Which domains of the theoretical domains framework should be targeted in interventions to increase adherence to antihypertensives? A systematic review

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Nonadherence to antihypertensives is prevalent and is associated with poorer health outcomes. This study aimed to identify psychological factors associated with adherence in patients taking antihypertensives. However, adherence within the first year of being prescribed antihypertensives is estimated to be less than 50%, with estimates of adherence ranging from 30 to 70% \cite{2}. Uncontrolled blood pressure persists in nonadherent patients, with almost 75% of patients failing to reach optimal blood pressure control \cite{3}. The risk of hospitalization has been found to be significantly higher in patients with hypertension who were nonadherent to antihypertensives \cite{4}.

Interventions that have been developed to increase adherence have been found to be moderately effective in reducing blood pressure \cite{4}. However, Morrissey \textit{et al.} \cite{4} noted that the effects of interventions can be limited and have varied effects often because of the ‘lack of explicit rationale for the intervention choice and the use of inappropriate methods to design the interventions’ \cite{1}.

The use of theory can help in the design of behaviour change interventions that are more likely to be effective. The TDF was developed and validated to summarize a comprehensive range of domains, from 33 psychological theories that can influence behaviour. It consists of 14 individual, nonoverlapping domains that are summarized in Table 1. Few studies have used theories, such as the TDF to inform interventions to increase adherence to antihypertensives. However, Morrissey \textit{et al.} \cite{4} conducted a review of interventions designed to increase antihypertensives and categorized their components using the Theoretical Domains Framework (TDF) \cite{5}. Morrissey \textit{et al.} \cite{4} did not reach any definitive conclusions about the domains that were likely to result in a greater reduction in both SBP and DBP whenever included in the intervention. In addition, they did not find that more complex interventions (those addressing a greater number of domains) were more likely to be effective. Although interventions addressing ‘memory, attention and decision processes’ were associated with a larger effect size, the authors noted that this domain was present in most studies and the remaining interventions (which did not address ‘memory, attention and decision processes’) may have only provided minimal support, which may be why they were less effective.

Although Morrissey \textit{et al.} \cite{4} identified the intervention components that have been addressed by interventions, to date, no study has synthesized evidence on the psychological factors that are associated with nonadherence to antihypertensives. This study aimed to identify psychological factors associated with adherence in patients taking antihypertensives, mapped onto the TDF, in order to inform the development of more targeted and effective interventions. Comparison between the results of the current review, and the study by Morrissey \textit{et al.} \cite{4}, was used to...
TABLE 1. The Theoretical Domains Framework

| Theoretical domain                  | Definition                                                                 |
|-------------------------------------|-----------------------------------------------------------------------------|
| Knowledge                           | An awareness of the existence of something                                  |
| Skills                              | An ability or proficiency acquired through practice                         |
| Social/professional role and identity | A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting |
| Beliefs about capabilities          | Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use |
| Optimism                            | The confidence that things will happen for the best or that desired goals will be attained |
| Beliefs about consequences          | Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation |
| Reinforcement                       | Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus |
| Intention                           | A conscious decision to perform a behaviour or a resolve to act in a certain way |
| Goals                               | Mental representations of outcomes or end states that an individual wants to achieve |
| Memory, attention and decision processes | The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives |
| Environmental context and resources | Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence and adaptive behaviour |
| Social influences                   | Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours |
| Emotion                             | A complex reaction pattern, involving experiential, behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event |
| Behavioural regulation              | Anything aimed at managing or changing objectively observed or measured actions |

Data from [5].

Methods

Search strategy
Studies were retrieved from PubMed, EMBASE and PsychINFO using search terms related to hypertension, adherence, determinants and quantitative studies (see, e.g. Supplementary File 1, http://links.lww.com/HJH/B901). The bibliography list of selected articles were searched to identify further studies. Studies were included if they tested for statistical associations between adherence and psychological/motivational determinants in patients over 18 years of age taking antihypertensives for hypertension. There were no restrictions on the geographical location or the intensity of antihypertensive treatment. Studies were excluded if they included patients who did not have hypertension or were not published in the English language. Studies were also excluded if insufficient information was given to allow mapping of determinants of adherence on to the TDF.

Review process
The search results were exported to Endnote. Duplicates were removed and the titles and abstracts of the articles were screened by M.R. A 10% random sample was screened by S.G. (agreement level 100%). Full texts of eligible articles were then retrieved. S.G. and M.R. independently screened all full text articles and all disagreements were resolved through discussion.

S.G. and M.R. carried out a quality assessment of the included studies using the National Institute of Clinical Excellence critical appraisal checklist for questionnaires [6]. Ten percent of studies were independently reviewed by both S.G. and M.R. and inter-rater reliability was 100%. Studies were not excluded on the basis of the quality assessment, rather the quality assessment was used to assess the strength of the evidence.

Data were extracted related to country, study design, sample size, age and gender of participants and psychological factors associated with adherence. M.R., S.G. and D.M. extracted the data. Ten percent of the studies that M.R. and D.M. extracted data for were checked by S.G. and the agreement rate was 100%.

Psychological factors were mapped on to the TDF by M. R., S.G. and D.M. Subdomains were developed for domains for which more than one clearly distinguishable component was identified after reviewing the studies. G.J. checked the TDF mapping for all included studies and any disagreements were resolved through discussion.

Results
Thirty-one studies were included (Fig. 1).

Table 2 describes the characteristics of included studies (see Supplementary File 2 for more detail, http://links.lww.com/HJH/B901). Overall the studies included a wide range of countries including high-income, middle-income and low-income countries and spanning five continents (no studies were identified from Australia). The majority of studies used a cross-sectional design. Sample sizes ranged from 115 to 8692. Studies differed in the length of time patients needed to have been on antihypertensives to be eligible for recruitment. Some did not specify any length of time, whereas others ranged from 3 to 12 months. All but one study used self-report to measure adherence.

The majority of studies assessing beliefs about consequences used the Beliefs about Medicines Questionnaire [38] that divides beliefs about medicines into necessity and concerns. Necessity assesses beliefs about the need for prescribed medication. Concerns assesses beliefs about the danger of dependence on medicines, and short-term and long-term toxicity. Necessity and concerns are, therefore, reported as two separate subdomains of ‘beliefs about consequences’ where these were reported separately in the
original studies. Environmental factors reported in the studies either related to the complexity of the medication regime or the resources available to the patients. As they appeared to be quite different concepts they are reported as separate subdomains. Finally, ‘social influences’ were either from family and friends or from healthcare professionals. Again, as these seemed to be two separate concepts, they are reported as two subdomains.

None of the studies tested all domains of the TDF for associations with medication adherence. The number of studies testing each domain/subdomain, and the proportion of these that found a significant association with adherence, are shown in Table 3. Thirteen out of 14 of the domains were tested in less than half of the studies.

The domains most frequently tested were ‘beliefs about consequences’, ‘knowledge’, ‘environmental context and resources’ and ‘social influences’ (Table 3). All studies that measured skills, measured health literacy; no studies measured physical skills. No studies included the domain of ‘goals’. In addition: ‘skills’, ‘social professional identity’, ‘optimism’, ‘emotion’ and ‘behavioural regulation’ were investigated in less than 10% of the studies.

Concerns about medicines (a subdomain of ‘beliefs about consequences’), and ‘beliefs about capabilities’, were tested in over three studies, all of which found them to be statistically significant (Table 3). ‘Memory/attention决策 processes’, health literacy (a subdomain of ‘skills’), ‘social identity’ and ‘intentions’ were also found to be

FIGURE 1 PRISMA diagram showing studies identified.
TABLE 2. Study characteristics

| Author, year | Country       | Study design      | Sample size | Participants mean age (MA) and gender |
|--------------|---------------|-------------------|-------------|-------------------------------------|
| Ahn and Ham, 2016 [7] | South Korea | Cross-sectional | 289 | MA = 69, Male = 66%, Female = 44% |
| Al-Ramahi et al., 2019 [8] | Palestine | Cross-sectional | 450 | MA = 59, Male = 44%, Female = 56% |
| Schoent en al., 2016 [9] | USA | Randomized clinical trial | 1058 | MA = 57, Male = 29%, Female = 71% |
| Aziz et al., 2020 [10] | Malaysia | Cross-sectional | 160 | MA = 65, Male = 71%, Female = 29% |
| Bane et al., 2006 [11] | Northern Ireland | Cross-sectional | 139 | MA = 52, Male = 51%, Female = 49% |
| Da Silva Barreto et al., 2014 [12] | Brazil | Cross-sectional | 422 | MA = not reported, Male = 41%, Female = 59% |
| Bersia and DeDede, 2017 [13] | Ethiopia | Cross-sectional | 172 | MA = 52, Male = 44%, Female = 56% |
| Boma et al., 2017 [14] | Sub-Saharan Africa | Cross-sectional | 357 | MA = 57, Male = 43%, Female = 53% |
| Dillon et al., 2016 [15] | Ireland | Prospective cohort study | 1211 | MA = 7, Male = 47%, Female = 53% |
| Durand et al., 2018 [16] | UK | Cross-sectional | 204 | MA = 70, Male = 58%, Female = 42% |
| Fernandez-Arias et al., 2014 [17] | Peru | Cross-sectional | 115 | MA = 63, Male = 33%, Female = 67% |
| Ghem baza et al., 2014 [18] | Algeria | Cross-sectional | 462 | MA = 62, Male = 24%, Female = 76% |
| Hassan et al., 2019 [19] | Malaysia | Cross-sectional | 240 | MA = 54.5, Male = 50%, Female = 50% |
| Horne et al., 2010 [20] | UK | Longitudinal | 230 | MA = 67, Male = 88%, Female = 12% |
| Karakurt and Kasikci, 2012 [21] | Turkey | Descriptive | 750 | MA = 61, Male = 22%, Female = 88% |
| Li et al., 2012 [22] | Taiwan | Cross-sectional | 200 | MA = 60, Male = 62%, Female = 38% |
| Lo et al., 2016 [23] | China | Cross-sectional | 195 | MA = 76, Male = 21%, Female = 79% |
| Lor et al., 2019 [24] | USA | Cross-sectional | 1355 | MA = 62, Male = 24%, Female = 76% |
| Morrison et al., 2015 [25] | 11 European countries | Cross-sectional | 2595 | MA = 54–64, Male = 64–51%, Female = 36–49% (reported separately for each country) |
| Nair et al., 2011 [26] | USA | Cross-sectional | 8692 | MA = 63, Male = 46%, Female = 56% |
| Osamor and Owumi, 2011 [27] | Nigeria | Cross-sectional | 440 | MA = 60, Male = 35%, Female = 65% |
| Patel and Taylor, 2022 [28] | USA | Prospective, cross-sectional | 240 | MA = 59, Male = 45, Female = 5% |
| Quine et al. 2011 [29] | UK | Longitudinal | 934 | MA = 69, Male = 42%, Female = 58% |
| Rahmawati and Bajorek, 2018 [30] | Indonesia | Cross-sectional | 384 | MA = 66, Male = 25%, Female = 75% |
| Sarkar et al., 2018 [31] | India | Cross-sectional | 400 | Over 60 = 41%, 40–59 = 52%, 30–39 = 7%, Male = 43%, Female = 57% |
| Da Silva Barreto, 2014 [32] | Brazil | Cross-sectional | 422 | Female = 59.48%, 63.25% over the age of 60 |
| Tan et al., 2020 [33] | Malaysia | Cross-sectional | 384 | MA = 57, Male = 40 Female = 60% |
| Turner et al., 2009 [34] | USA | Cross-sectional | 202 | MA = 65, Male = 34%, Female = 66% |
| Wang et al., 2002 [35] | USA | Cross-sectional | 496 | MA = not known, Male = 39%, Female = 61% |
| Yue et al., 2014 [36] | China | Cross-sectional | 232 | MA = 66, Male = 48%, Female = 52% |
| Zhang et al., 2018 [37] | China | Cross-sectional | 1916 | MA = 72, Male = 40%, Female = 60% |

TABLE 3. Determinants of antihypertensive adherence mapped on to the Theoretical Domains Framework, along with the number of studies and significant studies, subdomains totals are indicated when these were seen in the data

| TDF domain (subdomain) | Subdomain | Number of studies testing for this domain/subdomain(%) | Number of studies showing significant association with adherence (percent of studies that tested for association) |
|------------------------|-----------|-----------------------------------------------------|------------------------------------------------------------------------------------------------|
| Knowledge              | Health literacy | 14 (44) | 11 (79) |
| Skills                 | 2 (6)   | 2 (100) |
| Social/professional role and identity | 2 (6) | 2 (100) |
| Beliefs about capabilities | 6 (19) | 6 (100) |
| Optimism               | 2 (6)   | 1 (50) |
| Beliefs about consequences | 18 (58) | 15 (83) |
| Concerns               | 7 (12)  | 7 (100) |
| Necessity              | 8 (25)  | 5 (63) |
| Combined concerns and necessity (when not presented separately) | 6 (19) | 3 (50) |
| Reinforcement          | 5 (16)  | 3 (60) |
| Intentions             | 2 (6)   | 2 (100) |
| Goals                  | 0 (0)   | NA |
| Memory/attention/decision processes | 2 (6) | 2 (100) |
| Environmental context and resources | 11 (35) | 11 (100) |
| Resources              | 7 (12)  | 5 (71) |
| Complexity of regimen  | 8 (25)  | 4 (50) |
| Social influences      | 10 (32) | 6 (60) |
| Family and friends     | 7 (23)  | 3 (43) |
| Healthcare professionals | 7 (23) | 3 (43) |
| Emotion                | 2 (6)   | 1 (50) |
| Behavioural regulation | 1 (3)   | 1 (100) |
Comparison to existing literature
Morrissey et al. [4] found that the TDF domains that were commonly targeted in interventions to reduce nonadherence of antihypertensives were: 'memory attention and decision processes' (31/31 interventions), 'environmental context and resources' (27/31 interventions), 'social influences' (22/31 interventions) and 'knowledge' (20/31 interventions). Our review has shown that other domains/subdomains that may be important to target in future interventions are concerns about medicines and 'beliefs about capabilities'. Those with less concerns about medicines and a greater belief in their ability to control their illness were more likely to take their medicines; however, 'beliefs about capabilities' has not been well tested in existing interventions. A study comparing healthcare professionals to patients' concerns about safe care for adults with complex needs has shown that patients have more concerns than healthcare professionals about medicines' side effects and interactions, and that that is a potential barrier to adherence [39].

Implications for practice
Our findings suggest that healthcare professionals should focus on addressing patients' concerns about their medicines and their belief in their ability to control their blood pressure, through taking their medicines. Whilst higher knowledge was found to be associated with greater adherence in over three quarters of studies that tested for this, a higher level of health literacy was also associated with greater adherence. This suggests that in order to increase knowledge, healthcare professionals need to provide information in a way that is accessible to patients. Previous research [40] has shown the importance of tailoring interventions to address individual causes of nonadherence. The domains of the TDF that are associated with nonadherence address a broad range of factors some of which are likely to be associated with intentional nonadherence, for example, 'knowledge' and concerns about medicines, and others, which may be associated with unintentional nonadherence, such as 'memory' attention and decision 'processes' and 'behavioural regulation'. Understanding the types of factors that are likely to cause nonadherence can be helpful in knowing what questions to ask patients, and then tailoring interventions towards specific barriers to adherence and potential facilitators that are identified.

Strengths and limitations
To our knowledge, this is the first review synthesizing evidence of psychological factors associated with adherence. Limitations were that studies that were not published in English were excluded, which could have led to the exclusion of relevant articles. However, we identified studies in high-income, middle-income and low-income countries. There is also the possibility of publication bias with studies only being submitted for publication if they showed a significant effect, especially given the high level of significance observed across all domains measured.

Concluding remarks
The review findings showed that concerns about medicines and personal beliefs about capabilities to take medicine to control hypertension were key factors associated with adherence to antihypertensives. However, 'beliefs about capabilities' is currently incorporated into few of the interventions that have been designed to increase adherence [4].
Knowledge about hypertension, is also likely to be associated with adherence. More investigation is needed in relation to factors that may be associated with unintentional nonadherence. Healthcare professionals can potentially increase adherence by asking patients about all the above factors and tailoring their consultations and recommendations accordingly. Researchers should more comprehensively measure a wider range of potential barriers and facilitators to adherence.

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Conflicts of interest

There are no conflicts of interest.

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