and avoid misconception about the drugs and its side
37
38 effects, good family support, making the medication accessible and available free of cost were
39
40 suggested as major suggestions to improve medication adherence. Similar interventions were
41
42 also suggested by previous qualitative evidences on medication adherence among CVD and
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44 DM patients.⁴⁰⁻⁴³
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48 *Strengths and limitations of the study*

50 To the best of our knowledge, this is the first review exploring and synthesizing the qualitative
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52 factors associated with medication adherence among CVD and DM patients in India. We
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54 provided a comprehensive and systematic evidence on the barriers, facilitators related to
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56 medication adherence, adhering to the ENTREQ statement and ensuring transparency and
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3 reproducibility of our findings. We examined these evidences through the lenses of well-
4 established theoretical framework model. Moreover, our study was able to provide valuable
5 suggestions to promote the medication adherence from both patients and provider's
6 perspective. In addition to these strengths, we found that the highest rated studies contributed
7 to majority of the factors found in our review. This in turn ensures the transferability (external
8 validity) of our review findings.
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11 However, our review has certain limitations. We did not search the grey literature, possibly
12 missing some insights for our review. Hence, we cannot rule out of the dissemination bias with
13 respect to accurate and complete representation of phenomenon of interest. We focussed
14 primarily on the patient and provider perspective on medication adherence.⁴⁴ Hence, we cannot
15 comment on the organizational or political influences on the adherence to long-term therapies
16 as mentioned in the WHO report.¹⁶ The sample size of the included studies can be considered
17 as relatively low (median sample size - 30). However, all the studies were conducted till the
18 achievement of data saturation.
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20 *Implications for clinical and public health practice*

21
22 Improving medication adherence is essential to achieve better control and prevent life-
23 threatening complications. Factors related to patients such as self-awareness and fear about the
24 condition and its complications acted as major facilitator for medication adherence. We also
25 found certain modifiable barriers related to medical intake such as forgetfulness, lack of
26 knowledge, and misconception about medications. Interventions should focus on these
27 modifiable barriers such as knowledge barriers, intention barriers and health system-related
28 barriers to achieve better adherence. In addition, it is important for the family members to help
29 the patients in mapping the daily routine and link the medicine intake with these routines to
30 facilitate the adherence. Our review also suggested that healthcare providers play an important
31 role in promoting the medication adherence. Hence, the interventions should not only target
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3 the patients, but also the family members and healthcare providers and it should be tailored to
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5 the differences in setting, culture and type of the patients.
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8 *Implications for future research*
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10 More evidences need to be generated with respect to the solutions obtained in our review such
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12 as memory tools including the digital solutions, polypills, peer support groups etc. Further
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14 qualitative studies including the subgroup of patients with CVD and DM under different stages
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16 and treatment regimens and are required to contextualize the medication adherence. Exploring
17
18 the barriers using theoretical framework with the same methodological approach, can provide
19
20 a more reliable evidence to develop patient-centered interventions and achieve better control
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22 among CVD and DM patients.
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32 **Competing interests' statement:** None declared
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38 **Author contribution statement:** Conceived and designed the study: YK & SR, Data
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40 management and extraction: YK, SR and TR, Analysed the data and wrote the paper: YK, SR,
41
42 TR and MT, Provided comments and inputs to revise the manuscript: YK, SR, TR and MT
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45 **Data sharing statement:** Data will be available upon reasonable request by investigators
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48 **Word count:** 4070 (Being a Qualitative Evidence Synthesis we had to quote regarding the
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50 studies in our results and also we had elaborated the methods in an elaborate manner)
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Table 1: Characteristics of the studies included (N=18)

S.No	Author and year	State	Data collection method	Study participants	Study setting	Approach	Coding	Theoretical framework used	Method of analysis	Sample size	Mean Age in years	Study quality
1.	Agarwal 2019	Kerala	IDI	Clinical and administrative staff	Facility based	NR	Inductive	NR	Dedoose Software	21	NR	***
2.	Dhar et al 2016	Delhi	IDI	Hypertensive women aged 35-59 years	Community based	NR	Inductive	Yes	Manual content analysis	30	48	***
3.	George et al 2016	Karnataka	IDI	Physicians providing Non communicable disease care	Community based	NR	Inductive	NR	Manual content analysis	36	46	***
4.	Gupta et al 2019	Rajasthan	IDI	Hypertensive women	Facility based	NR	NR	NR	Manual content analysis	30	56	**
5.	Gupta et al 2020	Haryana	IDI	Hypertension patients	Facility based	NR	NR	NR	Manual content analysis	100	38-76	***
6.	Jayanna et al 2019	Karnataka	IDI & FGD	Diabetes and Hypertension patients	Facility based	NR	NR	Yes	Manual content analysis	10 IDI + 20 FGDs	NR	***
7.	Krishnamoorthy et al 2018	Puducherry	IDI & KII	Diabetes and Hypertension patients & Healthcare workers	Community based	NR	Inductive	NR	Manual content analysis	6 IDI + 4 KII	NR	***
8.	Kusuma et al 2010	Delhi	KII & FGD	Recent and Settled Migrants having hypertension inhabited in Delhi	Community based	NR	NR	NR	Manual content analysis	14 (KII) + 20 (FGD)	38 – 50 (KII) & 25 – 40 (FGD)	***
9.	Miller et al 2017	Delhi	IDI	Cardiovascular disease patients	Trial based	Descriptive	NR	NR	Manual content analysis	14	NR	***
10.	Newtonraj et al 2017	Tamil Nadu	Personal interviews	Hypertensive patients	Community based	NR	NR	NR	Manual content analysis	40	NR	**

11.	Nimesh et al 2019	Madhya Pradesh	IDI	Individuals with diabetes	Community based	NR	Inductive	Yes	Manual content analysis	60	52	***
12.	Patti et al 2020	Orissa	IDI	Primary care physicians	Facility based	NR	NR	NR	Manual content analysis	17	40	***
13.	Rani et al 2019	Tamil Nadu	FGD	Individuals with diabetes	Community based	Descriptive	NR	NR	Manual content analysis	50	50	**
14.	Salaam et al 2019	Andhra Pradesh	IDI	Patients with Cardiovascular disease	Community based	NR	NR	Yes	NVivo version 11 software	12	62	***
15.	Satish et al 2019	West Bengal	FGD	Patients with hypertension and/or diabetes	Trial based	NR	NR	Yes	Manual content analysis	70	53	***
16.	Thakur et al 2016	Chandigarh	IDI & FGD	Coronary artery disease patients	Facility based	NR	NR	NR	Manual Thematic analysis	20	NR	*
17.	Venkatesan et al 2018	Tamil Nadu	IDI	Health care workers	Community based	NR	NR	NR	Anthropac software	10	NR	***
18.	Wood et al 2015	Hyderabad and Delhi	IDI	Patients with Cardiovascular diseases	Trial based	NR	NR	Yes	Nvivo software	52	57	***

NR – Not Reported

IDI – In depth Interview

FGD – Focussed Group Discussion

KII – Key informant interview

Table 2: Thematic framework analysis for summarizing barriers in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Barriers in Medication Adherence	Studies
PATIENTS	1. Lack of awareness/knowledge: Lack of knowledge and understanding about the disease, its complications and treatment among the patients	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Patti et al 2020, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Forgetfulness: Patients forget to take medicine because of busy schedule	Dhar et al 2016, Gupta et al 2019, Gupta et al 2020, Rani et al 2019, Venkatesan et al 2018, Wood et al 2015, Tan et al 2017, Thakur et al 2016
	3. Misconception about medications: Patient has wrong perception about the medications, especially about its side effects and quality	George et al 2016, Gupta et al 2020, Patti et al 2020, Rani et al 2019, Salaam et al 2019, Tan et al 2017, Venkatesan et al 2018
	4. Preference to alternate system of medicine: Patients prefers taking herbal and other alternate system of medicines for their condition	George et al 2016, Tan et al 2017, Venkatesan et al 2018
	5. Ill effects of substance abuse: Patients have difficulty in adhering to medications during the bout of tobacco or alcohol consumption	Jayanna et al 2019, Krishnamoorthy et al 2018
	6. Effect of side effects: Patients stop their medication once they develop side effects related to the drugs	Venkatesan et al 2018, Wood et al 2015
	7. Stress: Patients developing stress due to personal or work-related problems are more non-adherent to medications	Krishnamoorthy et al 2018
	8. Stigma: Patients feel stigmatised in revealing their disease status to other family/friends leading to lack of support from them	Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Lack of physical, emotional and social support as the family members are pre-occupied with domestic works, crisis, other priorities and commitments	Dhar et al 2016, George et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Rani et al 2019, Wood et al 2015
	2. Risk communication: Poor risk communication or counselling to patients and family members about non-adherence to medication by the treating physicians	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Thakur et al 2016
	3. Physician attitude: Lack of respect, empathy, communication and attention towards patients by the treating physicians	Dhar et al 2016, Gupta et al 2019, Kusuma et al 2010, Jayanna et al 2019

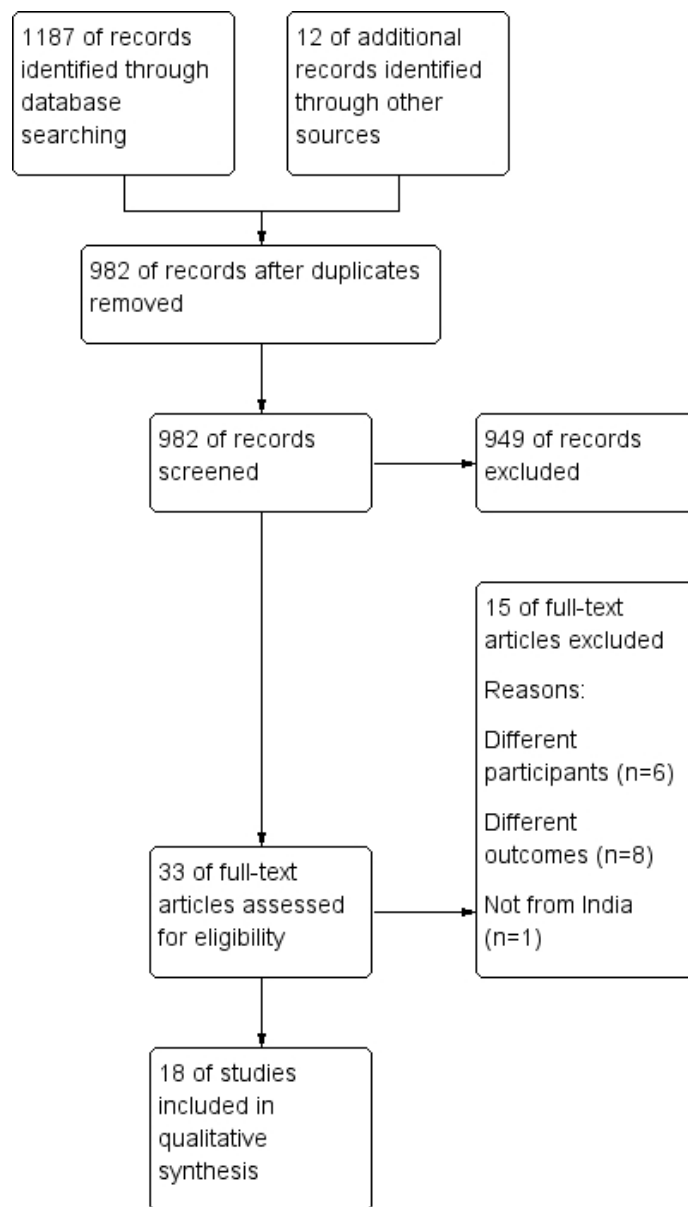
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Affordability: Patients lose their daily wages due to inconvenient consultation timings in public facilities, which is aggravated by travel costs due to poor access, and higher medication costs while preferring private facilities	Agarwal et al 2019, Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Nimesh et al 2019, Salaam et al 2019, Satish et al 2019, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Accessibility: Lack of access to healthcare facilities (more distance) requiring longer travel and waiting time.	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	3. Availability: Non-availability of essential medicines in public healthcare facilities	Dhar et al 2016, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Salaam et al 2019, Wood et al 2015
	4. Acceptability: Medications from public health facilities are not acceptable to the patients due to poorer quality	
	5. Overburdening of primary health centres: Burdening of primary health facilities lead to time constraints in patient counselling regarding medication adherence	Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Venkatesan et al 2018

Table 3: Thematic framework for summarizing facilitators in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Facilitators in Medication Adherence	Studies
PATIENTS	1. Self-awareness and fear: Patient's understanding about medicine adherence and fear about complications of non-adherence keeps them healthy	Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Satish et al 2019, Tan et al 2017, Wood et al 2015
	2. Medicine Reminder system: Separate pill boxes/cases/covers, personalized shelf, and maintaining drug record notebook helps them in remembering daily doses	Dhar et al 2016, Krishnamoorthy et al 2018, Miller et al 2017, Tan et al 2017
	3. Integrating drug intake with the daily routine: Fixed time for medicine intake, separate place for keeping drug, and making arrangements during travel helps them in adherence	Dhar et al 2016, Krishnamoorthy et al 2018
	4. Positive peer influence: Good adherence to medication by the patient's peers motivates the patient to be compliance to their own drug intake	Gupta et al 2019, Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Constant reminders by family members for drug intake	Dhar et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Miller et al 2017, Wood et al 2015
	2. Past adverse experiences: Death of patients' own family members due to complications of the condition has motivated them to adhere to medication	Dhar et al 2016, Krishnamoorthy et al 2018
	3. Healthcare provider counselling and empathy: Patients described that counselling from their healthcare providers has motivated them to remain adherent	Kusuma et al 2010, Miller et al 2017, Patti et al 2020, Salaam et al 2019, Tan et al 2017
	4. Trust in physician: Adherence is more when a positive rapport and trust is established between the patient and health care providers.	Dhar et al 2016, Krishnamoorthy et al 2018, Satish et al 2019
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Dedicated pill boxes/covers: Provision of different medications in separate boxes/covers in the healthcare facility has helped as the patient to remember which medication to take at what time	Krishnamoorthy et al 2018, Wood et al 2015
	2. Combination drugs (polypills): Polypills had the following advantages to facilitate the medication adherence: a smaller number of pills, lower frequency, less chance of forgetting, potential for lower cost, and convenient simpler regimen	Salaam et al 2019, Wood et al 2015
	3. Availability of medications: Proper pharmacy inventory control and stock delivery has aided in medication adherence	Miller et al 2017
ENVIRONMENT (Regulatory, market and policy framework)	1. NGO Support: Patients has reported that sharing their concerns and receiving counselling from NGO/ Health officers acted as a facilitator for drug intake	Tan et al 2017, Wood et al 2015

Table 4: Thematic framework for summarizing suggestions to improve medication adherence among CVD & DM patients in India

Main theme/Sub-themes	Suggestions to improve medication adherence	Studies
PATIENTS	1. Peer support groups: Patients can motivate each other by forming support groups among themselves	Krishnamoorthy et al 2018
	2. Digital reminder system: Patient can use digital reminders such as watch, mobile phone to adhere to their drug schedule	Krishnamoorthy et al 2018, Miller et al 2017
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Social support: Family members can be educated and asked to provide support by reinforcing compliance, reminding about drug intake, motivating them patients to avoid substance abuse	Agarwal et al 2019, Dhar et al 2016, Krishnamoorthy et al 2018, Nimesh et al 2019, Wood et al 2015
	2. Financial support: Family members can provide financial support to cover the cost of medications, travel etc.	Gupta et al 2019
	3. Regular training of healthcare workers: Physicians and other healthcare workers involved in prescribing drugs and counselling should undergo regular training on standard treatment protocols	George et al 2016, Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019
	4. Team work approach: Integration of AYUSH, mental health counsellors, physiotherapist and geriatric clinics at primary healthcare level	George et al 2016, Miller et al 2017, Patti et al 2020
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Innovations in patient care: Healthcare workers can make innovations like dedicated day for specific conditions (diabetes day, etc), dedicated counselling station/session with additional staff for detailing the importance of adherence and complications related to non-adherence, unique pill dispensing mechanism (colour coding)	Agarwal et al 2019, Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Satish et al 2019, Venkatesan et al 2018, Wood et al 2015
	2. IEC/BCC/Awareness campaigns: Putting up of IEC materials and conducting campaigns on importance of adherence in public places and workplaces	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Newtonraj et al 2017, Patti et al 2020, Rani et al 2019
	3. Digitalizing patient treatment record: Digitalizing a dedicated treatment record for each patient can help in better follow-up of the patient and improve adherence	Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019, Wood et al 2015
	4. Polypills: Disseminating the advantages of polypills to healthcare professionals by CME/conferences and patients by public education campaigns; Integration of polypills into clinical practice. etc	Salaam et al 2019, Wood et al 2015
ENVIRONMENT (Regulatory, market and policy framework)	1. Linkage of health services with NGO and community-based organizations: Community members, volunteers, anganwadi workers, self-help groups and NGO workers can be trained in counselling the patients to improve medication adherence	Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Tan et al 2017



141x246mm (72 x 72 DPI)

Supplementary Table 1 Search strategy

Key word	Alternative word
Qualitative studies	((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))
Medication Adherence	((((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])
Barriers, Facilitators and solutions	Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions
Diabetes mellitus and CVDs	((((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))

India	(India[MeSH Terms] OR Republic of India[MeSH Terms]))
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Search results (PubMed):

(((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms])) AND (((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms]) OR Life Change Events[MeSH Terms]) OR Trust[MeSH Terms]))) AND (((((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms])) AND (India[MeSH Terms] OR Republic of India[MeSH Terms])) – 199 (Filters: Years between 2010 and 2020 and English language publication)

((((((((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))) AND (((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])) AND (Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions)) AND ((((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))) AND ((India[MeSH Terms] OR Republic of India[MeSH Terms])) – 31 results (Filters: Years between 2010 and 2020 and English language publication)

Google scholar: 635 + 22 + 6 + 12 = 675

1
2
3 **ScienceDirect:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
4 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 238 articles
5

6 **Cochrane library:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
7 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 34 articles
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Patient and Provider's perspective on barriers and facilitators for medication adherence among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A qualitative evidence synthesis

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3 1 **Patient and Provider's perspective on barriers and facilitators for medication adherence**
4
5 2 **among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A**
6
7 3 **qualitative evidence synthesis**

8
9
10 4 **Running head:** Barriers and facilitators for medication adherence among CVD and DM
11
12 5 patients in India

13
14
15 6 **Article category:** Systematic Review

16
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14
15 6 **Key messages:**

- 16
17 7 • This is the first review exploring factors associated with drug adherence among CVD
18 & DM patients in India
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20 8
21 9 • Patient-related barriers were lack of knowledge about their condition, forgetfulness,
22 stigma and stress
23
24 10
25 11 • Care team-related barriers were lack of family support, risk communication and
26 physician attitude
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28 12
29 13 • Health system-related barriers were accessibility, affordability, availability and
30 acceptability
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32 14
33 15 • Solutions to address these barriers were peer support group, digital reminders and
34 innovations in patient care
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41 17 **Abstract:**

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43 18 **Objective:**

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46 19 To explore the various stakeholders' perspectives on barriers and facilitators for medication
47 adherence among CVD and DM patients in India.

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50 21 **Methods:**

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52 22 A comprehensive systematic search was conducted in Medline, Cochrane library, Science
53 Direct and Google Scholar from January 2010 to July 2020. We used the framework of the
54 systems approach for healthcare delivery to conduct thematic analysis, using published
55 23
56 24
57 25 qualitative literature to derive relevant themes, sub-themes and codes.

1 **Setting:** A Qualitative Evidence Synthesis of qualitative published studies from India

2 **Subjects:** A Qualitative Evidence Synthesis of the available qualitative evidence on the
3 barriers and facilitating factors for medication adherence among CVD and DM patients in India

4 **Results:**

5 In total, 18 studies were included. Major barriers reported were lack of understanding about
6 the disease, complications related to non-adherence, followed by forgetfulness, lack of family
7 support and risk communication. Health system-related barriers such as accessibility,
8 affordability, and acceptability were also reported by majority of the studies. Creation of peer
9 support group, digital reminder system, integration of AYUSH, mental health, physiotherapy
10 and geriatric clinics at primary healthcare level and innovations in patient care were suggested
11 to counter these barriers in medication adherence.

12 **Conclusion:**

13 Such patient-specific targeted interventions needs to be developed to achieve better control
14 among CVD and DM patients.

15 **Keywords:** Cardiovascular Diseases, Diabetes Mellitus, Medication Adherence, Qualitative
16 Research

17

1 INTRODUCTION

2 Cardiovascular diseases (CVDs) are the leading cause of mortality globally and in India.^{1,2}
3 More than a quarter (28%) of all deaths in India are attributable to CVDs with Ischemic heart
4 disease (IHD) and stroke constituting the majority (83%).³ On the other hand, India ranks
5 second after China in the global diabetes epidemic, with a prevalence of around 10%.⁴ Both
6 diabetes mellitus (DM) and hypertension have long been recognized as independent risk factors
7 for CVDs, whereas adherence to prescribed hypoglycaemic and antihypertensive drug
8 therapies have significantly reduced the risk.⁵⁻⁸ At least half of hypertensive & DM patients
9 stop taking their medication within a year, often without informing their provider. With further
10 non adherence and attrition over time, medication adherence has emerged as a significant
11 public health priority.⁹

12 Medication adherence is defined as the extent to which a person's behaviour coincides with the
13 agreed medication regimen or health advice from a health care provider.¹⁰ It has three
14 components: initiation (when the patient takes the first dose of prescribed medication),
15 implementation (the extent to which a patient's actual dosing corresponds to the prescribed
16 dosing regimen), and discontinuation (when no more doses are taken after that).¹¹ Medication
17 adherence is of growing interest to clinicians, healthcare systems, and other stakeholders (e.g.,
18 payers). There is soaring evidence that establishes nonadherence is often associated with lower
19 quality of life, adverse clinical events, increased need for medical interventions, mortality, and
20 thus giving rise to avoidable out-of-pocket expenditure in health.¹² Non-adherent hypertensive
21 and stable coronary heart disease (CHD) patients have a four to five times higher risk of
22 developing CHD and death, when compared to adherent patients.^{13,14} Similarly, the likelihood
23 of hospitalization is doubled among DM & hypertensive patients who are non-adherent to
24 prescribed therapies compared to the general population. Despite recent advancements in
25 pharmacologic treatment and technology to treat and monitor DM and CVD patients,

1 medication adherence is of particular concern in low-and-middle-income countries (LMIC)
2 like India, where accessibility and affordability are still issues.^{3,15}
3 Barriers to adherence can be comprehended as the patient, medication, provider, and health
4 system factors, with interactions among them.^{16,17} Patient factors that influence adherence
5 include poor health literacy, cultural beliefs regarding medication effectiveness, and religious
6 healing practices.¹⁷ Low income, forgetting to take medication, and perceptions regarding pills
7 like safety concerns, convenience, and necessity add to the above list.^{16,17} Inadequate
8 knowledge about a drug and its use, not being convinced of the need for medication, fear of
9 adverse effects, and long-term treatment regimens also prompt medication discontinuation.¹⁵
10 Clinician factors cover failure to recognize nonadherence, prescription of complex and
11 multidrug regimens, ineffective communication of benefits of medications, and excluding
12 patients in the treatment decision-making process.¹⁷ Health system factors comprise limited
13 insurance coverage, poor coordination of care between inpatient and outpatient settings, and
14 inadequate communication between prescribers (i.e., specialists and primary care clinicians).
15 In addition, the caregivers' aspect also becomes relevant in determining patients' adherence as
16 CVD patients with a caregiver are more likely to be adherent to medications.¹⁸ Hence
17 identifying specific barriers for each patient and adopting suitable techniques to overcome them
18 is imperative to improve medication adherence. Some of the facilitators successful in
19 overcoming these barriers include a personal medication counsellor in the care continuum to
20 guide patients with medication use, single-pill fixed-dose combinations, training pharmacists
21 as coaches for drug therapies, building peer groups for chronic conditions, and developing
22 information systems in the follow-up of patients.¹⁹
23 Quantitative studies have focused on medication adherence incidence, and identification of its
24 potential risk factors. They do not, however, uncover life circumstances that may influence
25 adherence from the patient perspective. The inclusion of qualitative studies in our review will

1
2
3 1 provide a better understanding of the barriers and facilitators from the perspective and
4
5 2 experiences of patients, healthcare providers, and caregivers.²⁰ Qualitative evidence synthesis,
6
7 3 a novel research method, brings together the available qualitative evidence from primary
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9 4 studies through a systematic review process. Despite the evidence obtained from primary
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11 5 qualitative studies could be conceptually richer, a qualitative evidence synthesis can aid us in
12
13 6 getting an overall view of the findings, and help us in addressing subtle and sensitive issues
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15 7 that most primary studies encounter. The findings from a qualitative evidence synthesis can
16
17 8 guide us in crucial making policy recommendations in health care, retaining the impact of
18
19 9 individual studies and group experiences. ²¹ Therefore, the current review was done to
20
21 10 understand the perspective of various stakeholders (patients, caregivers, and healthcare
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23 11 providers) on the barriers and facilitators for medication adherence among CVD and DM
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25 12 patients in India. We also explored the suggestions and solutions provided by these
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27 13 stakeholders in overcoming the reported barriers.
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34 **METHODS**

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37 15 This review was performed by adhering to the “enhancing transparency in reporting the
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39 16 synthesis of qualitative research (ENTREQ)” statement.²² We registered our protocol in the
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41 17 PROSPERO database (Registration number - CRD42020199529). We also searched
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43 18 PROSPERO and Cochrane to ensure that no similar review protocol has been reported. We
44
45 19 also performed a preliminary search to ensure that no previous reviews of our similar topic
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47 20 targeting the Indian population were published.
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51 **Study design**

52
53 22 We performed an evidence synthesis of the available qualitative evidence on the barriers and
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55 23 facilitating factors for medication adherence among CVD and DM patients. This review would
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1 help to aggregate the evidence of peer-reviewed articles in this field and build an organized
2 empirical research outline based on prior knowledge.

3 ***Eligibility criteria***

4 *Study type*

5 We have included qualitative peer-reviewed studies conducted in India for our current review.
6 Furthermore, qualitative evidence from other mixed methods studies was screened for
7 eligibility and included in the qualitative component was relevant to our review. In addition,
8 we included studies using qualitative techniques for data collection such as focussed group
9 discussion (FGD), in-depth interviews (IDI), and Key Informant Interviews (KII).

10 *Participant type*

11 We have included the studies reporting the barriers and facilitators of medication adherence
12 from patients' perspectives (CVD and DM), family members, healthcare workers (HCWs), or
13 health system policymakers in India. HCWs were defined as per WHO recommendation as "all
14 the persons involved in the actions whose primary intent is to enhance the health."²³

15 *Outcome*

16 The phenomenon of interest in our review was to explore the barriers and facilitators for
17 medication adherence among CVD and DM patients in India. We also explored the possible
18 suggestions and solutions to address the barriers and improve compliance, as experienced by
19 the patients, caregivers, family members, HCWs, and other relevant stakeholders.

20 ***Exclusion criteria***

21 We have excluded the studies not available in English, books or conference abstracts or grey
22 literature, or editorial comments. We have also excluded the studies reporting only quantitative
23 data such as cross-sectional surveys, case-control, cohort studies, or intervention trials.

24 ***Search strategy***

1 We have conducted a comprehensive and systematic search in databases and search engines
2 such as Medline, Cochrane library, ScienceDirect, and Google Scholar. A combination of
3 medical subject heading (MeSH) and free-full text terms were used for carrying out a literature
4 search. The detailed search strategy and search results in the databases mentioned above and
5 search engines are provided in Supplementary File 1. In addition to this, we also checked the
6 reference list of primary studies obtained via electronic search and included articles relevant to
7 our review and analysis. The search was conducted in all the databases from January 2010 to
8 July 2020 with English language restriction for publication. Furthermore, the search timeline
9 was restricted to ensure that our work provides a broader view and identifies the emerging
10 issues.

11 **Study selection process**

12 Two investigators (YK and TR) independently performed the literature search, screened the
13 title and abstract of all the identified studies, and retrieved the full text for articles relevant to
14 our review. Further full-text screening of the retrieved articles was done again independently
15 by the two investigators (YK, TR) to select the studies matching the eligibility criteria of our
16 review. Disagreements during this process between the two investigators were resolved
17 through consultation with a third investigator (SR).

18 **Data Extraction and Management**

19 After the study selection, two investigators (YK and TR) independently extracted the relevant
20 data and study characteristics onto a predetermined data extraction format. Data entry was
21 double-checked for accuracy by a third investigator (SR) by comparing the data presented in
22 the review and individual study reports. As a result, we have extracted the following study
23 characteristics: general information such as the name of the first author, the country in which
24 the study was done, and year of publication, in the methods section, data collection period,
25 study design, study participants, sample size, sampling technique, and data collection

1 procedure. In addition, barriers, facilitators, suggestions, and solutions to medication adherence
2 were identified systematically.

3 **Quality assessment**

4 Two investigators (YK and SR) independently performed the quality check using the Critical
5 Appraisal Skills Programme (CASP) criteria.²⁴ This checklist has been widely used for
6 assessing the quality of studies included in this Qualitative Evidence synthesis.²⁵ This has
7 helped determine whether the studies included are coherent with the quality appraisal standard
8 for qualitative studies. This checklist consists of 10 questions concerning the study's clarity,
9 methodology, and results to rank the included studies. Subsequently, these studies were
10 stratified into high quality (three stars for studies scoring 8 to 10 points), medium quality (two
11 stars for studies scoring 4 to 7 points), and low rate (one star for studies scoring 0 to 3 points).
12 We did not exclude the low-quality studies, but the interpretation of results was made with
13 caution. Disagreements during the quality assessment process were resolved by discussion with
14 the third investigator (TR).

15 **Data Analysis**

16 We analysed and reported the findings in separate clusters such as patients, caregivers, family
17 members, HCWs, and policymakers to demonstrate the differences among these subgroups.
18 We have adopted a thematic framework analysis to analyse and synthesize the data. Thematic
19 framework analysis has been helpful as the evidence was primarily descriptive and improved
20 our understanding of the barriers and facilitators in medication adherence among CVD and DM
21 patients. This framework synthesis has five stages of synthesizing the qualitative data.

22 ***First stage - Familiarisation with the data:*** Primary investigator (YK) did the process of
23 familiarisation with data by reviewing all the selected articles against the objective of our
24 review and found the recurrent themes across the included studies.

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2
3 1 **The second stage - Identifying the thematic framework:** The investigators used a
4
5 2 predetermined thematic framework developed using literature to guide the thematic analysis.
6
7 3 The final framework comprised of a detailed list of facilitators and barriers for medication
8
9 4 adherence and also solutions to address the issue.

10
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12 5 **Third stage - Indexing:** Two independent investigators (YK and SR) read the extracted
13
14 6 information and searched for themes as per the predetermined thematic framework and found
15
16 7 additional emerging themes. The framework underwent several revisions as and when a new
17
18 8 theme emerged. This has been performed through discussion and agreement between the entire
19
20 9 team of investigators. Next, all the studies were completely read and examined till there was
21
22 10 no new emergent theme. Coding of the data was then done as per the themes identified in our
23
24 11 analysis. Finally, each preliminary study indexing was done using the codes related to the
25
26 12 thematic framework. Whenever appropriate, sections of the studies were indexed with one or
27
28 13 more codes.

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33 14 **Fourth stage - Charting:** The investigators have sorted the data based on the themes and
34
35 15 presented these themes in the tabular format (chart). The rows and columns of the table indicate
36
37 16 the themes related to the studies, which enabled us to compare the study findings across various
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39 17 themes and subthemes.

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42 18 **Fifth stage - Mapping and interpretation:** The investigators used these charts to define the
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44 19 concepts identified, and mapped the nature and range of the phenomena. Our review explored
45
46 20 the associations between the various themes and helped in clarifying the findings. Finally, we
47
48 21 mapped and interpreted the findings in line with our objectives and emergent themes.

52 **Results**

56 **Study selection**

1 A comprehensive and systematic search was done to identify the relevant studies from January
2 2010 to July 2020. In total, we identified 1187 citations, and after the removal of duplicates
3 from multiple databases, 982 records were screened for their title and abstract and assessed for
4 eligibility. From these records, we retrieved 33 articles, and after going through the full text of
5 these articles, 18 studies were included in the review. (**Figure 1**).²⁶⁻⁴³

6 **Characteristics of the studies included**

7 Characteristics of the included studies are reported in **Table 1**. Of the 18 studies included, 9
8 (50%) were from the Southern region, followed by 7 (38%) from the Northern part of India.
9 The mean age of the participants ranged from 25-76 years. The typology of the studies
10 comprised of in-depth interviews (IDIs) and focussed group discussions (FGDs). The study
11 participants were primarily patients with diabetes, hypertension, or any cardiovascular diseases
12 (to explore the patient perspective), and health care workers (4 studies) providing care to them
13 (to obtain the provider perspective). The total sample size of the included studies ranged from
14 6 to 100. The majority (10 of the included studies) were done in a community setting, while
15 the rest were either facility-based or had participants from ongoing trials. Four of the included
16 studies used software for analysing the qualitative data, while the rest followed manual
17 methods. Most of the included studies (14 out of 18) had higher ratings indicating high-quality
18 evidence.

19 **Narrative synthesis**

20 Significant findings from the review showed that factors contributory to adherence come under
21 three themes: patient-related, family-related, and health system-related factors. The barriers,
22 facilitators, and suggestions to improve medication adherence were summarized under these
23 three themes.

24 **Barriers in medication adherence**

1 **Table-2** shows the thematic framework analysis related to barriers in medication adherence
2 among CVD and DM patients. All the 18 included studies have explored and reported on these
3 barriers.

4 *Patient-related factors*

5 Significant patient-related barriers (10 studies) reported were lack of knowledge or
6 understanding about the disease, its complications related to nonadherence, and the treatment
7 schedule, followed by forgetfulness to take medicine (7 studies). Reasons provided for the same
8 were the patients' busy schedule, laziness, or forgetting to take the medication while traveling
9 out-of-station. Patients have also reported certain misconceptions about the medicines like the
10 risk of long-term neurological illness because of medication intake, inferior quality of drugs
11 provided in hospitals, and wrong perception about stopping the medications once the patient
12 feels normal. Patients in some studies have reported that they practice alternate systems of
13 medicine such as herbal medicines and avoid taking allopathic medicines leading to poorer
14 control of their condition. Substance use such as alcohol or tobacco use, side effects related to
15 drugs, stress, and stigma were reported to be other barriers

16 *Family-related factors*

17 The patients and providers have reported a lack of family support as a significant contributing
18 factor for nonadherence. In addition, the lack of social and emotional support to the patients
19 further contributes to the nonadherence among the patients suffering from CVDs and DM.
20 Domestic works, personal priorities, commitments, or other issues hinder the family members
21 from providing the above-mentioned support to the patients.

22 *Health system-related factors*

23 In most of these studies, providers were also interviewed to understand the factors related to
24 the health system responsible for nonadherence among CVD and DM patients. Healthcare
25 providers and patients interviewed, in almost all these studies, have reported affordability,

1 accessibility, and acceptability as the major factors hindering medication adherence.
2
3 Affordability is an issue with patients seeking healthcare in private facilities and patients
4
5 getting care in public healthcare facilities. Though there was no direct medical cost related to
6
7 government hospitals or primary healthcare centres, direct non-medical costs such as transport
8
9 (due to poor accessibility) and indirect costs such as loss of wages (due to inconvenient
10
11 consultation timing) were higher amongst these patients. In addition, patients have a wrong
12
13 perception that medications in public facilities are of poorer quality, making them choose
14
15 private health facilities, including those belonging to lower socioeconomic status. Lack of risk
16
17 communication, counselling, or empathy by the physicians mainly due to overburdening public
18
19 health facilities and time constraints were the other health system-related barriers reported by
20
21 the providers and patients.
22
23

24 **Facilitators in medication adherence**

25 Facilitators in medication adherence were also summarized using the pre-existing thematic
26
27 framework (**Table-3**). In total, ten studies have explored the facilitators in medication
28
29 adherence from the patient or providers' perspective.
30
31

32 *Patient-related factors*

33 Most of the studies (5 studies) reported fear of complications due to nonadherence and self-
34
35 perception of being healthy (once they adhere to the medications) as the significant facilitators.
36
37 In addition, having a reminder system in the form of a reminder notebook, separate
38
39 pillboxes/cases/covers or personalized shelf facilitate the patients in adhering to the
40
41 medications. Some studies have also reported that integrating drug intake into daily routine
42
43 activities and peer influence acts as a good facilitator in compliance with medications.
44
45

46 *Family-related factors*

47 Family support was reported as a major facilitating factor for compliance with medication.
48
49 Apart from the support, adverse experiences in the past, such as death or severe complications
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1 among the family members, instilled fear in the patients, making them more compliant to the
2 medications.

3 *Health system-related factors*

4 Barriers reported in some of the studies, such as empathy and counselling by healthcare
5 providers, were considered facilitators by the other studies' patients. Another major facilitator
6 from the health system side is the trust that patient has in their physician and their willingness
7 to effectively follow advice related to self-care and adherence. Other familiar facilitators
8 reported by the patients and providers were the use of dedicated pill cover/boxes for each drug
9 provided in the clinic, linkage of health services with NGO for provision of counselling and
10 generating awareness, availability of medication, and use of polypills.

11 **Suggestions to improve medication adherence**

12 Suggestions and solutions to enhance the compliance to medication were reported in 16 out of
13 the 18 included studies based on either patient or provider's perspective (**Table-4**). Few
14 suggestions were related to patients and family members, while the majority were related to
15 the change in the health system.

16 *Patient and family-related factors*

17 Creating or joining a peer support group was one of the major suggestions related to the
18 patients. This will help by motivating the patients to be more compliant with medications and
19 other self-care practices. Digital reminder systems using a watch and a mobile phone can also
20 improve medication adherence.

21 *Health system-related factors*

22 Innovations in patient care, have been necessitated as an important factor to promote drug
23 adherence. Some of the innovations suggested were dedicated days for specific disease
24 conditions to avoid overburdening the facilities, a dedicated counselling station for drug
25 adherence during the clinic with separate human resource, and a unique pill dispensing

1
2
3 1 mechanism like colour coding, etc. In addition, Information Education and Communication
4
5 2 (IEC)/Behaviour change communication (BCC) campaigns, digitalizing the patient treatment
6
7 3 records, linkage of healthcare services with NGOs or community-based organizations, regular
8
9 4 training of healthcare workers, and promotion of polypill use were other common suggestions
10
11 5 offered by the healthcare providers.
12
13

14 6 **Discussion**

15
16
17 7 We conducted this review to integrate the qualitative evidence on barriers and facilitators for
18
19 8 medication adherence among CVD and DM patients in India. We also further explored the
20
21 9 suggestions to improve the same. The studies included in our review involved a total of 636
22
23 10 participants (534 CVD and DM patients, 102 healthcare providers). The majority of the
24
25 11 included studies were of high quality with respect to study clarity, methodology and results.
26
27 12 We summarized under three major themes: barriers, facilitators, suggestions and reported the
28
29 13 findings under the following four sub-themes: patients, care team, healthcare organization and
30
31 14 environment-related factors.
32
33

34 15 *Comparison of findings with previous literature*

35 16 *Barriers in medication adherence*

36
37
38 17 Major barriers were lack of patient's understanding about the disease and its complications,
39
40 18 forgetfulness and misconception about the medications. Lack of family support was seen as a
41
42 19 major barrier from both patient's and provider's perspectives. In addition to these factors, stress
43
44 20 and stigma were also mentioned as important factors among patients to not take medicine on
45
46 21 time. In addition to the above, medication adherence could also be highly hindered by the
47
48 22 patients' cultural beliefs, perceived discrimination, and social customs, which are highly
49
50 23 prevalent in a culturally influenced country like India. A few studies have also shown evidence
51
52 24 of improvisation in medication adherence where efforts were taken to overcome the cultural
53
54 25 barriers.⁴⁴ We also found major health system-related barriers were lack of accessibility and
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1
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3 1 availability, higher cost of medications and poor physician attitude. These findings were in line
4
5 2 with the previous review conducted among South-East Asian DM patients.^{44,46} In addition, our
6
7 3 findings about patients related factors were found to be similar to other patients belonging to
8
9 4 non-English speaking Hispanic, South American ethnic groups, as they also had
10
11 5 misconceptions related to therapy, lack of understanding about their condition, with additional
12
13 6 stress and stigma as a factor for non-adherence.⁴⁷⁻⁴⁹
14
15
16

17 *Facilitators in medication adherence*

18
19 8 Fear of complications, self-perception of being healthy, having a reminder system were
20
21 9 reported as major facilitators by patients. Physician trust, advice, empathy, and counselling
22
23 10 were the other provider-related facilitators in adhering to medications. Common facilitators as
24
25 11 reported by the patients and providers were: dedicated pill cover/boxes for each drug provided
26
27 12 in the clinic, availability of medication and use of polypills. These findings were also in line
28
29 13 with the previous qualitative reviews conducted in low middle-income countries including
30
31 14 India.⁴⁷⁻⁵⁰
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35 *Suggestions to improve medication adherence*

36
37 16 The solutions provided by the patients and health professionals were in line with the barriers
38
39 17 identified in our review. Proper physician counselling to make the patients understand their
40
41 18 own condition, complications of the disease and avoid misconception about the drugs and their
42
43 19 side effects, good family support, making the medication accessible and available free of cost
44
45 20 were suggested as major suggestions to improve medication adherence. Similar interventions
46
47 21 were also suggested by previous qualitative evidence on medication adherence among CVD
48
49 22 and DM patients.⁴⁵⁻⁴⁹ It is also interesting to note that medication adherence is also hurdled by
50
51 23 the patients' intention towards adherence, and this intention might vary across nations and
52
53 24 cultural groups. The patient's intention not to refill prescriptions due to cost, not to take
54
55 25 medication because the patient feels better, also influence the patient's decision. Thus future
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1 research exploring these reasons on patient's choice to adhere or not, rather than an inability to
2 adhere (e.g., forgetting, no access) needs to be encouraged.

3 *Strengths and limitations of the study*

4 To the best of our knowledge, this is the first review exploring and synthesizing the qualitative
5 factors associated with medication adherence among CVD and DM patients in India. We have
6 provided comprehensive and systematic evidence on the barriers, facilitators related to
7 medication adherence, adhering to the ENTREQ statement and ensuring transparency and
8 reproducibility. We examined this evidence through the lenses of a well-established theoretical
9 framework model. Moreover, our study was able to provide valuable suggestions to promote
10 medication adherence from both patients and provider's perspectives. In addition to these
11 strengths, we found that the highest-rated studies contributed to the majority of the factors
12 found in our review. This in turn ensures the transferability (external validity) of our review
13 findings.

14 However, our review has certain limitations. We did not search grey literature, possibly missing
15 some insights for our review. Hence, we cannot rule out of the dissemination bias with respect
16 to accurate and complete representation of the phenomenon of interest. We focussed primarily
17 on the patient and provider perspective on medication adherence.⁵¹ Hence, we cannot comment
18 on the organizational or political influences on the adherence to long-term therapies as
19 mentioned in the WHO report.¹⁶ The sample size of the included studies can be considered
20 relatively low (median sample size - 30). However, all the studies were conducted till the
21 achievement of data saturation. In addition to the above, these results and suggestions need to
22 be considered after taking into account India's cross-cultural adaptations, customs, linguistic
23 variations and genetic susceptibility and higher prevalence of risk factor profile.

24 *Implications for clinical and public health practice*

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2
3 1 Improving medication adherence is essential to achieve better control and prevent life-
4
5 2 threatening complications. Factors related to patients such as self-awareness and fear about the
6
7 3 condition and its complications acted as a major facilitator for medication adherence. We also
8
9 4 found more modifiable barriers related to medication intakes such as forgetfulness, lack of
10
11 5 knowledge, and misconception about medications. Interventions should focus on these
12
13 6 modifiable barriers such as knowledge barriers, intention barriers and health system-related
14
15 7 barriers to achieve better adherence. In addition, it is important for the family members to help
16
17 8 the patients in mapping their daily routine and link the medicine intake with these routines to
18
19 9 facilitate adherence. Our review also suggested that healthcare providers play an important role
20
21 10 in promoting medication adherence. Hence, the interventions should not only target the patients
22
23 11 but also the family members and healthcare providers and they should be tailored to suit
24
25 12 differences in setting, culture and type of the patients.

31 *Implications for future research*

32
33 14 More evidence need to be generated with respect to the solutions obtained in our review such
34
35 15 as memory tools including the digital solutions, polypills, peer support groups etc. Further
36
37 16 qualitative studies including the subgroup of patients with CVD and DM under different stages
38
39 17 and treatment regimens are required to contextualize the medication adherence. Exploring the
40
41 18 barriers using a theoretical framework with the same methodological approach, can provide
42
43 19 more reliable evidence to develop patient-centred interventions and achieve better control
44
45 20 among CVD and DM patients.

49 **Conclusion:**

50
51 22 In our review, we categorised the facilitating factors and barriers influencing medication
52
53 23 adherence into patient related, health system related and care team related factors. Thus, we
54
55 24 advocate creation of peer support group, use of digital reminder system for overcoming patients
56
57 25 related factors, and integration of AYUSH services, mental health, physiotherapy and geriatric
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3 1 clinics even at the primary healthcare level for overcoming the health system related barriers
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5 2 towards medication adherence.
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Table 1: Characteristics of the studies included (N=18)

S.No	Author and year	State	Data collection method	Study participants	Study setting	Approach	Coding	Theoretical framework used	Method of analysis	Sample size	Mean Age in years	Study quality
1.	Agarwal 2019	Kerala	IDI	Clinical and administrative staff	Facility based	NR	Inductive	NR	Dedoose Software	21	NR	***
2.	Dhar et al 2016	Delhi	IDI	Hypertensive women aged 35-59 years	Community based	NR	Inductive	Yes	Manual content analysis	30	48	***
3.	George et al 2016	Karnataka	IDI	Physicians providing Non communicable disease care	Community based	NR	Inductive	NR	Manual content analysis	36	46	***
4.	Gupta et al 2019	Rajasthan	IDI	Hypertensive women	Facility based	NR	NR	NR	Manual content analysis	30	56	**
5.	Gupta et al 2020	Haryana	IDI	Hypertension patients	Facility based	NR	NR	NR	Manual content analysis	100	38-76	***
6.	Jayanna et al 2019	Karnataka	IDI & FGD	Diabetes and Hypertension patients	Facility based	NR	NR	Yes	Manual content analysis	10 IDI + 20 FGDs	NR	***
7.	Krishnamoorthy et al 2018	Puducherry	IDI & KII	Diabetes and Hypertension patients & Healthcare workers	Community based	NR	Inductive	NR	Manual content analysis	6 IDI + 4 KII	NR	***
8.	Kusuma et al 2010	Delhi	KII & FGD	Recent and Settled Migrants having hypertension inhabited in Delhi	Community based	NR	NR	NR	Manual content analysis	14 (KII) + 20 (FGD)	38 – 50 (KII) & 25 – 40 (FGD)	***
9.	Miller et al 2017	Delhi	IDI	Cardiovascular disease patients	Trial based	Descriptive	NR	NR	Manual content analysis	14	NR	***
10.	Newtonraj et al 2017	Tamil Nadu	Personal interviews	Hypertensive patients	Community based	NR	NR	NR	Manual content analysis	40	NR	**

11.	Nimesh et al 2019	Madhya Pradesh	IDI	Individuals with diabetes	Community based	NR	Inductive	Yes	Manual content analysis	60	52	***
12.	Patti et al 2020	Orissa	IDI	Primary care physicians	Facility based	NR	NR	NR	Manual content analysis	17	40	***
13.	Rani et al 2019	Tamil Nadu	FGD	Individuals with diabetes	Community based	Descriptive	NR	NR	Manual content analysis	50	50	**
14.	Salaam et al 2019	Andhra Pradesh	IDI	Patients with Cardiovascular disease	Community based	NR	NR	Yes	NVivo version 11 software	12	62	***
15.	Satish et al 2019	West Bengal	FGD	Patients with hypertension and/or diabetes	Trial based	NR	NR	Yes	Manual content analysis	70	53	***
16.	Thakur et al 2016	Chandigarh	IDI & FGD	Coronary artery disease patients	Facility based	NR	NR	NR	Manual Thematic analysis	20	NR	*
17.	Venkatesan et al 2018	Tamil Nadu	IDI	Health care workers	Community based	NR	NR	NR	Anthropac software	10	NR	***
18.	Wood et al 2015	Hyderabad and Delhi	IDI	Patients with Cardiovascular diseases	Trial based	NR	NR	Yes	Nvivo software	52	57	***

NR – Not Reported

IDI – In depth Interview

FGD – Focussed Group Discussion

KII – Key informant interview

Table 2: Thematic framework analysis for summarizing barriers in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Barriers in Medication Adherence	Studies
PATIENTS	1. Lack of awareness/knowledge: Lack of knowledge and understanding about the disease, its complications and treatment among the patients	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Patti et al 2020, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Forgetfulness: Patients forget to take medicine because of busy schedule	Dhar et al 2016, Gupta et al 2019, Gupta et al 2020, Rani et al 2019, Venkatesan et al 2018, Wood et al 2015, Tan et al 2017, Thakur et al 2016
	3. Misconception about medications: Patient has wrong perception about the medications, especially about its side effects and quality	George et al 2016, Gupta et al 2020, Patti et al 2020, Rani et al 2019, Salaam et al 2019, Tan et al 2017, Venkatesan et al 2018
	4. Preference to alternate system of medicine: Patients prefers taking herbal and other alternate system of medicines for their condition	George et al 2016, Tan et al 2017, Venkatesan et al 2018
	5. Ill effects of substance abuse: Patients have difficulty in adhering to medications during the bout of tobacco or alcohol consumption	Jayanna et al 2019, Krishnamoorthy et al 2018
	6. Effect of side effects: Patients stop their medication once they develop side effects related to the drugs	Venkatesan et al 2018, Wood et al 2015
	7. Stress: Patients developing stress due to personal or work-related problems are more non-adherent to medications	Krishnamoorthy et al 2018
	8. Stigma: Patients feel stigmatised in revealing their disease status to other family/friends leading to lack of support from them	Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Lack of physical, emotional and social support as the family members are pre-occupied with domestic works, crisis, other priorities and commitments	Dhar et al 2016, George et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Rani et al 2019, Wood et al 2015
	2. Risk communication: Poor risk communication or counselling to patients and family members about non-adherence to medication by the treating physicians	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Thakur et al 2016
	3. Physician attitude: Lack of respect, empathy, communication and attention towards patients by the treating physicians	Dhar et al 2016, Gupta et al 2019, Kusuma et al 2010, Jayanna et al 2019

HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Affordability: Patients lose their daily wages due to inconvenient consultation timings in public facilities, which is aggravated by travel costs due to poor access, and higher medication costs while preferring private facilities	Agarwal et al 2019, Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Nimesh et al 2019, Salaam et al 2019, Satish et al 2019, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Accessibility: Lack of access to healthcare facilities (more distance) requiring longer travel and waiting time.	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	3. Availability: Non-availability of essential medicines in public healthcare facilities	Dhar et al 2016, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Salaam et al 2019, Wood et al 2015
	4. Acceptability: Medications from public health facilities are not acceptable to the patients due to poorer quality	
	5. Overburdening of primary health centres: Burdening of primary health facilities lead to time constraints in patient counselling regarding medication adherence	Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Venkatesan et al 2018

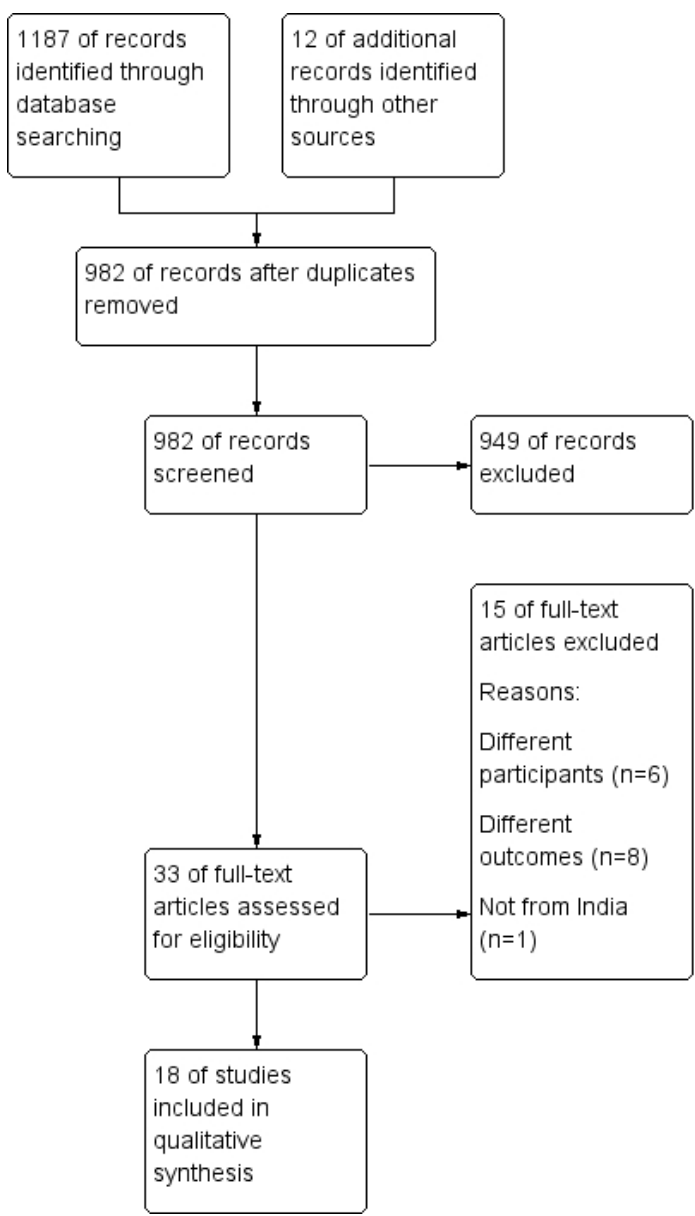
Table 3: Thematic framework for summarizing facilitators in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Facilitators in Medication Adherence	Studies
PATIENTS	1. Self-awareness and fear: Patient's understanding about medicine adherence and fear about complications of non-adherence keeps them healthy	Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Satish et al 2019, Tan et al 2017, Wood et al 2015
	2. Medicine Reminder system: Separate pill boxes/cases/covers, personalized shelf, and maintaining drug record notebook helps them in remembering daily doses	Dhar et al 2016, Krishnamoorthy et al 2018, Miller et al 2017, Tan et al 2017
	3. Integrating drug intake with the daily routine: Fixed time for medicine intake, separate place for keeping drug, and making arrangements during travel helps them in adherence	Dhar et al 2016, Krishnamoorthy et al 2018
	4. Positive peer influence: Good adherence to medication by the patient's peers motivates the patient to be compliance to their own drug intake	Gupta et al 2019, Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Constant reminders by family members for drug intake	Dhar et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Miller et al 2017, Wood et al 2015
	2. Past adverse experiences: Death of patients' own family members due to complications of the condition has motivated them to adhere to medication	Dhar et al 2016, Krishnamoorthy et al 2018
	3. Healthcare provider counselling and empathy: Patients described that counselling from their healthcare providers has motivated them to remain adherent	Kusuma et al 2010, Miller et al 2017, Patti et al 2020, Salaam et al 2019, Tan et al 2017
	4. Trust in physician: Adherence is more when a positive rapport and trust is established between the patient and health care providers.	Dhar et al 2016, Krishnamoorthy et al 2018, Satish et al 2019
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Dedicated pill boxes/covers: Provision of different medications in separate boxes/covers in the healthcare facility has helped as the patient to remember which medication to take at what time	Krishnamoorthy et al 2018, Wood et al 2015
	2. Combination drugs (polypills): Polypills had the following advantages to facilitate the medication adherence: a smaller number of pills, lower frequency, less chance of forgetting, potential for lower cost, and convenient simpler regimen	Salaam et al 2019, Wood et al 2015
	3. Availability of medications: Proper pharmacy inventory control and stock delivery has aided in medication adherence	Miller et al 2017
ENVIRONMENT (Regulatory, market and policy framework)	1. NGO Support: Patients has reported that sharing their concerns and receiving counselling from NGO/ Health officers acted as a facilitator for drug intake	Tan et al 2017, Wood et al 2015

Table 4: Thematic framework for summarizing suggestions to improve medication adherence among CVD & DM patients in India

Main theme/Sub-themes	Suggestions to improve medication adherence	Studies
PATIENTS	1. Peer support groups: Patients can motivate each other by forming support groups among themselves	Krishnamoorthy et al 2018
	2. Digital reminder system: Patient can use digital reminders such as watch, mobile phone to adhere to their drug schedule	Krishnamoorthy et al 2018, Miller et al 2017
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Social support: Family members can be educated and asked to provide support by reinforcing compliance, reminding about drug intake, motivating them patients to avoid substance abuse	Agarwal et al 2019, Dhar et al 2016, Krishnamoorthy et al 2018, Nimesh et al 2019, Wood et al 2015
	2. Financial support: Family members can provide financial support to cover the cost of medications, travel etc.	Gupta et al 2019
	3. Regular training of healthcare workers: Physicians and other healthcare workers involved in prescribing drugs and counselling should undergo regular training on standard treatment protocols	George et al 2016, Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019
	4. Team work approach: Integration of AYUSH, mental health counsellors, physiotherapist and geriatric clinics at primary healthcare level	George et al 2016, Miller et al 2017, Patti et al 2020
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Innovations in patient care: Healthcare workers can make innovations like dedicated day for specific conditions (diabetes day, etc), dedicated counselling station/session with additional staff for detailing the importance of adherence and complications related to non-adherence, unique pill dispensing mechanism (colour coding)	Agarwal et al 2019, Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Satish et al 2019, Venkatesan et al 2018, Wood et al 2015
	2. IEC/BCC/Awareness campaigns: Putting up of IEC materials and conducting campaigns on importance of adherence in public places and workplaces	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Newtonraj et al 2017, Patti et al 2020, Rani et al 2019
	3. Digitalizing patient treatment record: Digitalizing a dedicated treatment record for each patient can help in better follow-up of the patient and improve adherence	Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019, Wood et al 2015
	4. Polypills: Disseminating the advantages of polypills to healthcare professionals by CME/conferences and patients by public education campaigns; Integration of polypills into clinical practice. etc	Salaam et al 2019, Wood et al 2015
ENVIRONMENT (Regulatory, market and policy framework)	1. Linkage of health services with NGO and community-based organizations: Community members, volunteers, anganwadi workers, self-help groups and NGO workers can be trained in counselling the patients to improve medication adherence	Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Tan et al 2017

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141x246mm (72 x 72 DPI)

Supplementary Table 1 Search strategy

Key word	Alternative word
Qualitative studies	((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))
Medication Adherence	((((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])
Barriers, Facilitators and solutions	Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions
Diabetes mellitus and CVDs	((((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))

India	(India[MeSH Terms] OR Republic of India[MeSH Terms]))
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Search results (PubMed):

(((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms])) AND (((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms]) OR Life Change Events[MeSH Terms]) OR Trust[MeSH Terms]))) AND (((((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms])) AND (India[MeSH Terms] OR Republic of India[MeSH Terms])) – 199 (Filters: Years between 2010 and 2020 and English language publication)

((((((((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))) AND (((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])) AND (Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions)) AND ((((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))) AND ((India[MeSH Terms] OR Republic of India[MeSH Terms])) – 31 results (Filters: Years between 2010 and 2020 and English language publication)

Google scholar: 635 + 22 + 6 + 12 = 675

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3 **ScienceDirect:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
4 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 238 articles
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6 **Cochrane library:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
7 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 34 articles
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For peer review only

S1 Table. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ Checklist (Tong, *et al.*, 2012)

Item No.	Guide and Description	Report Location
1. Aim	State the research question the synthesis addresses	P 6, 1-13
2. Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology (e.g. meta-ethnography, thematic synthesis, critical interpretive synthesis, grounded theory synthesis, realist synthesis, meta-aggregation, meta-study, framework synthesis)	P9, 16-25 P10, 1-22
3. Approach to searching	Indicate whether the search was pre-planned (comprehensive search strategies to seek all available studies) or iterative (to seek all available concepts until they theoretical saturation is achieved)	P8, 1-10
4. Inclusion criteria	Specify the inclusion/exclusion criteria (e.g. in terms of population, language, year limits, type of publication, study type)	P7, 3-23
5. Data sources	Describe the information sources used (e.g. electronic databases (MEDLINE, EMBASE, CINAHL, psycINFO), grey literature databases (digital thesis, policy reports), relevant organisational websites, experts, information specialists, generic web searches (Google Scholar) hand searching, reference lists) and when the searches conducted; provide the rationale for using the data sources	P8, 1-10
6. Electronic Search strategy	Describe the literature search (e.g. provide electronic search strategies with population terms, clinical or health topic terms, experiential or social phenomena related terms, filters for qualitative research, and search limits)	Supplementary file 1
7. Study screening methods	Describe the process of study screening and sifting (e.g. title, abstract and full text review, number of independent reviewers who screened studies)	Figure 1
8. Study characteristics	Present the characteristics of the included studies (e.g. year of publication, country, population, number of participants, data collection, methodology, analysis, research questions)	Table 1
9. Study selection results	Identify the number of studies screened and provide reasons for study exclusion (e.g. for comprehensive searching, provide numbers of studies screened and reasons for exclusion indicated in a figure/flowchart; for iterative searching describe reasons for study exclusion and inclusion based on modifications to the research question and/or contribution to theory development)	Fig 1 - PRISMA flow diagram P11, 6-18
10. Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings (e.g. assessment of conduct (validity and robustness),	P11, 14-18 Table 1

	assessment of reporting (transparency), assessment of content and utility of the findings)	
11. Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings (e.g. Existing tools: CASP, QARI, COREQ, Mays and Pope [25]; reviewer developed tools; describe the domains assessed: research team, study design, data analysis and interpretations, reporting)	P9, 3-14 Table 1
12. Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required	P8, 11-17
13. Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale	P11, 14-18 Table 1
14. Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies? (e.g. all text under the headings "results /conclusions" were extracted electronically and entered into a computer software)	P8, 18-25
15. Software	State the computer software used, if any	None used
16. Number of reviewers	Identify who was involved in coding and analysis	P9, 16-22
17. Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts)	P9, 23-35 P10, 1-22
18. Study comparison	Describe how were comparisons made within and across studies (e.g. subsequent studies were coded into pre-existing concepts, and new concepts were created when deemed necessary)	Table 2
19. Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive	Inductive process Table 2
20. Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation	Table 2
21. Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies (e.g. new interpretation, models of evidence, conceptual models, analytical framework, development of a new theory or construct)	P11-14

BMJ Open

Patient and Provider's perspective on barriers and facilitators for medication adherence among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A qualitative evidence synthesis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055226.R2
Article Type:	Original research
Date Submitted by the Author:	15-Dec-2021
Complete List of Authors:	Krishnamoorthy, Yuvaraj; JIPMER PSM, Rajaa, Sathish; Jawaharlal Institute of Postgraduate Medical Education, Rehman, Tanveer; PGIMER Thulasingam, Mahalakshmi ; JIPMER, Department of Preventive and Social Medicine
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Cardiovascular medicine, Diabetes and endocrinology
Keywords:	QUALITATIVE RESEARCH, PREVENTIVE MEDICINE, PRIMARY CARE, Coronary heart disease < CARDIOLOGY, DIABETES & ENDOCRINOLOGY

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3 1 **Patient and Provider's perspective on barriers and facilitators for medication adherence**
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5 2 **among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A**
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7 3 **qualitative evidence synthesis**

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10 4 **Running head:** Barriers and facilitators for medication adherence among CVD and DM
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12 5 patients in India

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15 6 **Article category:** Systematic Review

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14 6 **Abstract:**

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16 7 **Objective:**

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18 8 To explore the various stakeholders' perspectives on barriers and facilitators for medication
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20 9 adherence among CVD and DM patients in India.

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22 10 **Methods:**

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24 11 A comprehensive systematic search was conducted in Medline, Cochrane library, Science
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26 12 Direct and Google Scholar from January 2010 to July 2020. We used the framework of the
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28 13 systems approach for healthcare delivery to conduct thematic analysis, using published
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30 14 qualitative literature to derive relevant themes, sub-themes and codes.

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32 15 **Setting:** A Qualitative Evidence Synthesis of qualitative published studies from India

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34 16 **Subjects:** A Qualitative Evidence Synthesis of the available qualitative evidence on the
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36 17 barriers and facilitating factors for medication adherence among CVD and DM patients in India

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38 18 **Results:**

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40 19 In total, 18 studies were included. Major barriers reported were lack of understanding about
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42 20 the disease, complications related to non-adherence, followed by forgetfulness, lack of family
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44 21 support and risk communication. Health system-related barriers such as accessibility,
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46 22 affordability, and acceptability were also reported by majority of the studies. Creation of peer
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48 23 support group, digital reminder system, integration of AYUSH, mental health, physiotherapy
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50 24 and geriatric clinics at primary healthcare level and innovations in patient care were suggested
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52 25 to counter these barriers in medication adherence.

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3 1 **Conclusion:**
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5 2 Such patient-specific targeted interventions need to be developed to achieve better control
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8 3 among CVD and DM patients.
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10 4 **Keywords:** Cardiovascular Diseases, Diabetes Mellitus, Medication Adherence, Qualitative
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12 5 Research
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15 6 **Strengths and Limitations:**
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- 17 7 1. This is the first review exploring factors associated with drug adherence among CVD
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19 8 & DM patients in India
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21 9 2. We have adhered to the ENTREQ statement ensuring transparency and reproducibility
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24 10 of the study findings.
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26 11 3. We cannot rule out of the dissemination bias with respect to accurate and complete
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28 12 representation of the phenomenon of interest.
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31 13 4. We focussed primarily on the patient and provider perspective on medication
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33 14 adherence. Hence, we cannot comment on the organizational or political influences on
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35 15 the adherence to long-term therapies.
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38 16 5. The sample size of the included studies can be considered relatively low (median
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40 17 sample size - 30).
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1 INTRODUCTION

2 Cardiovascular diseases (CVDs) are the leading cause of mortality globally and in India.^{1,2}
3 More than a quarter (28%) of all deaths in India are attributable to CVDs with Ischemic heart
4 disease (IHD) and stroke constituting the majority (83%).³ On the other hand, India ranks
5 second after China in the global diabetes epidemic, with a prevalence of around 10%.⁴ Both
6 diabetes mellitus (DM) and hypertension have long been recognized as independent risk factors
7 for CVDs, whereas adherence to prescribed hypoglycaemic and antihypertensive drug
8 therapies have significantly reduced the risk.⁵⁻⁸ At least half of hypertensive & DM patients
9 stop taking their medication within a year, often without informing their provider. With further
10 nonadherence and attrition over time, medication adherence has emerged as a significant public
11 health priority.⁹

12 Medication adherence is defined as the extent to which a person's behaviour coincides with the
13 agreed medication regimen or health advice from a health care provider.¹⁰ It has three
14 components: initiation (when the patient takes the first dose of prescribed medication),
15 implementation (the extent to which a patient's actual dosing corresponds to the prescribed
16 dosing regimen), and discontinuation (when no more doses are taken after that).¹¹ Medication
17 adherence is of growing interest to clinicians, healthcare systems, and other stakeholders (e.g.,
18 payers). There is soaring evidence that establishes nonadherence is often associated with lower
19 quality of life, adverse clinical events, increased need for medical interventions, mortality, and
20 thus giving rise to avoidable out-of-pocket expenditure in health.¹² Non-adherent hypertensive
21 and stable coronary heart disease (CHD) patients have a four to five times higher risk of
22 developing CHD and death, when compared to adherent patients.^{13,14} Similarly, the likelihood
23 of hospitalization is doubled among DM & hypertensive patients who are non-adherent to
24 prescribed therapies compared to the general population. Despite recent advancements in
25 pharmacologic treatment and technology to treat and monitor DM and CVD patients,

1 medication adherence is of particular concern in low-and-middle-income countries (LMIC)
2 like India, where accessibility and affordability are still issues.^{3,15}
3 Barriers to adherence can be comprehended as the patient, medication, provider, and health
4 system factors, with interactions among them.^{16,17} Patient factors that influence adherence
5 include poor health literacy, cultural beliefs regarding medication effectiveness, and religious
6 healing practices.¹⁷ Low income, forgetting to take medication, and perceptions regarding pills
7 like safety concerns, convenience, and necessity add to the above list.^{16,17} Inadequate
8 knowledge about a drug and its use, not being convinced of the need for medication, fear of
9 adverse effects, and long-term treatment regimens also prompt medication discontinuation.¹⁵
10 Clinician factors cover failure to recognize nonadherence, prescription of complex and
11 multidrug regimens, ineffective communication of benefits of medications, and excluding
12 patients in the treatment decision-making process.¹⁷ Health system factors comprise limited
13 insurance coverage, poor coordination of care between inpatient and outpatient settings, and
14 inadequate communication between prescribers (i.e., specialists and primary care clinicians).
15 In addition, the caregivers' aspect also becomes relevant in determining patients' adherence as
16 CVD patients with a caregiver are more likely to be adherent to medications.¹⁸ Hence
17 identifying specific barriers for each patient and adopting suitable techniques to overcome them
18 is imperative to improve medication adherence. Some of the facilitators successful in
19 overcoming these barriers include a personal medication counsellor in the care continuum to
20 guide patients with medication use, single-pill fixed-dose combinations, training pharmacists
21 as coaches for drug therapies, building peer groups for chronic conditions, and developing
22 information systems in the follow-up of patients.¹⁹
23 Quantitative studies have focused on medication adherence incidence and identification of its
24 potential risk factors. They do not, however, uncover life circumstances that may influence
25 adherence from the patient perspective. The inclusion of qualitative studies in our review will

1
2
3 1 provide a better understanding of the barriers and facilitators from the perspective and
4
5 2 experiences of patients, healthcare providers, and caregivers.²⁰ Qualitative evidence synthesis,
6
7 3 a novel research method, brings together the available qualitative evidence from primary
8
9 4 studies through a systematic review process. Despite the evidence obtained from primary
10
11 5 qualitative studies could be conceptually richer, a qualitative evidence synthesis can aid us in
12
13 6 getting an overall view of the findings, and help us in addressing subtle and sensitive issues
14
15 7 that most primary studies encounter. The findings from a qualitative evidence synthesis can
16
17 8 guide us in crucial making policy recommendations in health care, retaining the impact of
18
19 9 individual studies and group experiences. ²¹ Therefore, the current review was done to
20
21 10 understand the perspective of various stakeholders (patients, caregivers, and healthcare
22
23 11 providers) on the barriers and facilitators for medication adherence among CVD and DM
24
25 12 patients in India. We also explored the suggestions and solutions provided by these
26
27 13 stakeholders in overcoming the reported barriers.
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34 **METHODS**

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37 15 This review was performed by adhering to the “enhancing transparency in reporting the
38
39 16 synthesis of qualitative research (ENTREQ)” statement. (Supplementary file 2) ²² We
40
41 17 registered our protocol in the PROSPERO database (Registration number -
42
43 18 CRD42020199529). We also searched PROSPERO and Cochrane to ensure that no similar
44
45 19 review protocol has been reported. We also performed a preliminary search to ensure that no
46
47 20 previous reviews of our similar topic targeting the Indian population were published.
48
49

50 **Study design**

51
52 22 We performed an evidence synthesis of the available qualitative evidence on the barriers and
53
54 23 facilitating factors for medication adherence among CVD and DM patients. This review would
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60

1 help to aggregate the evidence of peer-reviewed articles in this field and build an organized
2 empirical research outline based on prior knowledge.

3 ***Eligibility criteria***

4 *Study type*

5 We have included qualitative peer-reviewed studies conducted in India for our current review.
6 Furthermore, qualitative evidence from other mixed methods studies was screened for
7 eligibility and included in the qualitative component was relevant to our review. In addition,
8 we included studies using qualitative techniques for data collection such as focussed group
9 discussion (FGD), in-depth interviews (IDI), and Key Informant Interviews (KII).

10 *Participant type*

11 We have included the studies reporting the barriers and facilitators of medication adherence
12 from patients' perspectives (CVD and DM), family members, healthcare workers (HCWs), or
13 health system policymakers in India. HCWs were defined as per WHO recommendation as "all
14 the persons involved in the actions whose primary intent is to enhance the health."²³

15 *Outcome*

16 The phenomenon of interest in our review was to explore the barriers and facilitators for
17 medication adherence among CVD and DM patients in India. We also explored the possible
18 suggestions and solutions to address the barriers and improve compliance, as experienced by
19 the patients, caregivers, family members, HCWs, and other relevant stakeholders.

20 ***Exclusion criteria***

21 We have excluded the studies not available in English, books or conference abstracts or grey
22 literature, or editorial comments. We have also excluded the studies reporting only quantitative
23 data such as cross-sectional surveys, case-control, cohort studies, or intervention trials.

24 **Search strategy**

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2
3 1 We have conducted a comprehensive and systematic search in databases and search engines
4
5 2 such as Medline, Cochrane library, ScienceDirect, and Google Scholar. A combination of
6
7 3 medical subject heading (MeSH) and free-full text terms was used for carrying out a literature
8
9 4 search. The detailed search strategy and search results in the databases mentioned above and
10
11 5 search engines are provided in Supplementary File 1. In addition to this, we also checked the
12
13 6 reference list of primary studies obtained via electronic search and included articles relevant to
14
15 7 our review and analysis. The search was conducted in all the databases from January 2010 to
16
17 8 July 2020 with English language restriction for publication. Furthermore, the search timeline
18
19 9 was restricted to ensure that our work provides a broader view and identifies the emerging
20
21 10 issues.

26 11 **Study selection process**

28 12 Two investigators (YK and TR) independently performed the literature search, screened the
29
30 13 title and abstract of all the identified studies, and retrieved the full text for articles relevant to
31
32 14 our review. Further full-text screening of the retrieved articles was done again independently
33
34 15 by the two investigators (YK, TR) to select the studies matching the eligibility criteria of our
35
36 16 review. Disagreements during this process between the two investigators were resolved
37
38 17 through consultation with a third investigator (SR).

42 18 **Data Extraction and Management**

44 19 After the study selection, two investigators (YK and TR) independently extracted the relevant
45
46 20 data and study characteristics onto a predetermined data extraction format. Data entry was
47
48 21 double-checked for accuracy by a third investigator (SR) by comparing the data presented in
49
50 22 the review and individual study reports. As a result, we have extracted the following study
51
52 23 characteristics: general information such as the name of the first author, the country in which
53
54 24 the study was done, and year of publication, in the methods section, data collection period,
55
56 25 study design, study participants, sample size, sampling technique, and data collection
57
58
59
60

1 procedure. In addition, barriers, facilitators, suggestions, and solutions to medication adherence
2 were identified systematically.

3 **Quality assessment**

4 Two investigators (YK and SR) independently performed the quality check using the Critical
5 Appraisal Skills Programme (CASP) criteria.²⁴ This checklist has been widely used for
6 assessing the quality of studies included in this Qualitative Evidence synthesis.²⁵ This has
7 helped determine whether the studies included are coherent with the quality appraisal standard
8 for qualitative studies. This checklist consists of 10 questions concerning the study's clarity,
9 methodology, and results to rank the included studies. Subsequently, these studies were
10 stratified into high quality (three stars for studies scoring 8 to 10 points), medium quality (two
11 stars for studies scoring 4 to 7 points), and low rate (one star for studies scoring 0 to 3 points).
12 We did not exclude the low-quality studies, but the interpretation of results was made with
13 caution. Disagreements during the quality assessment process were resolved by discussion with
14 the third investigator (TR).

15 **Data Analysis**

16 We analysed and reported the findings in separate clusters such as patients, caregivers, family
17 members, HCWs, and policymakers to demonstrate the differences among these subgroups.
18 We have adopted a thematic framework analysis to analyse and synthesize the data. Thematic
19 framework analysis has been helpful as the evidence was primarily descriptive and improved
20 our understanding of the barriers and facilitators in medication adherence among CVD and DM
21 patients. This framework synthesis has five stages of synthesizing the qualitative data.

22 ***First stage - Familiarisation with the data:*** Primary investigator (YK) did the process of
23 familiarisation with data by reviewing all the selected articles against the objective of our
24 review and found the recurrent themes across the included studies.

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2
3 1 **The second stage - Identifying the thematic framework:** The investigators used a
4
5 2 predetermined thematic framework developed using literature to guide the thematic analysis.
6
7 3 The final framework comprised of a detailed list of facilitators and barriers for medication
8
9 4 adherence and also solutions to address the issue.

10
11
12 5 **Third stage - Indexing:** Two independent investigators (YK and SR) read the extracted
13
14 6 information and searched for themes as per the predetermined thematic framework and found
15
16 7 additional emerging themes. The framework underwent several revisions as and when a new
17
18 8 theme emerged. This has been performed through discussion and agreement between the entire
19
20 9 team of investigators. Next, all the studies were completely read and examined till there was
21
22 10 no new emergent theme. Coding of the data was then done as per the themes identified in our
23
24 11 analysis. Finally, each preliminary study indexing was done using the codes related to the
25
26 12 thematic framework. Whenever appropriate, sections of the studies were indexed with one or
27
28 13 more codes.

29
30
31
32
33 14 **Fourth stage - Charting:** The investigators have sorted the data based on the themes and
34
35 15 presented these themes in the tabular format (chart). The rows and columns of the table indicate
36
37 16 the themes related to the studies, which enabled us to compare the study findings across various
38
39 17 themes and subthemes.

40
41
42 18 **Fifth stage - Mapping and interpretation:** The investigators used these charts to define the
43
44 19 concepts identified, and mapped the nature and range of the phenomena. Our review explored
45
46 20 the associations between the various themes and helped in clarifying the findings. Finally, we
47
48 21 mapped and interpreted the findings in line with our objectives and emergent themes.

22 **Ethical considerations**

23
24 23 Approval from an ethics committee is not required since our review included only publicly
25
26 24 available data without involving the human participants directly.

1 **Patient and Public Involvement:**

2 Patients or the public were not involved in the design, or conduct, or reporting, or dissemination
3 plans of our research.

4 **Results**

5 **Study selection**

6 A comprehensive and systematic search was done to identify the relevant studies from January
7 2010 to July 2020. In total, we identified 1187 citations, and after the removal of duplicates
8 from multiple databases, 982 records were screened for their title and abstract and assessed for
9 eligibility. From these records, we retrieved 33 articles, and after going through the full text of
10 these articles, 18 studies were included in the review. (**Figure 1**).²⁶⁻⁴³

11 **Characteristics of the studies included**

12 Characteristics of the included studies are reported in **Table 1**. Of the 18 studies included, 9
13 (50%) were from the Southern region, followed by 7 (38%) from the Northern part of India.
14 The mean age of the participants ranged from 25-76 years. The typology of the studies
15 comprised of in-depth interviews (IDIs) and focussed group discussions (FGDs). The study
16 participants were primarily patients with diabetes, hypertension, or any cardiovascular diseases
17 (to explore the patient perspective), and health care workers (4 studies) providing care to them
18 (to obtain the provider perspective). The total sample size of the included studies ranged from
19 6 to 100. The majority (10 of the included studies) were done in a community setting, while
20 the rest were either facility-based or had participants from ongoing trials. Four of the included
21 studies used software for analysing the qualitative data, while the rest followed manual
22 methods. Most of the included studies (14 out of 18) had higher ratings indicating high-quality
23 evidence.

24 **Narrative synthesis**

1
2
3 1 Significant findings from the review showed that factors contributory to adherence come under
4
5 2 three themes: patient-related, family-related, and health system-related factors. The barriers,
6
7 3 facilitators, and suggestions to improve medication adherence were summarized under these
8
9 4 three themes.

5 **Barriers in medication adherence**

6 **Table-2** shows the thematic framework analysis related to barriers in medication adherence
7 among CVD and DM patients. All the 18 included studies have explored and reported on these
8 barriers.

9 *Patient-related factors*

10 Significant patient-related barriers (10 studies) reported were lack of knowledge or
11 understanding about the disease, its complications related to nonadherence, and the treatment
12 schedule, followed by forgetfulness to take medicine (7 studies). Reasons provided for the same
13 were the patients' busy schedule, laziness, or forgetting to take the medication while traveling
14 out-of-station. Patients have also reported certain misconceptions about the medicines like the
15 risk of long-term neurological illness because of medication intake, inferior quality of drugs
16 provided in hospitals, and wrong perception about stopping the medications once the patient
17 feels normal. Patients in some studies have reported that they practice alternate systems of
18 medicine such as herbal medicines and avoid taking allopathic medicines leading to poorer
19 control of their condition. Substance use such as alcohol or tobacco use, side effects related to
20 drugs, stress, and stigma were reported to be other barriers

21 *Family-related factors*

22 The patients and providers have reported a lack of family support as a significant contributing
23 factor for nonadherence. In addition, the lack of social and emotional support to the patients
24 further contributes to the nonadherence among the patients suffering from CVDs and DM.

1
2
3 1 Domestic works, personal priorities, commitments, or other issues hinder the family members
4
5 2 from providing the above-mentioned support to the patients.
6

7 3 *Health system-related factors*

8
9
10 4 In most of these studies, providers were also interviewed to understand the factors related to
11
12 5 the health system responsible for nonadherence among CVD and DM patients. Healthcare
13
14 6 providers and patients interviewed, in almost all these studies, have reported affordability,
15
16 7 accessibility, and acceptability as the major factors hindering medication adherence.
17
18 8 Affordability is an issue with patients seeking healthcare in private facilities and patients
19
20 9 getting care in public healthcare facilities. Though there was no direct medical cost related to
21
22 10 government hospitals or primary healthcare centres, direct non-medical costs such as transport
23
24 11 (due to poor accessibility) and indirect costs such as loss of wages (due to inconvenient
25
26 12 consultation timing) were higher amongst these patients. In addition, patients have a wrong
27
28 13 perception that medications in public facilities are of poorer quality, making them choose
29
30 14 private health facilities, including those belonging to lower socioeconomic status. Lack of risk
31
32 15 communication, counselling, or empathy by the physicians mainly due to overburdening public
33
34 16 health facilities and time constraints were the other health system-related barriers reported by
35
36 17 the providers and patients.
37
38
39

40 18 **Facilitators in medication adherence**

41
42
43 19 Facilitators in medication adherence were also summarized using the pre-existing thematic
44
45 20 framework (**Table-3**). In total, ten studies have explored the facilitators in medication
46
47 21 adherence from the patient or providers' perspective.
48
49

50 22 *Patient-related factors*

51
52
53 23 Most of the studies (5 studies) reported fear of complications due to nonadherence and self-
54
55 24 perception of being healthy (once they adhere to the medications) as the significant facilitators.
56
57 25 In addition, having a reminder system in the form of a reminder notebook, separate
58
59
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1 pillboxes/cases/covers, or personalized shelf facilitates the patients in adhering to the
2 medications. Some studies have also reported that integrating drug intake into daily routine
3 activities and peer influence acts as a good facilitator in compliance with medications.

4 *Family-related factors*

5 Family support was reported as a major facilitating factor for compliance with medication.
6 Apart from the support, adverse experiences in the past, such as death or severe complications
7 among the family members, instilled fear in the patients, making them more compliant to the
8 medications.

9 *Health system-related factors*

10 Barriers reported in some of the studies, such as empathy and counselling by healthcare
11 providers, were considered facilitators by the other studies' patients. Another major facilitator
12 from the health system side is the trust that patient has in their physician and their willingness
13 to effectively follow advice related to self-care and adherence. Other familiar facilitators
14 reported by the patients and providers were the use of dedicated pill cover/boxes for each drug
15 provided in the clinic, linkage of health services with NGO for provision of counselling and
16 generating awareness, availability of medication, and use of polypills.

17 **Suggestions to improve medication adherence**

18 Suggestions and solutions to enhance the compliance to medication were reported in 16 out of
19 the 18 included studies based on either patient or provider's perspective (**Table-4**). Few
20 suggestions were related to patients and family members, while the majority were related to
21 the change in the health system.

22 *Patient and family-related factors*

23 Creating or joining a peer support group was one of the major suggestions related to the
24 patients. This will help by motivating the patients to be more compliant with medications and

1 other self-care practices. Digital reminder systems using a watch and a mobile phone can also
2 improve medication adherence.

3 *Health system-related factors*

4 Innovations in patient care, have been necessitated as an important factor to promote drug
5 adherence. Some of the innovations suggested were dedicated days for specific disease
6 conditions to avoid overburdening the facilities, a dedicated counselling station for drug
7 adherence during the clinic with separate human resources, and a unique pill dispensing
8 mechanism like colour coding, etc. In addition, Information Education and Communication
9 (IEC)/Behaviour change communication (BCC) campaigns, digitalizing the patient treatment
10 records, linkage of healthcare services with NGOs or community-based organizations, regular
11 training of healthcare workers, and promotion of polypill use were other common suggestions
12 offered by the healthcare providers.

13 **Discussion**

14 We conducted this review to integrate the qualitative evidence on barriers and facilitators for
15 medication adherence among CVD and DM patients in India. We also further explored the
16 suggestions to improve the same. The studies included in our review involved a total of 636
17 participants (534 CVD and DM patients, 102 healthcare providers). The majority of the
18 included studies were of high quality concerning study clarity, methodology, and results. We
19 summarized under three major themes: barriers, facilitators, suggestions and reported the
20 findings under the following four sub-themes: patients, care team, healthcare organization, and
21 environment-related factors.

22 *Comparison of findings with previous literature*

23 *Barriers in medication adherence*

24 Major barriers were lack of patient's understanding about the disease and its complications,
25 forgetfulness, and misconception about the medications. Lack of family support was seen as a

1 major barrier from both patient's and provider's perspectives. In addition to these factors, stress
2 and stigma were also mentioned as important factors among patients to not take medicine on
3 time. In addition to the above, medication adherence could also be highly hindered by the
4 patients' cultural beliefs, perceived discrimination, and social customs, which are highly
5 prevalent in a culturally influenced country like India. A few studies have also shown evidence
6 of improvement in medication adherence where efforts were taken to overcome the cultural
7 barriers.⁴⁴ We also found major health system-related barriers were lack of accessibility and
8 availability, higher cost of medications, and poor physician attitude. These findings were in
9 line with the previous review conducted among South-East Asian DM patients.^{44,46} In addition,
10 our findings of patients related factors were found to be similar to other patients belonging to
11 non-English speaking Hispanic, South American ethnic groups, as they also had
12 misconceptions related to therapy, lack of understanding about their condition, with additional
13 stress and stigma as a factor for non-adherence.⁴⁷⁻⁴⁹

14 *Facilitators in medication adherence*

15 Fear of complications, self-perception of being healthy, having a reminder system was reported
16 as major facilitators by patients. Physician trust, advice, empathy, and counselling were the
17 other provider-related facilitators in adhering to medications. Common facilitators as reported
18 by the patients and providers were: dedicated pill cover/boxes for each drug provided in the
19 clinic, availability of medication, and use of polypills. These findings were also in line with the
20 previous qualitative reviews conducted in low middle-income countries including India.⁴⁷⁻⁵⁰

21 *Suggestions to improve medication adherence*

22 The solutions provided by the patients and health professionals were in line with the barriers
23 identified in our review. Proper physician counselling to make the patients understand their
24 own condition, complications of the disease and avoid misconception about the drugs and their
25 side effects, good family support, making the medication accessible and available free of cost

1 were suggested as major suggestions to improve medication adherence. Similar interventions
2 were also suggested by previous qualitative evidence on medication adherence among CVD
3 and DM patients.⁴⁵⁻⁴⁹ It is also interesting to note that medication adherence is also hurdled by
4 the patients' intention towards adherence, and this intention might vary across nations and
5 cultural groups. The patient's intention not to refill prescriptions due to cost, not to take
6 medication because the patient feels better, also influences the patient's decision. Thus future
7 research exploring these reasons on patient's choice to adhere or not, rather than an inability to
8 adhere (e.g., forgetting, no access) needs to be encouraged.

9 *Strengths and limitations of the study*

10 To the best of our knowledge, this is the first review exploring and synthesizing the qualitative
11 factors associated with medication adherence among CVD and DM patients in India. We have
12 provided comprehensive and systematic evidence on the barriers, facilitators related to
13 medication adherence, adhering to the ENTREQ statement, and ensuring transparency and
14 reproducibility. We examined this evidence through the lenses of a well-established theoretical
15 framework model. Moreover, our study was able to provide valuable suggestions to promote
16 medication adherence from both patient's and provider's perspectives. In addition to these
17 strengths, we found that the highest-rated studies contributed to the majority of the factors
18 found in our review. This in turn ensures the transferability (external validity) of our review
19 findings.

20 However, our review has certain limitations. We did not search grey literature, possibly missing
21 some insights for our review. Hence, we cannot rule out the dissemination bias for an accurate
22 and complete representation of the phenomenon of interest. We focussed primarily on the
23 patient and provider perspective on medication adherence.⁵¹ Hence, we cannot comment on the
24 organizational or political influences on the adherence to long-term therapies as mentioned in
25 the WHO report.¹⁶ The sample size of the included studies can be considered relatively low

1 (median sample size - 30). However, all the studies were conducted till the achievement of data
2 saturation. In addition to the above, these results and suggestions need to be considered after
3 taking into account India's cross-cultural adaptations, customs, linguistic variations, and
4 genetic susceptibility, and higher prevalence of risk factor profile.

5 *Implications for clinical and public health practice*

6 Improving medication adherence is essential to achieve better control and prevent life-
7 threatening complications. Factors related to patients such as self-awareness and fear about the
8 condition and its complications acted as a major facilitator for medication adherence. We also
9 found more modifiable barriers related to medication intakes such as forgetfulness, lack of
10 knowledge, and misconception about medications. Interventions should focus on these
11 modifiable barriers such as knowledge barriers, intention barriers, and health system-related
12 barriers to achieve better adherence. In addition, the family members need to help the patients
13 in mapping their daily routine and link the medicine intake with these routines to facilitate
14 adherence. Our review also suggested that healthcare providers play an important role in
15 promoting medication adherence. Hence, the interventions should not only target the patients
16 but also the family members and healthcare providers and they should be tailored to suit
17 differences in setting, culture, and type of the patients.

18 *Implications for future research*

19 More evidence needs to be generated concerning the solutions obtained in our review such as
20 memory tools including the digital solutions, polypills, peer support groups, etc. Further
21 qualitative studies including the subgroup of patients with CVD and DM under different stages
22 and treatment regimens are required to contextualize the medication adherence. Exploring the
23 barriers using a theoretical framework with the same methodological approach, can provide
24 more reliable evidence to develop patient-centered interventions and achieve better control
25 among CVD and DM patients.

1
2
3 **1 Conclusion:**
4

5
6 2 In our review, we categorised the facilitating factors and barriers influencing medication
7
8 3 adherence into patient-related, health system-related, and care team-related factors. Thus, we
9
10 4 advocate the creation of peer support groups, the use of a digital reminder system for
11
12 5 overcoming patients related factors, and integration of AYUSH services, mental health,
13
14 6 physiotherapy, and geriatric clinics even at the primary healthcare level for overcoming the
15
16 7 health system-related barriers towards medication adherence.
17
18

19
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21

22
23 9 **Competing interests statement:** None declared
24

25
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27

28 11 **Author contribution statement:** Conceived and designed the study: YK & SR, Data
29
30 12 management and extraction: YK, SR & TR, Analysed the data and wrote the paper: SR, YK
31
32 13 & TR. Provided comments and inputs to revise the manuscript: SR, YK, TR & MT
33

34 14 **Data sharing statement:** The authors confirm that the data supporting the findings of this
35
36 15 study are available within the article
37
38

39 16 **References:**
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5 **Figure 1: Flow chart showing the search strategy and selection of studies**

For peer review only

Table 1: Characteristics of the studies included (N=18)

S.No	Author and year	State	Data collection method	Study participants	Study setting	Approach	Coding	Theoretical framework used	Method of analysis	Sample size	Mean Age in years	Study quality
1.	Agarwal 2019	Kerala	IDI	Clinical and administrative staff	Facility based	NR	Inductive	NR	Dedoose Software	21	NR	***
2.	Dhar et al 2016	Delhi	IDI	Hypertensive women aged 35-59 years	Community based	NR	Inductive	Yes	Manual content analysis	30	48	***
3.	George et al 2016	Karnataka	IDI	Physicians providing Non communicable disease care	Community based	NR	Inductive	NR	Manual content analysis	36	46	***
4.	Gupta et al 2019	Rajasthan	IDI	Hypertensive women	Facility based	NR	NR	NR	Manual content analysis	30	56	**
5.	Gupta et al 2020	Haryana	IDI	Hypertension patients	Facility based	NR	NR	NR	Manual content analysis	100	38-76	***
6.	Jayanna et al 2019	Karnataka	IDI & FGD	Diabetes and Hypertension patients	Facility based	NR	NR	Yes	Manual content analysis	10 IDI + 20 FGDs	NR	***
7.	Krishnamoorthy et al 2018	Puducherry	IDI & KII	Diabetes and Hypertension patients & Healthcare workers	Community based	NR	Inductive	NR	Manual content analysis	6 IDI + 4 KII	NR	***
8.	Kusuma et al 2010	Delhi	KII & FGD	Recent and Settled Migrants having hypertension inhabited in Delhi	Community based	NR	NR	NR	Manual content analysis	14 (KII) + 20 (FGD)	38 – 50 (KII) & 25 – 40 (FGD)	***
9.	Miller et al 2017	Delhi	IDI	Cardiovascular disease patients	Trial based	Descriptive	NR	NR	Manual content analysis	14	NR	***
10.	Newtonraj et al 2017	Tamil Nadu	Personal interviews	Hypertensive patients	Community based	NR	NR	NR	Manual content analysis	40	NR	**

11.	Nimesh et al 2019	Madhya Pradesh	IDI	Individuals with diabetes	Community based	NR	Inductive	Yes	Manual content analysis	60	52	***
12.	Patti et al 2020	Orissa	IDI	Primary care physicians	Facility based	NR	NR	NR	Manual content analysis	17	40	***
13.	Rani et al 2019	Tamil Nadu	FGD	Individuals with diabetes	Community based	Descriptive	NR	NR	Manual content analysis	50	50	**
14.	Salaam et al 2019	Andhra Pradesh	IDI	Patients with Cardiovascular disease	Community based	NR	NR	Yes	NVivo version 11 software	12	62	***
15.	Satish et al 2019	West Bengal	FGD	Patients with hypertension and/or diabetes	Trial based	NR	NR	Yes	Manual content analysis	70	53	***
16.	Thakur et al 2016	Chandigarh	IDI & FGD	Coronary artery disease patients	Facility based	NR	NR	NR	Manual Thematic analysis	20	NR	*
17.	Venkatesan et al 2018	Tamil Nadu	IDI	Health care workers	Community based	NR	NR	NR	Anthropac software	10	NR	***
18.	Wood et al 2015	Hyderabad and Delhi	IDI	Patients with Cardiovascular diseases	Trial based	NR	NR	Yes	NVivo software	52	57	***

NR – Not Reported

IDI – In depth Interview

FGD – Focussed Group Discussion

KII – Key informant interview

Table 2: Thematic framework analysis for summarizing barriers in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Barriers in Medication Adherence	Studies
PATIENTS	1. Lack of awareness/knowledge: Lack of knowledge and understanding about the disease, its complications and treatment among the patients	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Patti et al 2020, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Forgetfulness: Patients forget to take medicine because of busy schedule	Dhar et al 2016, Gupta et al 2019, Gupta et al 2020, Rani et al 2019, Venkatesan et al 2018, Wood et al 2015, Tan et al 2017, Thakur et al 2016
	3. Misconception about medications: Patient has wrong perception about the medications, especially about its side effects and quality	George et al 2016, Gupta et al 2020, Patti et al 2020, Rani et al 2019, Salaam et al 2019, Tan et al 2017, Venkatesan et al 2018
	4. Preference to alternate system of medicine: Patients prefers taking herbal and other alternate system of medicines for their condition	George et al 2016, Tan et al 2017, Venkatesan et al 2018
	5. Ill effects of substance abuse: Patients have difficulty in adhering to medications during the bout of tobacco or alcohol consumption	Jayanna et al 2019, Krishnamoorthy et al 2018
	6. Effect of side effects: Patients stop their medication once they develop side effects related to the drugs	Venkatesan et al 2018, Wood et al 2015
	7. Stress: Patients developing stress due to personal or work-related problems are more non-adherent to medications	Krishnamoorthy et al 2018
	8. Stigma: Patients feel stigmatised in revealing their disease status to other family/friends leading to lack of support from them	Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Lack of physical, emotional and social support as the family members are pre-occupied with domestic works, crisis, other priorities and commitments	Dhar et al 2016, George et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Rani et al 2019, Wood et al 2015
	2. Risk communication: Poor risk communication or counselling to patients and family members about non-adherence to medication by the treating physicians	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Thakur et al 2016
	3. Physician attitude: Lack of respect, empathy, communication and attention towards patients by the treating physicians	Dhar et al 2016, Gupta et al 2019, Kusuma et al 2010, Jayanna et al 2019

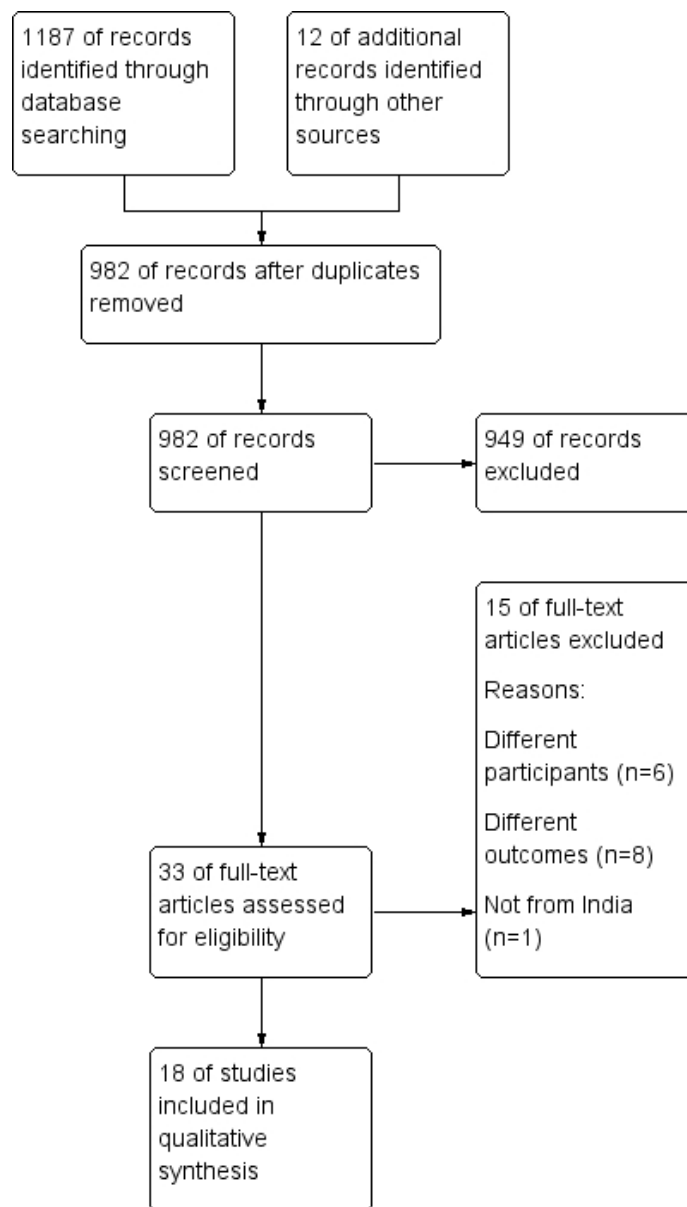
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Affordability: Patients lose their daily wages due to inconvenient consultation timings in public facilities, which is aggravated by travel costs due to poor access, and higher medication costs while preferring private facilities	Agarwal et al 2019, Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Nimesh et al 2019, Salaam et al 2019, Satish et al 2019, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Accessibility: Lack of access to healthcare facilities (more distance) requiring longer travel and waiting time.	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	3. Availability: Non-availability of essential medicines in public healthcare facilities	Dhar et al 2016, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Salaam et al 2019, Wood et al 2015
	4. Acceptability: Medications from public health facilities are not acceptable to the patients due to poorer quality	
	5. Overburdening of primary health centres: Burdening of primary health facilities lead to time constraints in patient counselling regarding medication adherence	Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Venkatesan et al 2018

Table 3: Thematic framework for summarizing facilitators in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Facilitators in Medication Adherence	Studies
PATIENTS	1. Self-awareness and fear: Patient's understanding about medicine adherence and fear about complications of non-adherence keeps them healthy	Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Satish et al 2019, Tan et al 2017, Wood et al 2015
	2. Medicine Reminder system: Separate pill boxes/cases/covers, personalized shelf, and maintaining drug record notebook helps them in remembering daily doses	Dhar et al 2016, Krishnamoorthy et al 2018, Miller et al 2017, Tan et al 2017
	3. Integrating drug intake with the daily routine: Fixed time for medicine intake, separate place for keeping drug, and making arrangements during travel helps them in adherence	Dhar et al 2016, Krishnamoorthy et al 2018
	4. Positive peer influence: Good adherence to medication by the patient's peers motivates the patient to be compliance to their own drug intake	Gupta et al 2019, Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Constant reminders by family members for drug intake	Dhar et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Miller et al 2017, Wood et al 2015
	2. Past adverse experiences: Death of patients' own family members due to complications of the condition has motivated them to adhere to medication	Dhar et al 2016, Krishnamoorthy et al 2018
	3. Healthcare provider counselling and empathy: Patients described that counselling from their healthcare providers has motivated them to remain adherent	Kusuma et al 2010, Miller et al 2017, Patti et al 2020, Salaam et al 2019, Tan et al 2017
	4. Trust in physician: Adherence is more when a positive rapport and trust is established between the patient and health care providers.	Dhar et al 2016, Krishnamoorthy et al 2018, Satish et al 2019
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Dedicated pill boxes/covers: Provision of different medications in separate boxes/covers in the healthcare facility has helped as the patient to remember which medication to take at what time	Krishnamoorthy et al 2018, Wood et al 2015
	2. Combination drugs (polypills): Polypills had the following advantages to facilitate the medication adherence: a smaller number of pills, lower frequency, less chance of forgetting, potential for lower cost, and convenient simpler regimen	Salaam et al 2019, Wood et al 2015
	3. Availability of medications: Proper pharmacy inventory control and stock delivery has aided in medication adherence	Miller et al 2017
ENVIRONMENT (Regulatory, market and policy framework)	1. NGO Support: Patients has reported that sharing their concerns and receiving counselling from NGO/ Health officers acted as a facilitator for drug intake	Tan et al 2017, Wood et al 2015

Table 4: Thematic framework for summarizing suggestions to improve medication adherence among CVD & DM patients in India

Main theme/Sub-themes	Suggestions to improve medication adherence	Studies
PATIENTS	1. Peer support groups: Patients can motivate each other by forming support groups among themselves	Krishnamoorthy et al 2018
	2. Digital reminder system: Patient can use digital reminders such as watch, mobile phone to adhere to their drug schedule	Krishnamoorthy et al 2018, Miller et al 2017
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Social support: Family members can be educated and asked to provide support by reinforcing compliance, reminding about drug intake, motivating them patients to avoid substance abuse	Agarwal et al 2019, Dhar et al 2016, Krishnamoorthy et al 2018, Nimesh et al 2019, Wood et al 2015
	2. Financial support: Family members can provide financial support to cover the cost of medications, travel etc.	Gupta et al 2019
	3. Regular training of healthcare workers: Physicians and other healthcare workers involved in prescribing drugs and counselling should undergo regular training on standard treatment protocols	George et al 2016, Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019
	4. Team work approach: Integration of AYUSH, mental health counsellors, physiotherapist and geriatric clinics at primary healthcare level	George et al 2016, Miller et al 2017, Patti et al 2020
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Innovations in patient care: Healthcare workers can make innovations like dedicated day for specific conditions (diabetes day, etc), dedicated counselling station/session with additional staff for detailing the importance of adherence and complications related to non-adherence, unique pill dispensing mechanism (colour coding)	Agarwal et al 2019, Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Satish et al 2019, Venkatesan et al 2018, Wood et al 2015
	2. IEC/BCC/Awareness campaigns: Putting up of IEC materials and conducting campaigns on importance of adherence in public places and workplaces	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Newtonraj et al 2017, Patti et al 2020, Rani et al 2019
	3. Digitalizing patient treatment record: Digitalizing a dedicated treatment record for each patient can help in better follow-up of the patient and improve adherence	Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019, Wood et al 2015
	4. Polypills: Disseminating the advantages of polypills to healthcare professionals by CME/conferences and patients by public education campaigns; Integration of polypills into clinical practice. etc	Salaam et al 2019, Wood et al 2015
ENVIRONMENT (Regulatory, market and policy framework)	1. Linkage of health services with NGO and community-based organizations: Community members, volunteers, anganwadi workers, self-help groups and NGO workers can be trained in counselling the patients to improve medication adherence	Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Tan et al 2017



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Supplementary Table 1 Search strategy

Key word	Alternative word
Qualitative studies	((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))
Medication Adherence	((((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])
Barriers, Facilitators and solutions	Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions
Diabetes mellitus and CVDs	((((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))

India	(India[MeSH Terms] OR Republic of India[MeSH Terms]))
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Search results (PubMed):

(((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms])) AND (((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms]) OR Life Change Events[MeSH Terms]) OR Trust[MeSH Terms]))) AND (((((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms])) AND (India[MeSH Terms] OR Republic of India[MeSH Terms])) – 199 (Filters: Years between 2010 and 2020 and English language publication)

((((((((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))) AND (((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])) AND (Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions)) AND ((((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))) AND ((India[MeSH Terms] OR Republic of India[MeSH Terms])) – 31 results (Filters: Years between 2010 and 2020 and English language publication)

Google scholar: 635 + 22 + 6 + 12 = 675

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3 **ScienceDirect:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
4 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 238 articles
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6 **Cochrane library:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
7 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 34 articles
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For peer review only

Supplementary file 2. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ Checklist (Tong, *et al.*, 2012)

Item No.	Guide and Description	Report Location
1. Aim	State the research question the synthesis addresses	P 6, 1-13
2. Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology (e.g. meta-ethnography, thematic synthesis, critical interpretive synthesis, grounded theory synthesis, realist synthesis, meta-aggregation, meta-study, framework synthesis)	P9, 16-25 P10, 1-22
3. Approach to searching	Indicate whether the search was pre-planned (comprehensive search strategies to seek all available studies) or iterative (to seek all available concepts until they theoretical saturation is achieved)	P8, 1-10
4. Inclusion criteria	Specify the inclusion/exclusion criteria (e.g. in terms of population, language, year limits, type of publication, study type)	P7, 3-23
5. Data sources	Describe the information sources used (e.g. electronic databases (MEDLINE, EMBASE, CINAHL, psycINFO), grey literature databases (digital thesis, policy reports), relevant organisational websites, experts, information specialists, generic web searches (Google Scholar) hand searching, reference lists) and when the searches conducted; provide the rationale for using the data sources	P8, 1-10
6. Electronic Search strategy	Describe the literature search (e.g. provide electronic search strategies with population terms, clinical or health topic terms, experiential or social phenomena related terms, filters for qualitative research, and search limits)	Supplementary file 1
7. Study screening methods	Describe the process of study screening and sifting (e.g. title, abstract and full text review, number of independent reviewers who screened studies)	Figure 1
8. Study characteristics	Present the characteristics of the included studies (e.g. year of publication, country, population, number of participants, data collection, methodology, analysis, research questions)	Table 1
9. Study selection results	Identify the number of studies screened and provide reasons for study exclusion (e.g. for comprehensive searching, provide numbers of studies screened and reasons for exclusion indicated in a figure/flowchart; for iterative searching describe reasons for study exclusion and inclusion based on modifications to the research question and/or contribution to theory development)	Fig 1 - PRISMA flow diagram P11, 6-18
10. Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings (e.g. assessment of conduct (validity and robustness),	P11, 14-18 Table 1

	assessment of reporting (transparency), assessment of content and utility of the findings)	
11. Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings (e.g. Existing tools: CASP, QARI, COREQ, Mays and Pope [25]; reviewer developed tools; describe the domains assessed: research team, study design, data analysis and interpretations, reporting)	P9, 3-14 Table 1
12. Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required	P8, 11-17
13. Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale	P11, 14-18 Table 1
14. Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies? (e.g. all text under the headings "results /conclusions" were extracted electronically and entered into a computer software)	P8, 18-25
15. Software	State the computer software used, if any	None used
16. Number of reviewers	Identify who was involved in coding and analysis	P9, 16-22
17. Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts)	P9, 23-35 P10, 1-22
18. Study comparison	Describe how were comparisons made within and across studies (e.g. subsequent studies were coded into pre-existing concepts, and new concepts were created when deemed necessary)	Table 2
19. Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive	Inductive process Table 2
20. Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation	Table 2
21. Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies (e.g. new interpretation, models of evidence, conceptual models, analytical framework, development of a new theory or construct)	P11-14

BMJ Open

Patient and Provider's perspective on barriers and facilitators for medication adherence among adult patients with Cardiovascular Diseases and Diabetes Mellitus in India – A qualitative evidence synthesis

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Secondary Subject Heading:	Cardiovascular medicine, Diabetes and endocrinology
Keywords:	QUALITATIVE RESEARCH, PREVENTIVE MEDICINE, PRIMARY CARE, Coronary heart disease < CARDIOLOGY, DIABETES & ENDOCRINOLOGY

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3 1 **Patient and provider's perspective on barriers and facilitators for medication adherence**
4
5 2 **among adult patients with cardiovascular diseases and diabetes mellitus in India – A**
6
7 3 **qualitative evidence synthesis**

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9
10 4 **Running head:** Barriers and facilitators for medication adherence among cardiovascular
11
12 5 diseases and diabetes mellitus and DM patients in India

13
14 6 **Article category:** Systematic Review

15
16
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14 6 **Abstract:**

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17 7 **Objective:**

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19 8 To explore the various stakeholders' perspectives on barriers and facilitators for medication
20
21 9 adherence among cardiovascular diseases and diabetes mellitus patients in India.

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24 10 **Design:** Systematic review of qualitative studies

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26 11 **Data sources:**

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28 12 A comprehensive systematic search was conducted in Medline, Cochrane Library, Science
29
30 13 Direct and Google Scholar from January 2010 to July 2020. We included all qualitative peer-
31
32 14 reviewed studies, reporting barriers and facilitators of medication adherence, from India for
33
34 15 our current review.

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36
37 16 **Data extraction and synthesis:** Data extraction was performed by two independent authors
38
39 17 who also assessed the quality of included studies using the Critical Appraisal Skills Programme
40
41 18 (CASP) criteria. This qualitative evidence synthesis adhered to the Enhancing transparency in
42
43 19 reporting the synthesis of qualitative research (ENTREQ) checklist

44
45
46 20 **Results:**

47
48
49 21 In total, 18 studies were included. Major barriers reported were lack of understanding about
50
51 22 the disease, complications related to non-adherence, followed by forgetfulness, lack of family
52
53 23 support and risk communication. Health system-related barriers such as accessibility,
54
55 24 affordability, and acceptability were also reported by majority of the studies. Creation of peer
56
57 25 support groups, digital reminder systems, integration of native Indian systems of India,
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59
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1 physiotherapy and geriatric clinics at the primary healthcare level and innovations in patient
2 care were suggested to counter these barriers in medication adherence.

3 **Conclusion:**

4 Such patient-specific targeted interventions need to be developed to achieve better control
5 among CVD and DM patients.

6 **Keywords:** Cardiovascular Diseases, Diabetes Mellitus, Medication Adherence, Qualitative
7 Research

8 **Strengths and Limitations:**

- 9 1. This is the first review exploring factors associated with drug adherence among
10 cardiovascular diseases and diabetes mellitus patients in India
- 11 2. We have adhered to the ENTREQ statement ensuring transparency and reproducibility
12 of the study findings.
- 13 3. We cannot rule out dissemination bias, causing selective reporting of studies with more
14 non adherence to medications
- 15 4. We focussed primarily on the patient and provider perspective on medication
16 adherence. Hence, we cannot comment on the organizational or political influences on
17 the adherence to long-term therapies.
- 18 5. The sample size of the included studies can be considered relatively low (median
19 sample size - 30).

1 INTRODUCTION

2 Cardiovascular diseases (CVDs) are the leading cause of mortality globally and in India.^{1,2}
3 More than a quarter (28%) of all-cause mortality in India is attributed to CVDs, where ischemic
4 heart disease (IHD) and stroke constitute the majority (83%).³ On the other hand, India ranks
5 second after China in the global diabetes epidemic, with a prevalence of around 10%.⁴ Both
6 diabetes mellitus (DM) and hypertension have long been recognized as independent risk factors
7 for CVDs, whereas adherence to prescribed hypoglycaemic and antihypertensive drug
8 therapies have significantly reduced the risk.⁵⁻⁸ At least half of these chronic disease patients
9 stop taking medications within a year, often without informing their provider. With further
10 nonadherence and attrition over time, medication adherence has emerged as a significant public
11 health priority.⁹

12 Medication adherence is defined as the extent to which a person's behaviour coincides with the
13 agreed medication regimen or health advice from a health care provider.¹⁰ It has three
14 components: initiation (when the patient takes the first dose of prescribed medication),
15 implementation (the extent to which a patient's actual dosing corresponds to the prescribed
16 dosing regimen), and discontinuation (when no more doses are taken after that).¹¹ Medication
17 adherence is of growing interest to clinicians, healthcare systems, and other stakeholders. There
18 is soaring evidence that links nonadherence with lower quality of life, adverse clinical events,
19 increased need for medical interventions, and mortality, thus giving rise to avoidable out-of-
20 pocket expenditure in health.¹² Non-adherent hypertensive and stable coronary heart disease
21 (CHD) patients have a four to five times higher risk of developing CHD and death, when
22 compared to adherent patients.^{13,14} Similarly, the likelihood of hospitalization is doubled
23 among DM & hypertensive patients who are non-adherent to prescribed therapies compared to
24 the general population. Despite recent advancements in pharmacologic treatment and
25 technology to treat and monitor DM and CVD patients, medication adherence is of particular

1 concern in low-and-middle-income countries (LMIC) like India, where accessibility and
2 affordability issues are still pertinent.^{3,15}

3 Barriers to adherence are often related to patient, medication, provider, and health system
4 factors, with interactions between them.^{16,17} Patient factors that influence adherence include
5 poor health literacy, faulty cultural beliefs regarding medication effectiveness, and religious
6 healing practices.¹⁷ Low income, forgetting to take medication, and perceptions regarding pills
7 like safety concerns, convenience, and necessity add to the above list. Inadequate knowledge
8 about a drug and its use, not being convinced of the need for medication, fear of adverse effects,
9 and long-term treatment regimens also prompt medication discontinuation.¹⁵ Clinician factors
10 includes: failure to recognize nonadherence, prescription of complex and multidrug regimens,
11 ineffective communication of benefits of medications, and excluding patients in the treatment
12 decision-making process.¹⁷ Health system factors comprise limited insurance coverage, poor
13 coordination of care between inpatient and outpatient settings, and inadequate communication
14 between prescribers (i.e., specialists and primary care clinicians). In addition, the caregivers'
15 aspects also become relevant in determining patients' adherence, as it is proven that CVD
16 patients with caregivers are more likely to be adherent to medications.¹⁸ Hence identifying
17 patient-specific barriers and adopting suitable techniques to overcome them is imperative to
18 improve medication adherence. A few successful facilitators that has helped us overcoming
19 these barriers include: inclusion of medication counsellors into the continuum of care to guide
20 patients, single-pill fixed-dose combinations, training pharmacists as coaches for drug
21 therapies, building peer groups for chronic conditions, and developing information systems in
22 the follow-up of patients.¹⁹

23 Quantitative studies have extensively studied medication adherence and its determinants. They
24 do not, however, uncover life circumstances that may influence adherence from the patient
25 perspective. A systematic review of qualitative studies will provide us with a better

1 understanding of the barriers and facilitators from the first-hand experiences of patients,
2 healthcare providers, and caregivers.²⁰ Qualitative evidence synthesis, a novel research
3 method, brings together the available qualitative evidence from primary studies through a
4 systematic review process. Despite the conceptually rich evidence generated from primary
5 qualitative studies, a qualitative evidence synthesis can aid policymakers and clinicians to get
6 an overall insight of the findings, thereby enabling them to address all subtle and sensitive
7 issues that most primary studies encounter. The findings from this qualitative evidence
8 synthesis can guide various stakeholders to frame specific policy recommendations in non-
9 communicable disease care.²¹ Thus, we undertook this review to understand the perspective
10 of various stakeholders (patients, caregivers, and healthcare providers) on the barriers and
11 facilitators for medication adherence among CVD and DM patients in India. We also explored
12 the suggestions and solutions provided by these stakeholders in overcoming the reported
13 barriers.

14 **METHODS**

15 This review was performed by adhering to the “Enhancing transparency in reporting the
16 synthesis of qualitative research (ENTREQ)” statement. (Supplementary file 1)²² We
17 registered our protocol in the PROSPERO database (Registration number -
18 CRD42020199529). We also searched PROSPERO and Cochrane to ensure that no similar
19 review protocol has been reported. We also performed a preliminary search to ensure that no
20 previous reviews of our similar topic targeting the Indian population were published.

21 **Study design**

22 We performed a qualitative evidence synthesis of all available qualitative studies on the barriers
23 and facilitating factors for medication adherence among CVD and DM patients in India. This

1 review would help to aggregate the evidence of peer-reviewed articles and build an organized
2 empirical research outline based on prior knowledge.

3 ***Eligibility criteria***

4 *Study type*

5 We have included peer-reviewed qualitative studies conducted in India for our current review.
6 Furthermore, qualitative evidence from other mixed methods studies was screened for
7 eligibility and included in the qualitative component was relevant to our review. In addition,
8 we included studies using qualitative techniques for data collection such as focussed group
9 discussion (FGD), in-depth interviews (IDI), and Key Informant Interviews (KII).

10 *Participant type*

11 We have included the studies reporting the barriers and facilitators of medication adherence
12 from patients' perspectives (CVD and DM), family members, healthcare workers (HCWs), or
13 health system policymakers perspectives. HCWs were defined as per World health organisation
14 (WHO) recommendation as "all the persons involved in the actions whose primary intent is to
15 enhance the health."²³

16 *Outcome*

17 The phenomenon of interest was to explore the barriers and facilitators for medication
18 adherence among CVD and DM patients in India. We also explored the possible suggestions
19 and solutions to address the barriers and improve compliance, as experienced by the patients,
20 caregivers, family members, HCWs, and other relevant stakeholders.

21 ***Exclusion criteria***

22 We have excluded the studies not available in English, books, conference abstracts, grey
23 literature, or editorial comments. We have also excluded the studies reporting only quantitative
24 data such as cross-sectional surveys, case-control, cohort studies, or intervention trials.

25 **Search strategy**

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3 1 We have conducted a comprehensive and systematic search in databases and search engines
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5 2 such as Medline, Cochrane Library, ScienceDirect, and Google Scholar. A combination of
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7 3 medical subject heading (MeSH) and free-full text terms was used for carrying out a literature
8
9 4 search. The detailed search strategy and search results in the databases mentioned above and
10
11 5 search engines are provided in Supplementary File 2. In addition to this, we also checked the
12
13 6 reference list of primary studies obtained via electronic search and included articles relevant to
14
15 7 our review and analysis. The search was conducted in all above-mentioned databases from
16
17 8 January 2010 to July 2020. Our search timeline was restricted to the past decade alone to ensure
18
19 9 the identification of emerging issues.
20
21
22

23 24 10 **Study selection process**

25
26 11 Two investigators (YK and TR) independently performed the literature search, screened the
27
28 12 title and abstract of all the identified studies, and retrieved the full text for articles relevant to
29
30 13 our review. Further full-text screening of the retrieved articles was done again independently
31
32 14 by the two investigators (YK, TR) to select the studies matching the eligibility criteria of our
33
34 15 review. Disagreements during this process between the two investigators were resolved
35
36 16 through consultation with a third investigator (SR).
37
38
39

40 17 **Data Extraction and Management**

41
42 18 After the study selection, two investigators (YK and TR) independently extracted the relevant
43
44 19 data and study characteristics onto a predetermined data extraction format. Data entry was
45
46 20 double-checked for accuracy by a third investigator (SR) by comparing the data presented in
47
48 21 the review and individual study reports. As a result, we have extracted the following study
49
50 22 characteristics: general information such as the name of the first author, the country in which
51
52 23 the study was done, and year of publication, in the methods section, data collection period,
53
54 24 study design, study participants, sample size, sampling technique, and data collection
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1 procedure. In addition, barriers, facilitators, suggestions, and solutions to medication adherence
2 were identified systematically.

3 **Quality assessment**

4 Two investigators (YK and SR) independently performed the quality check using the Critical
5 Appraisal Skills Programme (CASP) criteria.²⁴ This checklist has been widely used for
6 assessing the quality of studies included in Qualitative Evidence synthesis.²⁵ This checklist
7 helps us to determine the coherence of included studies with the quality appraisal standard for
8 qualitative studies. This checklist consists of 10 questions concerning the study's clarity,
9 methodology, and results to rank the included studies. Subsequently, these studies were
10 stratified into high quality (three stars for studies scoring 8 to 10 points), medium quality (two
11 stars for studies scoring 4 to 7 points), and low rate (one star for studies scoring 0 to 3 points).
12 We did not exclude the low-quality studies, but the interpretation of results was made with
13 caution. Disagreements during the quality assessment process were resolved by discussion with
14 the third investigator (TR).

15 **Data Analysis**

16 We analysed and reported the findings in separate clusters such as patients, caregivers, family
17 members, HCWs, and policymakers to demonstrate the differences among these subgroups.
18 We have adopted a thematic framework analysis to analyse and synthesize the data. Thematic
19 framework analysis has been helpful as the evidence was primarily descriptive and improved
20 our understanding of the barriers and facilitators in medication adherence among CVD and DM
21 patients. This framework synthesis has five stages of synthesizing the qualitative data.

22 ***First stage - Familiarisation with the data:*** Primary investigator (YK) did the process of
23 familiarisation with data by reviewing all the selected articles against the objective of our
24 review and found the recurrent themes across the included studies.

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2
3 1 **The second stage - Identifying the thematic framework:** The investigators used a
4
5 2 predetermined thematic framework developed using literature to guide the thematic analysis.
6
7 3 The final framework comprised of a detailed list of facilitators and barriers for medication
8
9 4 adherence and also solutions to address the issue.

10
11
12 5 **Third stage - Indexing:** Two independent investigators (YK and SR) read the extracted
13
14 6 information and searched for themes as per the predetermined thematic framework and found
15
16 7 additional emerging themes. The framework underwent several revisions as and when a new
17
18 8 theme emerged, after discussing with the entire team of investigators. Next, all the studies were
19
20 9 completely read and examined till there was no new emergent theme. Coding of the data was
21
22 10 then done as per the themes identified in our analysis. Finally, each preliminary study indexing
23
24 11 was done using the codes related to the thematic framework. Whenever appropriate, sections
25
26 12 of the studies were indexed with one or more codes.

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30 13 **Fourth stage - Charting:** The investigators then sorted the data based on themes and presented
31
32 14 these themes in the tabular format (chart). The rows and columns of the table indicate the
33
34 15 themes related to the studies, which enabled us to compare the study findings across various
35
36 16 themes and subthemes.

37
38
39
40 17 **Fifth stage - Mapping and interpretation:** The investigators then used these charts to define
41
42 18 the concepts identified, and finally mapped the nature and range of the phenomena. Our review
43
44 19 explored the associations between the various emerging themes and helped in clarifying the
45
46 20 findings. Finally, we mapped and interpreted the findings in line with our objectives and
47
48 21 emergent themes.

22 **Ethics Approval:**

23 Approval from an ethics committee is not required since our review included only publicly
24 available data without involving the human participants directly.

1 **Patient and Public Involvement:**

2 Patients or the public were not involved in the design, or conduct, or reporting, or dissemination
3 plans of our research.

4 **Results**

5 **Study selection**

6 A comprehensive and systematic search was done to identify the relevant studies from January
7 2010 to July 2020. In total, we identified 1187 citations, and after the removal of duplicates
8 from multiple databases, 982 records were screened for their title and abstract, and assessed for
9 eligibility. From these records, we retrieved 33 articles, and after going through the full text of
10 these articles, 18 studies were included in the review. (**Figure 1**).²⁶⁻⁴³

11 **Characteristics of the studies included**

12 Characteristics of the included studies are reported in **Table 1**. Of the 18 studies included, 9
13 (50%) were from the southern region, followed by 7 (38%) from the northern part of India. The
14 mean age of the participants ranged from 25-76 years. The typology of the studies comprised
15 of in-depth interviews (IDIs) and focussed group discussions (FGDs). The study participants
16 were primarily patients with diabetes, hypertension, or any cardiovascular diseases (to explore
17 the patient perspective), and health care workers (4 studies) providing care to them (to obtain
18 the provider perspective). The total sample size of the included studies ranged from 6 to 100.
19 The majority (10 of the included studies) were from the community, while the rest were either
20 facility-based or had participants from ongoing trials. Four of the included studies used
21 software for analysing the qualitative data, while the rest followed manual methods. Most of
22 the included studies (14 out of 18) had high-quality evidence.

23 **Narrative synthesis**

1 Findings from our review showed that significant factors contributing to adherence were
2
3 grouped under three themes: patient-related, family-related, and health system-related factors.
4
5 The barriers, facilitators, and suggestions to improve medication adherence were summarized
6
7 under these three themes.
8
9

10 **Barriers in medication adherence**

11 **Table-2** shows the thematic framework analysis related to barriers in medication adherence
12 among CVD and DM patients. All the 18 included studies have explored and reported on these
13
14 barriers.
15

16 *Patient-related factors*

17 Significant patient-related barriers (10 studies) reported were lack of knowledge or
18 understanding about the disease, its complications, and the treatment schedule, followed by
19 forgetfulness to take medicines (7 studies). Reasons provided for the same were the patients'
20 busy schedule, laziness, or forgetting to take the medication while travelling out-of-station.
21 Patients have also reported certain misconceptions about the medicines like the risk of long-
22 term neurological illness because of medication intake, inferior quality of drugs provided in
23 hospitals, and wrong perception about stopping the medications once the patient feels normal.
24 Patients in some studies have reported that they practice alternate systems of medicine such as
25 herbal medicines and avoid taking allopathic medicines leading to poorer control. Substance
26 use such as alcohol or tobacco use, side effects related to drugs, stress, and stigma were reported
27 to be other barriers
28

29 *Family-related factors*

30 The patients and providers have reported lack of family support as a significant contributing
31 factor for nonadherence. In addition, the lack of social and emotional support to the patients
32 further promote nonadherence. Domestic works, personal priorities, commitments, or other
33 family-related issues hinder the family members from adequate support.
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1 *Health system-related factors*

2 In most of these studies, providers were also interviewed to understand the health system
3 barriers responsible for nonadherence among CVD and DM patients. Healthcare providers and
4 stakeholders interviewed, in almost all these studies, have reported affordability, accessibility,
5 and acceptability as major factors hindering medication adherence. Affordability is of prime
6 concern among patients seeking healthcare from private facilities. Though there are no direct
7 medical costs involved in availing services from the public sector or primary healthcare centres,
8 direct non-medical costs such as transport (due to poor accessibility) and indirect costs such as
9 loss of wages (due to inconvenient consultation timing) were contributory. In addition, studies
10 reported that patients, in general, had wrong perceptions about the quality of medications
11 provided in public facilities, influencing them to choose private health facilities, including
12 those belonging to lower socioeconomic status. Lack of risk communication, counselling, or
13 empathy by the physicians mainly due to overburdened public health facilities and time
14 constraints were the other health system-related barriers reported by the providers and patients.

15 **Facilitators in medication adherence**

16 Facilitators in medication adherence were also summarized using the pre-existing thematic
17 framework (**Table-3**). In total, ten studies have explored the facilitators in medication
18 adherence from the patient or providers' perspective.

19 *Patient-related factors*

20 Most of the studies (5 studies) reported fear of complications due to nonadherence and self-
21 perception of being healthy (once they adhere to the medications) as the significant facilitators.
22 In addition, having a reminder system in the form of reminder notebooks, separate
23 pillboxes/cases/covers, or personalized shelf facilitates the patients in adhering to the
24 medications. Some studies have also reported that integrating drug intake into daily routine
25 activities and peer influence acts as good facilitators for compliance with medications.

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2
3 1 *Family-related factors*
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5 2 Family support was reported as a major facilitating factor for compliance with medication.
6

7 3 Apart from the support, adverse experiences in the past, such as death or severe complications
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9 4 among the family members, instilled fear in the patients and making them more compliant to
10
11 5 the medications.
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14 6 *Health system-related factors*
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16 7 Barriers reported in some of the studies, such as empathy and counselling by healthcare
17
18 8 providers, were considered facilitators by other studies' patients. Another major facilitator from
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20 9 the health system side is the trust that patient has in their physician and their willingness to
21
22 10 effectively follow advices related to self-care and adherence. Other familiar facilitators
23
24 11 reported by the patients and providers were the use of dedicated pill cover/boxes for each drug
25
26 12 provided in the clinic, linkage of health services with other non-governmental organisations
27
28 13 (NGO) for provision of counselling and generating awareness, availability of medication, and
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30 14 use of polypills.
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35 15 **Suggestions to improve medication adherence**
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37 16 Suggestions and solutions to enhance the compliance to medication were reported in 16 out of
38
39 17 the 18 included studies based on either patient or provider's perspective (**Table-4**). Few
40
41 18 suggestions were related to patients and family members, while the majority were related to
42
43 19 the change in the health system.
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45

46 20 *Patient and family-related factors*
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48 21 Creating or joining a peer support group was one among the major suggestions related to the
49
50 22 patients. Digital reminder systems using a watch or a mobile phone were other uncommon
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52 23 suggestions to improve medication adherence.
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55 24 *Health system-related factors*
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3 1 Innovations in patient care, have been necessitated as an important factor to promote drug
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5 2 adherence. Some possible recommendations were hosting dedicated days for specific disease
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7 3 conditions to avoid overburdening the facilities, a dedicated counselling station for drug
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9 4 adherence during the clinic with separate human resources, and a unique pill dispensing
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11 5 mechanism like colour coding, etc were the other suggestions. In addition, information
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13 6 education and communication (IEC)/ behaviour change communication (BCC) campaigns,
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15 7 digitalizing the patient treatment records, linkage of healthcare services with NGOs or
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17 8 community-based organizations, regular training of healthcare workers, and promotion of
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19 9 polypill use were other common suggestions offered by the healthcare providers.
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23 24 **Discussion**

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26 11 We conducted this review to integrate qualitative evidence on barriers and facilitators for
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28 12 medication adherence among CVD and DM patients in India. We also further explored the
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30 13 suggestions to improve medication adherence. The studies included in our review involved a
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32 14 total of 636 participants (534 CVD and DM patients, 102 healthcare providers). The majority
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34 15 of the included studies were of high quality concerning study clarity, methodology, and results.
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36 16 We summarized the three major themes: barriers, facilitators, suggestions and reported our
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38 17 findings under the following four sub-themes: patients, care team, healthcare organization, and
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40 18 environment-related factors.
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44 *Comparison of findings with previous literature*

45 *Barriers in medication adherence*

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47 21 Major barriers were lack of patient's understanding about the disease and its complications,
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49 22 forgetfulness, and misconception about the medications. Lack of family support was seen as a
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51 23 major barrier from both patients' and providers' perspectives. In addition to these factors, stress
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53 24 and stigma were other contributory barriers. In addition to the above, adherence to medications
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55 25 was decided by patients' cultural beliefs, perceived discrimination, and social customs, which
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1 are largely prevalent in a culturally influenced country like India. A few studies have also
2 shown evidence of improvement in medication adherence in settings, where efforts were taken
3 to overcome the cultural barriers.⁴⁴ We also found that the major health system-related barriers
4 were lack of accessibility and availability, higher cost of medications, and poor physician
5 attitude. These findings were in line with the previous review conducted among South-East
6 Asian DM patients.⁴⁴⁻⁴⁶ In addition, our findings of patients related factors were found to be
7 similar to other patients belonging to non-English speaking Hispanic and south American
8 ethnic groups, such as lack of understanding about their condition, along with additional stress
9 and stigma.⁴⁷⁻⁴⁹

10 *Facilitators in medication adherence*

11 Fear of complications, self-perception of being healthy, having a reminder system were
12 reported as major facilitators by patients. Physician trust, advice, empathy, and counselling
13 were the common provider-related facilitators facilitating adherence. Common facilitators as
14 reported by the patients and providers were: dedicated pill cover/boxes for each drug provided
15 in the clinic, availability of medication, and use of polypills. These findings were also in line
16 with the previous qualitative reviews conducted in low middle-income countries including
17 India.⁴⁷⁻⁵⁰

18 *Suggestions to improve medication adherence*

19 The solutions provided by the patients and health professionals were in line with the barriers
20 identified in our review. Comprehensive physician counselling to make the patients understand
21 their own condition, complications of the disease and avoid misconception about the drugs and
22 their side effects, along with good family support, and making the medication accessible and
23 available free of cost were suggested as major suggestions to improve medication adherence.
24 Similar interventions were also suggested by previous qualitative evidence on medication
25 adherence among CVD and DM patients.⁴⁵⁻⁴⁹ It is also interesting to note that medication

1 adherence was also hurdled by the patients' intention towards adherence, and this intention
2 might vary across nations and cultural groups. The patient's intention not to refill prescriptions
3 due to cost, not to take medication because he feels better, also influences the patient's decision.
4 Thus future research exploring these reasons on patient's choice to adhere or not, rather than
5 an inability to adhere (e.g., forgetting, no access) needs to be encouraged.

6 *Strengths and limitations of the study*

7 To the best of our knowledge, this is the first review synthesizing all possible qualitative factors
8 associated with medication adherence among CVD and DM patients in India. We have
9 provided comprehensive and systematic evidence on the barriers, facilitators related to
10 medication adherence, adhering to the ENTREQ statement, thereby ensuring transparency and
11 reproducibility. We examined this evidence through the lenses of a well-established theoretical
12 framework model. Furthermore, our study was able to provide valuable suggestions to promote
13 medication adherence from both patient's and provider's perspectives. In addition to these
14 strengths, we found that the majority of the studies included in our review were of high quality
15 evidence. This in turn ensures the transferability (external validity) of our review findings.
16 However, our review has certain limitations. We did not search grey literature, possibly missing
17 some insights for our review. Hence, we cannot rule out the dissemination bias for an accurate
18 and complete representation of medication adherence. We focussed primarily on the patient
19 and provider perspective on medication adherence.⁵¹ Hence, we cannot comment on the
20 organizational or political influences on the adherence to long-term therapies as mentioned in
21 the WHO report.¹⁶ The sample size of the included studies can be considered relatively low
22 (median sample size - 30). However, all the studies were conducted till the achievement of data
23 saturation. In addition to the above, these results and suggestions need to be considered after
24 taking into account India's cross-cultural adaptations, customs, linguistic variations, and
25 genetic susceptibility, and higher prevalence of risk factor profile.

1 *Implications for clinical and public health practice*

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1 Improving medication adherence is essential to achieve better control and prevent life-threatening complications. Factors related to patients such as self-awareness and fear about the condition and its complications acted as a major facilitator for medication adherence. We also observed that most of the barriers identified were modifiable, in nature. Interventions should focus on these modifiable barriers such as knowledge barriers, intention barriers, and health system-related barriers to achieve better adherence. In addition, the family members need to help the patients in mapping their daily routine and link the medicine intake with these routines to facilitate adherence. Our review also suggested that healthcare providers play an important role in promoting medication adherence. Hence, the interventions should not only target the patients but also the family members and healthcare providers and they should be tailored to suit differences in setting, culture, and type of the patients.

13 *Implications for future research*

14 More evidence needs to be generated concerning the effectiveness and feasibility of possible solutions obtained in our review including the digital solutions, polypills, peer support groups, etc. Further qualitative studies including the subgroup of patients with CVD and DM under different stages and treatment regimens are required to contextualize the medication adherence on a larger scale. Exploring the barriers using a theoretical framework with the same methodological approach, can provide more reliable evidence to develop patient-centred interventions and achieve better control among CVD and DM patients.

21 **Conclusion:**

22 In our review, we categorised the facilitating factors and barriers influencing medication adherence into patient-related, health system-related, and care team-related factors. Thus, we advocate the creation of peer support groups, use of a digital reminder system for overcoming patients related factors, and integration of Indian systems of medicine, physiotherapy, and

1 geriatric clinics even at the primary healthcare level for overcoming the health system-related
2 barriers towards medication adherence.

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9 & TR. Provided comments and inputs to revise the manuscript: SR, YK, TR & MT

10 **Data sharing statement:** The authors confirm that the data supporting the findings of this
11 study are available within the article

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1 **Figure 1: Flow chart showing the search strategy and selection of studies**

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For peer review only

Table 1: Characteristics of the studies included (N=18)

S.No	Author and year	State	Data collection method	Study participants	Study setting	Approach	Coding	Theoretical framework used	Method of analysis	Sample size	Mean Age in years	Study quality
1.	Agarwal 2019	Kerala	IDI	Clinical and administrative staff	Facility based	NR	Inductive	NR	Dedoose Software	21	NR	***
2.	Dhar et al 2016	Delhi	IDI	Hypertensive women aged 35-59 years	Community based	NR	Inductive	Yes	Manual content analysis	30	48	***
3.	George et al 2016	Karnataka	IDI	Physicians providing Non communicable disease care	Community based	NR	Inductive	NR	Manual content analysis	36	46	***
4.	Gupta et al 2019	Rajasthan	IDI	Hypertensive women	Facility based	NR	NR	NR	Manual content analysis	30	56	**
5.	Gupta et al 2020	Haryana	IDI	Hypertension patients	Facility based	NR	NR	NR	Manual content analysis	100	38-76	***
6.	Jayanna et al 2019	Karnataka	IDI & FGD	Diabetes and Hypertension patients	Facility based	NR	NR	Yes	Manual content analysis	10 IDI + 20 FGDs	NR	***
7.	Krishnamoorthy et al 2018	Puducherry	IDI & KII	Diabetes and Hypertension patients & Healthcare workers	Community based	NR	Inductive	NR	Manual content analysis	6 IDI + 4 KII	NR	***
8.	Kusuma et al 2010	Delhi	KII & FGD	Recent and Settled Migrants having hypertension inhabited in Delhi	Community based	NR	NR	NR	Manual content analysis	14 (KII) + 20 (FGD)	38 – 50 (KII) & 25 – 40 (FGD)	***
9.	Miller et al 2017	Delhi	IDI	Cardiovascular disease patients	Trial based	Descriptive	NR	NR	Manual content analysis	14	NR	***
10.	Newtonraj et al 2017	Tamil Nadu	Personal interviews	Hypertensive patients	Community based	NR	NR	NR	Manual content analysis	40	NR	**

11.	Nimesh et al 2019	Madhya Pradesh	IDI	Individuals with diabetes	Community based	NR	Inductive	Yes	Manual content analysis	60	52	***
12.	Patti et al 2020	Orissa	IDI	Primary care physicians	Facility based	NR	NR	NR	Manual content analysis	17	40	***
13.	Rani et al 2019	Tamil Nadu	FGD	Individuals with diabetes	Community based	Descriptive	NR	NR	Manual content analysis	50	50	**
14.	Salaam et al 2019	Andhra Pradesh	IDI	Patients with Cardiovascular disease	Community based	NR	NR	Yes	NVivo version 11 software	12	62	***
15.	Satish et al 2019	West Bengal	FGD	Patients with hypertension and/or diabetes	Trial based	NR	NR	Yes	Manual content analysis	70	53	***
16.	Thakur et al 2016	Chandigarh	IDI & FGD	Coronary artery disease patients	Facility based	NR	NR	NR	Manual Thematic analysis	20	NR	*
17.	Venkatesan et al 2018	Tamil Nadu	IDI	Health care workers	Community based	NR	NR	NR	Anthropac software	10	NR	***
18.	Wood et al 2015	Hyderabad and Delhi	IDI	Patients with Cardiovascular diseases	Trial based	NR	NR	Yes	NVivo software	52	57	***

NR – Not Reported

IDI – In depth Interview

FGD – Focussed Group Discussion

KII – Key informant interview

Table 2: Thematic framework analysis for summarizing barriers in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Barriers in Medication Adherence	Studies
PATIENTS	1. Lack of awareness/knowledge: Lack of knowledge and understanding about the disease, its complications and treatment among the patients	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Patti et al 2020, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Forgetfulness: Patients forget to take medicine because of busy schedule	Dhar et al 2016, Gupta et al 2019, Gupta et al 2020, Rani et al 2019, Venkatesan et al 2018, Wood et al 2015, Tan et al 2017, Thakur et al 2016
	3. Misconception about medications: Patient has wrong perception about the medications, especially about its side effects and quality	George et al 2016, Gupta et al 2020, Patti et al 2020, Rani et al 2019, Salaam et al 2019, Tan et al 2017, Venkatesan et al 2018
	4. Preference to alternate system of medicine: Patients prefers taking herbal and other alternate system of medicines for their condition	George et al 2016, Tan et al 2017, Venkatesan et al 2018
	5. Ill effects of substance abuse: Patients have difficulty in adhering to medications during the bout of tobacco or alcohol consumption	Jayanna et al 2019, Krishnamoorthy et al 2018
	6. Effect of side effects: Patients stop their medication once they develop side effects related to the drugs	Venkatesan et al 2018, Wood et al 2015
	7. Stress: Patients developing stress due to personal or work-related problems are more non-adherent to medications	Krishnamoorthy et al 2018
	8. Stigma: Patients feel stigmatised in revealing their disease status to other family/friends leading to lack of support from them	Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Lack of physical, emotional and social support as the family members are pre-occupied with domestic works, crisis, other priorities and commitments	Dhar et al 2016, George et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Kusuma et al 2010, Newtonraj et al 2017, Rani et al 2019, Wood et al 2015
	2. Risk communication: Poor risk communication or counselling to patients and family members about non-adherence to medication by the treating physicians	Dhar et al 2016, George et al 2016, Gupta et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Thakur et al 2016
	3. Physician attitude: Lack of respect, empathy, communication and attention towards patients by the treating physicians	Dhar et al 2016, Gupta et al 2019, Kusuma et al 2010, Jayanna et al 2019

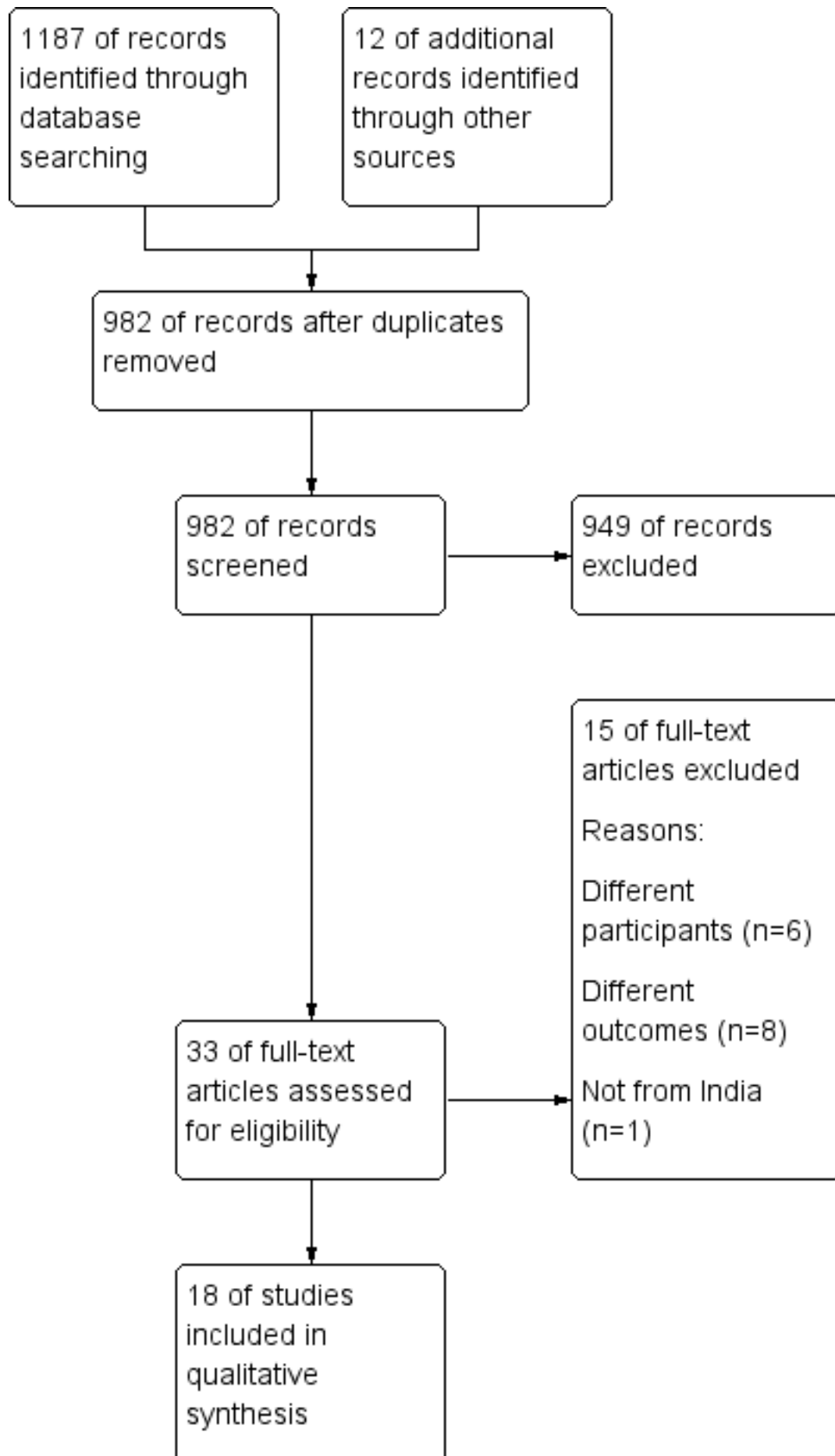
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Affordability: Patients lose their daily wages due to inconvenient consultation timings in public facilities, which is aggravated by travel costs due to poor access, and higher medication costs while preferring private facilities	Agarwal et al 2019, Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Nimesh et al 2019, Salaam et al 2019, Satish et al 2019, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	2. Accessibility: Lack of access to healthcare facilities (more distance) requiring longer travel and waiting time.	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Tan et al 2017, Thakur et al 2016, Venkatesan et al 2018, Wood et al 2015
	3. Availability: Non-availability of essential medicines in public healthcare facilities	Dhar et al 2016, Jayanna et al 2019, Kusuma et al 2010, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Salaam et al 2019, Wood et al 2015
	4. Acceptability: Medications from public health facilities are not acceptable to the patients due to poorer quality	
	5. Overburdening of primary health centres: Burdening of primary health facilities lead to time constraints in patient counselling regarding medication adherence	Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Venkatesan et al 2018

Table 3: Thematic framework for summarizing facilitators in medication adherence experienced by CVD & DM patients in India

Main theme/Sub-themes	Facilitators in Medication Adherence	Studies
PATIENTS	1. Self-awareness and fear: Patient's understanding about medicine adherence and fear about complications of non-adherence keeps them healthy	Krishnamoorthy et al 2018, Miller et al 2017, Patti et al 2020, Satish et al 2019, Tan et al 2017, Wood et al 2015
	2. Medicine Reminder system: Separate pill boxes/cases/covers, personalized shelf, and maintaining drug record notebook helps them in remembering daily doses	Dhar et al 2016, Krishnamoorthy et al 2018, Miller et al 2017, Tan et al 2017
	3. Integrating drug intake with the daily routine: Fixed time for medicine intake, separate place for keeping drug, and making arrangements during travel helps them in adherence	Dhar et al 2016, Krishnamoorthy et al 2018
	4. Positive peer influence: Good adherence to medication by the patient's peers motivates the patient to be compliance to their own drug intake	Gupta et al 2019, Krishnamoorthy et al 2018
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Family support: Constant reminders by family members for drug intake	Dhar et al 2016, Gupta et al 2020, Krishnamoorthy et al 2018, Miller et al 2017, Wood et al 2015
	2. Past adverse experiences: Death of patients' own family members due to complications of the condition has motivated them to adhere to medication	Dhar et al 2016, Krishnamoorthy et al 2018
	3. Healthcare provider counselling and empathy: Patients described that counselling from their healthcare providers has motivated them to remain adherent	Kusuma et al 2010, Miller et al 2017, Patti et al 2020, Salaam et al 2019, Tan et al 2017
	4. Trust in physician: Adherence is more when a positive rapport and trust is established between the patient and health care providers.	Dhar et al 2016, Krishnamoorthy et al 2018, Satish et al 2019
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Dedicated pill boxes/covers: Provision of different medications in separate boxes/covers in the healthcare facility has helped as the patient to remember which medication to take at what time	Krishnamoorthy et al 2018, Wood et al 2015
	2. Combination drugs (polypills): Polypills had the following advantages to facilitate the medication adherence: a smaller number of pills, lower frequency, less chance of forgetting, potential for lower cost, and convenient simpler regimen	Salaam et al 2019, Wood et al 2015
	3. Availability of medications: Proper pharmacy inventory control and stock delivery has aided in medication adherence	Miller et al 2017
ENVIRONMENT (Regulatory, market and policy framework)	1. NGO Support: Patients has reported that sharing their concerns and receiving counselling from NGO/ Health officers acted as a facilitator for drug intake	Tan et al 2017, Wood et al 2015

Table 4: Thematic framework for summarizing suggestions to improve medication adherence among CVD & DM patients in India

Main theme/Sub-themes	Suggestions to improve medication adherence	Studies
PATIENTS	1. Peer support groups: Patients can motivate each other by forming support groups among themselves	Krishnamoorthy et al 2018
	2. Digital reminder system: Patient can use digital reminders such as watch, mobile phone to adhere to their drug schedule	Krishnamoorthy et al 2018, Miller et al 2017
CARE TEAM (Frontline care providers - Healthcare professionals, family members and others)	1. Social support: Family members can be educated and asked to provide support by reinforcing compliance, reminding about drug intake, motivating them patients to avoid substance abuse	Agarwal et al 2019, Dhar et al 2016, Krishnamoorthy et al 2018, Nimesh et al 2019, Wood et al 2015
	2. Financial support: Family members can provide financial support to cover the cost of medications, travel etc.	Gupta et al 2019
	3. Regular training of healthcare workers: Physicians and other healthcare workers involved in prescribing drugs and counselling should undergo regular training on standard treatment protocols	George et al 2016, Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019
	4. Team work approach: Integration of AYUSH, mental health counsellors, physiotherapist and geriatric clinics at primary healthcare level	George et al 2016, Miller et al 2017, Patti et al 2020
HEALTHCARE ORGANIZATION (Infrastructure/Resources)	1. Innovations in patient care: Healthcare workers can make innovations like dedicated day for specific conditions (diabetes day, etc), dedicated counselling station/session with additional staff for detailing the importance of adherence and complications related to non-adherence, unique pill dispensing mechanism (colour coding)	Agarwal et al 2019, Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Miller et al 2017, Newtonraj et al 2017, Patti et al 2020, Satish et al 2019, Venkatesan et al 2018, Wood et al 2015
	2. IEC/BCC/Awareness campaigns: Putting up of IEC materials and conducting campaigns on importance of adherence in public places and workplaces	Dhar et al 2016, George et al 2016, Gupta et al 2019, Gupta et al 2020, Jayanna et al 2019, Krishnamoorthy et al 2018, Newtonraj et al 2017, Patti et al 2020, Rani et al 2019
	3. Digitalizing patient treatment record: Digitalizing a dedicated treatment record for each patient can help in better follow-up of the patient and improve adherence	Jayanna et al 2019, Miller et al 2017, Patti et al 2020, Satish et al 2019, Wood et al 2015
	4. Polypills: Disseminating the advantages of polypills to healthcare professionals by CME/conferences and patients by public education campaigns; Integration of polypills into clinical practice. etc	Salaam et al 2019, Wood et al 2015
ENVIRONMENT (Regulatory, market and policy framework)	1. Linkage of health services with NGO and community-based organizations: Community members, volunteers, anganwadi workers, self-help groups and NGO workers can be trained in counselling the patients to improve medication adherence	Dhar et al 2016, Jayanna et al 2019, Krishnamoorthy et al 2018, Kusuma et al 2010, Miller et al 2017, Tan et al 2017



Supplementary file 1. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ Checklist (Tong, *et al.*, 2012)

Item No.	Guide and Description	Report Location
1. Aim	State the research question the synthesis addresses	P 6, 1-13
2. Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology (e.g. meta-ethnography, thematic synthesis, critical interpretive synthesis, grounded theory synthesis, realist synthesis, meta-aggregation, meta-study, framework synthesis)	P9, 16-25 P10, 1-22
3. Approach to searching	Indicate whether the search was pre-planned (comprehensive search strategies to seek all available studies) or iterative (to seek all available concepts until they theoretical saturation is achieved)	P8, 1-10
4. Inclusion criteria	Specify the inclusion/exclusion criteria (e.g. in terms of population, language, year limits, type of publication, study type)	P7, 3-23
5. Data sources	Describe the information sources used (e.g. electronic databases (MEDLINE, EMBASE, CINAHL, psycINFO), grey literature databases (digital thesis, policy reports), relevant organisational websites, experts, information specialists, generic web searches (Google Scholar) hand searching, reference lists) and when the searches conducted; provide the rationale for using the data sources	P8, 1-10
6. Electronic Search strategy	Describe the literature search (e.g. provide electronic search strategies with population terms, clinical or health topic terms, experiential or social phenomena related terms, filters for qualitative research, and search limits)	Supplementary file 1
7. Study screening methods	Describe the process of study screening and sifting (e.g. title, abstract and full text review, number of independent reviewers who screened studies)	Figure 1
8. Study characteristics	Present the characteristics of the included studies (e.g. year of publication, country, population, number of participants, data collection, methodology, analysis, research questions)	Table 1
9. Study selection results	Identify the number of studies screened and provide reasons for study exclusion (e.g. for comprehensive searching, provide numbers of studies screened and reasons for exclusion indicated in a figure/flowchart; for iterative searching describe reasons for study exclusion and inclusion based on modifications to the research question and/or contribution to theory development)	Fig 1 - PRISMA flow diagram P11, 6-18
10. Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings (e.g. assessment of conduct (validity and robustness),	P11, 14-18 Table 1

	assessment of reporting (transparency), assessment of content and utility of the findings)	
11. Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings (e.g. Existing tools: CASP, QARI, COREQ, Mays and Pope [25]; reviewer developed tools; describe the domains assessed: research team, study design, data analysis and interpretations, reporting)	P9, 3-14 Table 1
12. Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required	P8, 11-17
13. Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale	P11, 14-18 Table 1
14. Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies? (e.g. all text under the headings "results /conclusions" were extracted electronically and entered into a computer software)	P8, 18-25
15. Software	State the computer software used, if any	None used
16. Number of reviewers	Identify who was involved in coding and analysis	P9, 16-22
17. Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts)	P9, 23-35 P10, 1-22
18. Study comparison	Describe how were comparisons made within and across studies (e.g. subsequent studies were coded into pre-existing concepts, and new concepts were created when deemed necessary)	Table 2
19. Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive	Inductive process Table 2
20. Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation	Table 2
21. Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies (e.g. new interpretation, models of evidence, conceptual models, analytical framework, development of a new theory or construct)	P11-14

Supplementary Table 2: Detailed search strategy

Key word	Alternative word
Qualitative studies	((((((((Qualitative Research[MeSH Terms]) OR Focus Groups[MeSH Terms]) OR Anthropology, Cultural[MeSH Terms]) OR Ethnopsychology[MeSH Terms]) OR Grounded Theory[MeSH Terms]) OR Nursing Methodology Research[MeSH Terms]) OR Narrative Medicine[MeSH Terms]) OR Tape Recording[MeSH Terms]) OR Culture[MeSH Terms]) OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))
Medication Adherence	((((((((((((((((Medication Adherence[MeSH Terms]) OR Patient Compliance[MeSH Terms]) OR No-Show Patients[MeSH Terms]) OR Health Personnel[MeSH Terms]) OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms]) OR Self Administration[MeSH Terms]) OR Patient Medication Knowledge[MeSH Terms]) OR Attitude to Health[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms]) OR Patient Acceptance of Health Care[MeSH Terms]) OR Motivation[MeSH Terms])
Barriers, Facilitators and solutions	Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions
Diabetes mellitus and CVDs	((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))

India	(India[MeSH Terms] OR Republic of India[MeSH Terms]))
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Search results (PubMed):

((((Diabetes Mellitus[MeSH Terms]) OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms])) AND (((((((((((((((Medication Adherence[MeSH Terms] OR Patient Compliance[MeSH Terms] OR No-Show Patients[MeSH Terms] OR Health Personnel[MeSH Terms] OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms] OR Self Administration[MeSH Terms] OR Patient Medication Knowledge[MeSH Terms] OR Attitude to Health[MeSH Terms] OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms] OR Patient Acceptance of Health Care[MeSH Terms] OR Motivation[MeSH Terms] OR Life Change Events[MeSH Terms] OR Trust[MeSH Terms]))) AND (((((((Qualitative Research[MeSH Terms] OR Focus Groups[MeSH Terms] OR Anthropology, Cultural[MeSH Terms] OR Ethnopsychology[MeSH Terms] OR Grounded Theory[MeSH Terms] OR Nursing Methodology Research[MeSH Terms] OR Narrative Medicine[MeSH Terms] OR Tape Recording[MeSH Terms] OR Culture[MeSH Terms] OR Attitude[MeSH Terms])) AND (India[MeSH Terms] OR Republic of India[MeSH Terms])) – 199 (Filters: Years between 2010 and 2020 and English language publication)

((((((((((((Qualitative Research[MeSH Terms] OR Focus Groups[MeSH Terms] OR Anthropology, Cultural[MeSH Terms] OR Ethnopsychology[MeSH Terms] OR Grounded Theory[MeSH Terms] OR Nursing Methodology Research[MeSH Terms] OR Narrative Medicine[MeSH Terms] OR Tape Recording[MeSH Terms] OR Culture[MeSH Terms] OR Attitude[MeSH Terms] Case studies OR Focused group discussions OR phenomenological studies OR ethnographic studies OR interviews))) AND (((((((((((Medication Adherence[MeSH Terms] OR Patient Compliance[MeSH Terms] OR No-Show Patients[MeSH Terms] OR Health Personnel[MeSH Terms] OR drug effects [Subheading]) OR (Treatment Adherence[MeSH Terms] OR Compliance[MeSH Terms])) OR Self Medication[MeSH Terms] OR Self Administration[MeSH Terms] OR Patient Medication Knowledge[MeSH Terms] OR Attitude to Health[MeSH Terms] OR Patient Acceptance of Health Care[MeSH Terms])) OR Patient Preference[MeSH Terms] OR Patient Acceptance of Health Care[MeSH Terms] OR Motivation[MeSH Terms])) AND (Challenges OR Challenge OR Problem OR Problems barriers OR Difficulties OR Issues OR Limitations OR Obstacles OR Facilitators OR Suggestions OR Solutions)) AND (((((((Diabetes Mellitus[MeSH Terms] OR Cardiovascular Diseases[MeSH Terms] OR Hypertension[MeSH Terms] OR Coronary Disease[MeSH Terms] OR Coronary Artery Disease[MeSH Terms] OR Heart Diseases[MeSH Terms] OR Cerebrovascular Diseases[MeSH Terms] OR Stroke[MeSH Terms]))) AND ((India[MeSH Terms] OR Republic of India[MeSH Terms])) – 31 results (Filters: Years between 2010 and 2020 and English language publication)

Google scholar: 635 + 22 + 6 + 12 = 675

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3 **ScienceDirect:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
4 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 238 articles
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6 **Cochrane library:** (Diabetes Mellitus OR Cardiovascular Diseases OR Hypertension) AND
7 (Qualitative Study OR Qualitative) AND (India) AND (Adherence) – 34 articles
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For peer review only