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Changing Medication-Related Beliefs: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Elizabeth Sheils[1], William Tillett[1, 2], Delyth James[3], Sarah Brown[3], Charlotte Dack[4], Hannah Family[5, 6], and Sarah C. E. Chapman[1, 7]

[1] Department of Life Sciences: Pharmacy and Pharmacology, University of Bath
[2] Royal National Hospital for Rheumatic Diseases, Royal United Hospital Bath, Bath, United Kingdom
[3] Department of Applied Psychology, Cardiff Metropolitan University
[4] Department of Psychology, University of Bath
[5] NIHR Health Protection Research Unit in Behavioural Science and Evaluation, University of Bristol
[6] The National Institute for Health and Care Research Applied Research Collaboration West, University Hospitals Bristol and Weston NHS Foundation Trust
[7] Institute of Pharmaceutical Science, Kings College London

Objective: Medication-related beliefs, for example, beliefs that medicines are unnecessary or that side effects are likely, can influence medication behaviors and experiences, potentially impacting quality of life and mortality. At times, it may be useful to change medication-related beliefs, for example, to reduce patients' concerns about side effects when extensive evidence suggests side effects are rare. Currently we do not know the most effective methods to address medication beliefs. ***Method:*** Systematic review and meta-analysis of randomized controlled trials that measured medication-related beliefs in people prescribed medication for long-term condition(s). We extracted data on behavior change techniques (BCTs), belief measure, study and patient characteristics, risk of bias, and quality of description. ***Results:*** We identified 56 trials randomizing 8,714 participants. In meta-analysis, interventions led to small-to-medium effects ($n = 36$, Hedges' $g = .362$, 95% confidence interval [CI] [.20, .52], $p < .001$) in increasing beliefs about medication need/benefit and reducing concerns about medication ($n = 21$, Hedges' $g = -.435$, 95% CI [−0.72, −0.15], $p < .01$). Effect sizes were higher for interventions that reported a significant effect on adherence. Problem solving, information about health consequences, and social support (unspecified) were the most prevalent BCTs. Fourteen BCTs were associated with significant effects on need/benefit beliefs and four BCTs were associated with significant effects on concern beliefs. ***Conclusion:*** It is possible to modify medication-related beliefs using a range of interventions and techniques. Future research should explore the best ways to operationalize these BCTs for specific health conditions to support medication beliefs and improve adherence.

Public Significance Statement

This review advances the field through highlighting techniques that can lead to a change in medication beliefs and as a consequence improved adherence. The meta-analysis indicated that beliefs regarding the necessity of medication and concerns about medication are modifiable. Importantly, it showed that these beliefs are strongly associated with medication adherence. Specific behavior change techniques that led to a significant change in medication belief were identified. These findings advance the field of medication adherence highlighting which techniques are most likely to be effective.

Elizabeth Sheils https://orcid.org/0000-0003-4499-3166

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Elizabeth Sheils served as lead for data curation, formal analysis, investigation, methodology, project administration, writing–original draft, and writing–review and editing. Sarah C. E. Chapman served as lead for funding acquisition and supervision. Elizabeth Sheils and Sarah C. E. Chapman contributed equally to conceptualization. William Tillett, Delyth James, Sarah Brown, Charlotte Dack, Hannah Family, and Sarah C. E. Chapman contributed equally to investigation, methodology, writing–review and editing, and formal analysis. William Tillett, Delyth James, Charlotte Dack, and Hannah Family contributed equally to supervision.

Correspondence concerning this article should be addressed to Elizabeth Sheils, Department of Life Sciences: Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, United Kingdom. Email: elizabeth.sheils@bath.edu

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Patients hold a plethora of beliefs about medication, going beyond a simple evaluation of efficacy and adverse effects and incorporating rich perceptions of the treatment in relation to themselves and the treatment context (Horne et al., 2019). Beliefs about prescribed medication are related to medication behaviors such as adherence (taking medication as prescribed; European Patients Forum, 2015) across a wide range of conditions (Horne et al., 2013) and can influence understanding of medication effects, for example, inducing negative expectations that affect experiences of side effects via nocebo effects (Heller et al., 2017) and predicting misattribution of symptoms as side effects of medication (Heller et al., 2015). Beliefs are integral to who we are and what we do, and can be distinguished from knowledge, as they do not necessitate objective truth (Connors & Halligan, 2015). Regardless of objective truth, beliefs are held with conviction, regarded as true, and provide a framework for behavior and understanding (Halligan & Aylward, 2006). Models such as the Necessity-Concerns Framework (Horne et al., 2013) and the Common-Sense or Self-Regulatory Model (Hagger & Orbell, 2022) propose that medication beliefs can influence responses to illness for example, engaging with healthcare and adhering to treatment if medications are perceived as effective and safe. Rates of long-term conditions (Department of Health and Social Care, 2012) managed using prescribed medication (NHS, 2017; Simpson et al., 2006) are increasing meaning it has become imperative to better understand and, where appropriate, change patients' medication-related beliefs.

Medication beliefs can be drawn from a wide range of sources including direct experience with treatment, observations of other people's experiences or information from diverse sources such as healthcare professionals (HCPs) and social media (Al Khaja et al., 2018). Linn et al. (2019) found that online information seeking was associated with greater concerns about medication and patients who sought information after consultation were found to be more nonadherent at 3 weeks compared to those who did not. Patients' medication-related beliefs are intrinsically subjective and often differ from the views of HCPs (Mårdby, 2008). Patients' beliefs regarding treatment can often be categorized into two main groups. These groups are based on their perceived need for treatment (referred to as "necessity beliefs") with the anticipated benefits (e.g., prevention of disease progression), and their concern about the potential negative outcomes of taking medication (known as "concern beliefs," e.g., dependency, potential adverse effects; Horne, 1997; Horne et al., 1999, 2013; Horne & Weinman, 1999). They can also include the likelihood that the medication can cure or control disease (Leventhal et al., 2003). Medication beliefs can also encompass general themes such as the nature of pharmaceuticals and whether they are overused (Horne & Weinman, 1999), beliefs about the manufacture of medications, efficacy of generic versus branded medication (Colgan et al., 2015; Keenum et al., 2012), and the trustworthiness of the pharmaceutical industry (Goff et al., 2008). Beliefs can also involve broader domains such as cultural beliefs and beliefs related to one's control over the disease.

The most extensively researched effect of medication-related beliefs is adherence. Treatment adherence is highly variable ranging from 0% to over 100% (Nieuwlaat et al., 2014). Overall, an estimated 30%–50% of patients are nonadherent (Brown & Bussell, 2011; Osterberg & Blaschke, 2005; Sabaté, 2003). Three meta-analyses have indicated stronger beliefs about the necessity of medication and fewer concerns about its potential negative effects are associated with greater adherence (Foot et al., 2016; Horne et al., 2013; Nie et al., 2019). While some nonadherence is unintentional (patients don't adhere due to reasons outside of their control), it is frequently intentional (deciding not to adhere often because of medication-related beliefs; Nunes et al., 2009). A recent systematic review (Shahin et al., 2019) found a statistically significant association between personal and cultural beliefs and medication adherence. Gonzalez et al. (2015) demonstrated through mediation analysis a significant indirect effect on diabetes distress and medication adherence through perceived control of the condition. While some nonadherence may have positive effects (e.g., by reducing adverse effects), it can lead to suboptimal therapeutic management (Cramer et al., 2008; DiMatteo et al., 2002), lost health gains, exacerbated symptoms, increased morbidity (Jimmy & Jose, 2011; Simpson et al., 2006), and financial burdens on healthcare systems (Cutler et al., 2018). It has been argued that above any other intervention, improving adherence creates more health gains (Sabaté, 2003); however, minimal improvement has been noted in adherence across the last 50 years (Nieuwlaat et al., 2014). Although we may be unable to cure conditions we have significant advances in treatment, thus finding ways to improve beliefs about medication is imperative to the treatment pathway.

It may be possible to modify patients' medication-related beliefs, supporting adherence, and other health outcomes. For example, pharmacist counseling of cancer patients decreased medication concerns, increased necessity beliefs, and increased adherence (Birand et al., 2019). Likewise, tailored text messages reduced medication concerns and increased adherence in patients with inflammatory bowel disease (Riaz & Nielsen, 2019). In addition, several randomized controlled trials (RCTs) that have aimed to change medication-related beliefs found a significant change between the intervention and the control group postintervention, including an individualized integrative nursing intervention for people with schizophrenia (Dahan et al., 2016), a relapse prevention program for depression (Lin et al., 2003), and a targeted text message intervention for asthma patients (Petrie et al., 2012). These three interventions also noted an improvement in adherence for the intervention group. To our knowledge, no systematic review has summarized evidence on the effectiveness of interventions to modify medication-related beliefs in RCTs.

The current systematic literature review and meta-analysis aims to: (a) identify which techniques are used within interventions which measure medication-related beliefs; (b) test the effectiveness of these interventions in changing medication-related beliefs using meta-analysis; (c) test whether the presence of specific intervention techniques moderate the effectiveness of interventions; and (d) assess the quality of reporting and risk of bias of included studies.

Method

See online supplemental material 1 for preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.

International Prospective Register of Systematic Review Registration Number CRD42018093966. The systematic review was originally conducted in July 2018 and updated in November 2020, with the addition of meta-analyses. The review process was conducted over an 18-month period.

Inclusion/Exclusion Criteria

Participants: Adults (aged 18 years old and older) prescribed medication for one or more long term conditions (typically lasting a year or longer). Interventions: Any method except those focused-on modification of patients' medication (e.g., titrating dose), targeting patients and/or HCPs, and taking place in any setting or geographical location. Comparison: Usual care or other control. Outcomes: Medication-related beliefs assessed postintervention. Study design: RCTs.

Literature Search

We searched CBI Medline, Embase, APA PsycINFO and PsycARTICLES, ProQuest, and Cochrane Library, from the earliest available date to November 20, 2020. Reference lists of included studies were screened to identify additional relevant articles. We explored "grey" literature such as conference presentations and theses. The search included terms relating to participants, intervention, outcome, and study design (see online supplemental material 2 for full description of search). We searched for words/phrases and used index terms such as MeSH and combined terms with Boolean logic. We identified online supplemental materials/websites and contacted authors for documents as needed.

Study Selection

We identified 13,540 results, of which 3,713 were duplicates. We removed 9,691 results during title/abstract screening, and 80 after full text screening, leaving 56 papers included. See Figure 1 for PRISMA diagram. Studies were independently screened by two reviewers (Elizabeth Sheils and Sarah C. E. Chapman) with high agreement (Cohen's $k = 99\%$). Disagreements were resolved by consensus.

Data Extraction

Data were extracted into Excel. Data extracted included the study aim and design, patient diagnosis/es and medication details, setting, country, sample characteristics, intervention and control characteristics, measure of medication-related beliefs and belief effect size, measure of adherence and effect size, follow-up duration, risk of bias, and intervention description quality.

Identification of Techniques Included in the Intervention/Control Conditions

We used the behavior change technique taxonomy v1 (BCTT; Michie et al., 2013) as the primary method to code techniques included within the interventions. A behavior change technique (BCT) has been described as the smallest component with the potential for behavior change which is replicable and observable (Michie et al., 2013). The BCTT, including 93 BCTs clustered in 16 domains, has been used to evaluate interventions across health domains including physical activity (Samdal et al., 2017), smoking cessation (Bartlett et al., 2014), and medication adherence smartphone applications (Morrissey et al., 2016). We selected it for this study because many of the terms used to describe interventions are used inconsistently, for example "pharmacist counseling" could involve didactic information provision or asking patients to share their thoughts whereas the BCTs are clearly defined. A program of work involving expert consensus exercises and systematic reviews has mapped BCTs to potential mechanisms of action including belief change. For example, the BCT "information about health consequences" is thought to affect behavior in part through modifying beliefs about the consequences of a behavior and perceptions of susceptibility to negative consequences (Carey et al., 2019; Connell et al., 2019). Although most of our studies were likely to consider medication-related beliefs linked to medication behaviors, making the BCTT relevant, there might be some studies which included techniques to change beliefs without the goal of changing behavior, and so we included a section on our data extraction form to record these.

To ensure accurate coding, coders completed training (BCT Taxonomy v1: Training, n.d.), checked codes against previous coding by other researchers (BCT Taxonomy v1: Interventions, 2018), examined available additional sources (e.g., protocols) for further details, built a coding manual with examples of BCTs (see online supplemental material 3), and extracted supporting evidence from text while coding. Following previous studies (Newby et al., 2021; Peters et al., 2015) only BCTs described in the intervention but not the control condition were coded. BCT coding took place in August–October 2020 and November–December 2020 following rerunning and updating the searches.

Risk of Bias

Cochrane's Risk of Bias tool (RoB 2; Sterne et al., 2019), was used to evaluate potential risk of bias in: randomization, fidelity, missing data, outcome measurement, and selective reporting. Each item was coded as: (possibly) yes/(possibly) no/not applicable/no information. An algorithm was used to make overall risk-of-bias judgements.

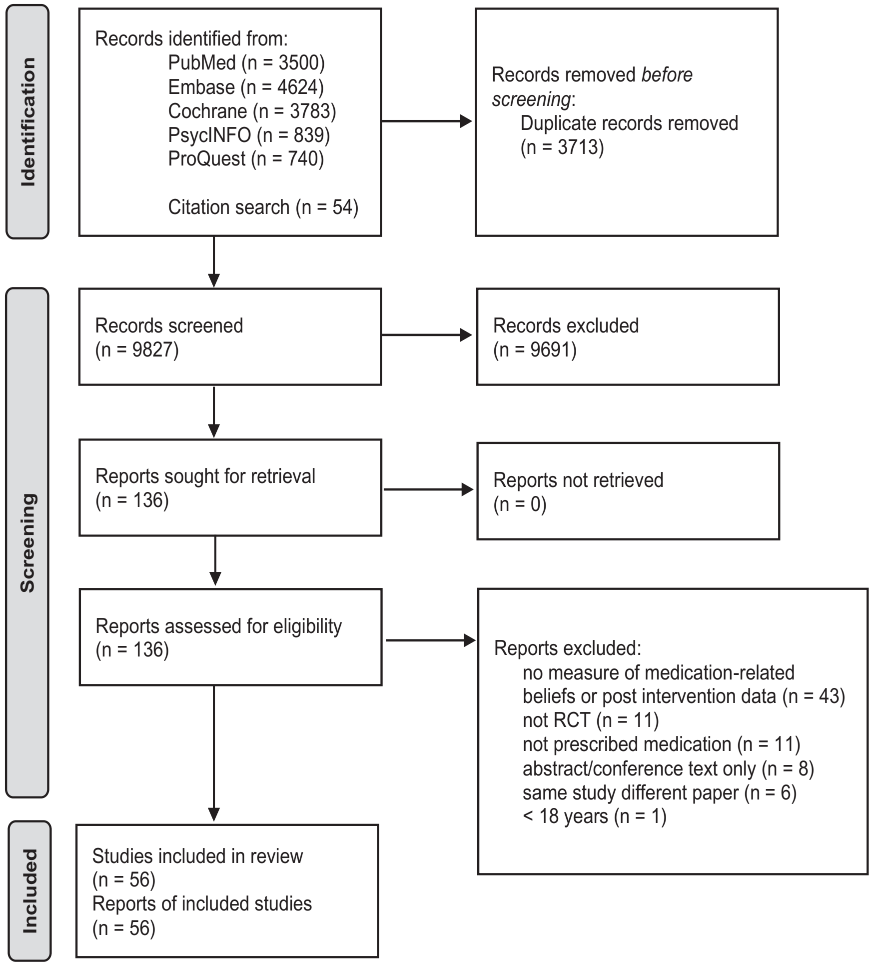
Quality of Intervention Description

The "template for intervention description and replication" (TIDieR; Hoffmann et al., 2014) was used to assess reporting quality (de Barra et al., 2019; MacDonald et al., 2016). It includes 12 items covering intervention name, rationale, materials and procedures, who provided, location, mode of delivery, when and how much, tailoring, modifications, and fidelity. Each item was coded as: adequately/inadequately/not reported or not applicable.

Coding Checks

All data were extracted by one reviewer (Elizabeth Sheils) and discussed with a second reviewer (Sarah C. E. Chapman). A random sample of 10% of studies were independently coded by a second reviewer (Sarah Brown) using RoB2 and TiDIER. There was a high rate of interrater reliability 70.8% for TiDIER and 84.0% for RoB2 with disagreement focused on coding of "not reported" versus "not applicable." Two coders (Elizabeth Sheils and Sarah Brown) coded all BCTs independently but met weekly to discuss and resolve disagreements, with input from the full team as needed. The

Figure 1
PRISMA Flow Chart



Note. PRISMA = preferred reporting items for systematic reviews and meta-analyses.

reviewers agreed about the presence of a BCT independently on 57.7% of occasions, and resolved the remainder of instances through discussion.

Meta-Analysis

Meta-analysis was performed in Stata 17. Studies were included studies in the meta-analysis if effect sizes on medication-related beliefs could be computed. Medication-related beliefs were grouped into those concerning perceived need for medication (e.g., Beliefs About Medication questionnaire [BMQ]-Necessity, Drug Attitude Inventory [DAI]) and perceived negative effects of medication (e.g., BMQ-Concern). A random-effects model was used to estimate effect sizes, given that we expected true effect sizes to be heterogeneous across different patient groups and interventions (Hunter & Schmidt, 2000). Hedges' *g* was used for effect sizes because of the presence of some studies with small samples (Hedges & Olkin, 1984). We conducted moderator analyses to examine whether effect sizes were larger for studies with versus without identified BCTs. We tested for heterogeneity using *Q* statistics and expressed the percentage of variation due to heterogeneity rather than chance using the I^2 statistic (50%–90% represents substantial heterogeneity; Deeks et al., 2019). Publication bias was assessed by examining funnel plot asymmetry and the Trim and Fill method (Thornton & Lee, 2000) and Egger's test for small study bias (Egger et al., 1997). Sensitivity analyses were performed by excluding studies with high risk of bias and exploring the outcome measures. Subgroup analyses by examining the studies which had measured and found significance in adherence for the intervention group versus control postintervention.

Results

Study and Participant Characteristics

There were 56 included studies (8,714 randomized participants, data reported on 7,730). They were conducted across four continents Europe ($n = 28$), Asia ($n = 12$), North America ($n = 9$), and Australia/Oceania ($n = 7$). Median publication year was 2013 (range 1982–2020). Four studies reported multiple intervention groups (two in Krasnoryadtseva et al., 2020; Linn et al., 2018; Polack et al., 2008, three in Mazor et al., 2007). Linn et al. (2018) also reported on two control groups. Therefore, 61 intervention and 57 control groups were identified. The average age of participants was 51.7 years in the intervention and 52.2 years in the control groups. Most studies had an equal number of males and females, average 46.5% female participants (range 0%–100%). Most samples ($n = 31$) had physical health conditions, 22 had mental health conditions, and three had comorbid physical and mental health conditions. See Table 1 and online supplemental material 4 for full details of the studies.

Intervention Characteristics

There was a wide range of interventions. The most common were: a combination of education, support, problem solving, medication reviews, and referral (delivered in 12 interventions); "adherence therapy," a manualized therapy combining principles of motivational interviewing and cognitive behavioral therapy (Gray et al., 2006) delivered in 11 interventions via between three weekly sessions to 14 sessions across 6 months; tailored problem solving (11 interventions); pharmacist consultations with/without follow-up via HCP or text message (seven interventions); and education/psychoeducation (six interventions). Five studies provided tailored visual and/or written information. Three studies used motivational interviewing (between three and seven sessions). Interventions were most frequently delivered by a pharmacist ($n = 18$).

Table 1
Intervention Group Details and Outcome Measures (n = 56)

Component	*n*
Intervention lead	
Pharmacist	18
Technology	9
Researcher	8
Nurse	7
Psychologist	3
Psychiatrist	3
Other	8
Delivery mode	
Face-to-face individual	35
Electronic device (app/text)	16
Face-to-face group	5
Setting	
Hospital outpatient clinic	14
Pharmacy	11
Inpatient	8
Mobile (text message/app/voice message)	7
GP/academic setting	5
Telephone	5
Home	2
Prison	2
Not specified	2
Primary outcome	
Adherence/compliance	30
Belief/attitude	11
Symptoms/quality of life	6
Knowledge	4
Other	5
Belief measure(s)	
BMQ-specific (Horne et al., 1999)	27
BMQ-general (Horne et al., 1999)	14
Two questions from BMQ	4
Drug Attitude Inventory (Hogan et al., 1983)	14
Antidepressant belief measure	3
Other	6
Adherence measure	
Morisky Medication Adherence Scale (Morisky et al., 1986)	7
Medication Adherence Report Scale (Horne & Hankins, 2008)	5
Medication Adherence Rating Scale (Thompson et al., 2000)	4
Dispensing records	4
Physiological	4
Interview	3
Medicine Adherence Questionnaire	3
Other/unspecified self-report	13

Note. GP = general practitioner; BMQ = Beliefs about medicines questionnaire.

Control Conditions

Forty-four control groups received usual care, 12 control groups received an active control (e.g., basic education). One paper did not describe the control condition.

Medication-Related Belief Measure

The majority of studies ($n = 33$) used a form of the BMQ (Horne et al., 1999) to measure beliefs, while 14 studies used the DAI (Hogan et al., 1983), which explores similar components to the BMQ.

Primary Outcome

The most common primary outcome was medication adherence ($n = 30$).

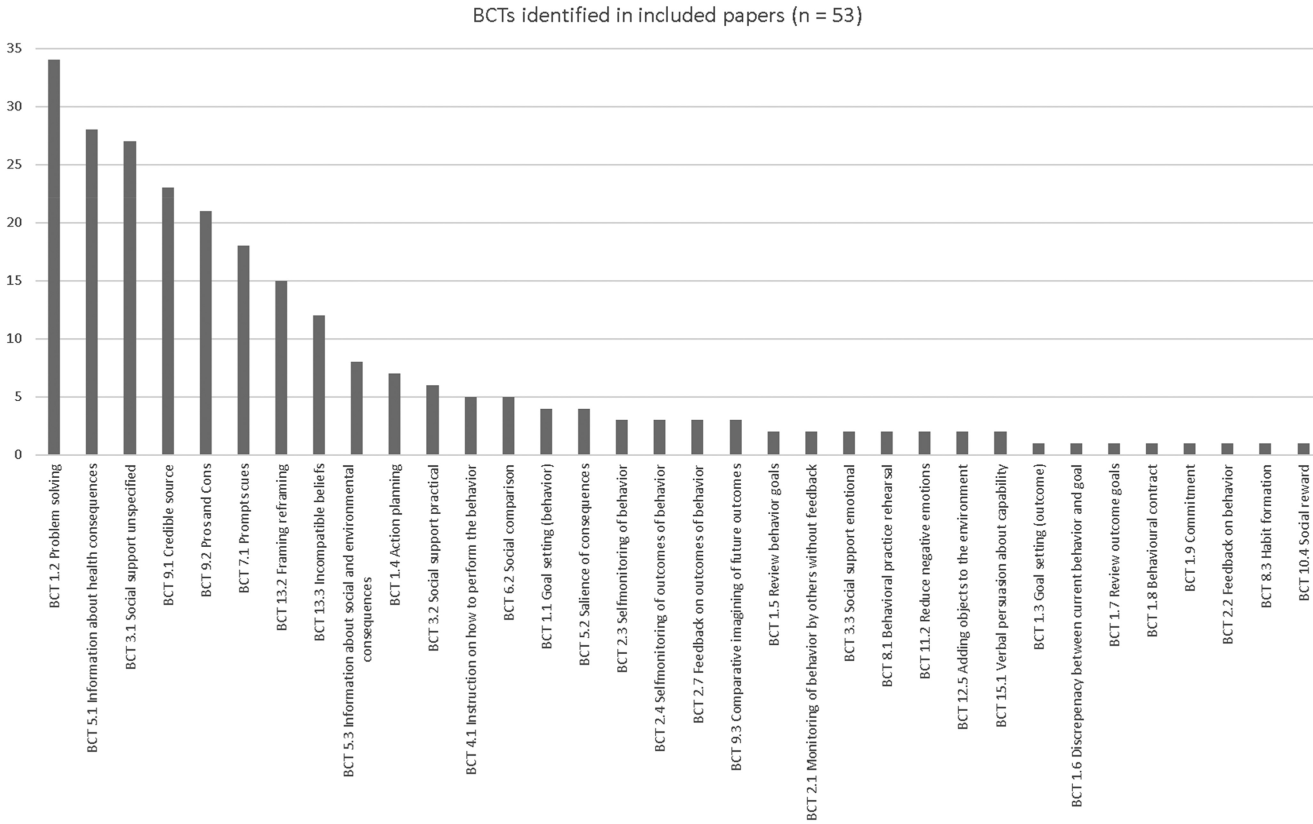
Medication Adherence

Forty-three studies measured medication adherence with 23 reporting a significant increase in adherence, one study reported significant increase in adherence at 6-month follow-up but not 12 months (Clarkesmith et al., 2013), 18 reporting nonsignificance, and one study excluding results due to ceiling effects (Uzenoff et al., 2008).

BCTs

A total of 251 BCTs were coded from 53 study reports. One study had no unique BCTs in the intervention group compared with the control (Krasnoryadtseva et al., 2020) and two studies had insufficient information (Adams et al., 2015; Prasetya et al., 2018). The mean number of BCTs in interventions was 4.74 (*SD* 2.98, range 1–14). See Figure 2 for frequency of BCTs. Of the 93 possible BCTs, 34 were identified from 14 of the 16 domains (all except scheduled consequences and covert learning) indicating the breadth of techniques used. The most common BCTs were "problem solving" (in 34 interventions), "information about health consequences" (in 28 interventions), and "social support (unspecified)" (in 27 interventions). The BCTs were operationalized in a wide variety of ways, for example, information about health consequences was provided via leaflets, videos, and face-to-face while social support (unspecified) was delivered via cognitive-behavior therapy, and support from family and friends (see Table 2 for definitions and examples). Many BCTs were used by very few studies, for example, eight BCTs used only once: goal setting (outcome), discrepancy between current behavior and goal, review outcome goals, behavioral contract, commitment, feedback on behavior, habit formation, and social reward. Ten of 11 studies which had belief/attitude as the primary outcome measure had codable

Figure 2
Number of Interventions Containing Each BCT



Note. BCT = behavior change technique.

BCTs (range 2–7 BCTs) with the most prevalent BCT being "social support (unspecified)" (eight interventions) followed by "problem solving" (seven interventions).

Quality of Description

The TIDieR checklist highlighted some aspects of interventions that were well reported (e.g., brief name and rationale were both reported by all studies and "who provided" the intervention was adequately reported in 84% of studies). Other aspects were less well described for example, 46% provided a detailed description of intervention materials, 7% reported modifications, and 30% reported fidelity (see Figure 3).

Risk of Bias

Overall, most studies had "some concerns" of bias, $n = 49$, and seven studies were "high risk" (see Figure 4). Most studies ($n = 48$) had low risk of bias for "randomization" and "deviation from intended interventions" ($n = 54$). The main sources of potential bias across all studies was "measurement outcome," primarily due to reliance on self-report outcomes (inevitable for studies exploring medication-related beliefs) in all studies, and that protocols were obtainable for only 10 studies making it difficult to assess if only a selection of outcomes were reported.

Intervention Effects on Medication-Related Beliefs

Meta-Analysis Results

We included 36 of the 56 studies in the meta-analysis, with 20 studies providing insufficient data to enable calculation of one or more effect sizes. Interventions were had a small-to-medium statistically significant effect on beliefs about medication need/benefit ($n = 36$), $g = .362$, $p < .001$, 95% confidence interval (CI) [0.204, 0.521], and small-to-medium statistically significant effect on concerns about medication ($n = 21$) $g = -.435$, $p < .01$, 95% CI [−0.721, −0.149]. There was high heterogeneity around both medication need, $Q(35) = 226.50$, $I^2 = 84.74$, and concerns estimates, $Q(20) = 246.31$, $p < .001$, $I^2 = 91.27$. See online supplemental material 5 for forest plots.

Sensitivity Analyses

To ensure the results were not driven by potential outliers, leave-one-out meta-analysis was conducted and revealed no single study had a dramatic impact on the overall model (overall model Hedges' g ranged from .311 to .382 for necessity and −.474 to −.36 for concerns). Next, we repeated the analyses with the studies at "high risk of bias" removed with minimal impacts on effect sizes or heterogeneity (necessity analysis: $n = 33$, Hedges' $g = .356$, $p < .001$, 95% CI [0.182, 0.531], $I^2 = 85.59$; concerns analysis: $n = 20$, Hedges' $g = -.429$, $p < .01$, 95% CI [−0.730, −0.129], $I^2 = 91.89$).

Table 2
Three Most Frequently Coded BCTs With Examples

BCT	Definition from BCT taxonomy (Michie et al., 2013)	Example of BCT in included study
1.2 Problem solving	Analyze, or prompt the person to analyze, factors influencing the behavior and generate or select strategies that include overcoming barriers and/or increasing facilitators	"Patients were helped to identify obstacles that might prevent them from taking medication, to identify strategies to overcome obstacles that arise, and to build self-efficacy." (Pakpour et al., 2017)
3.1 Social support (unspecified)	Advise on, arrange, or provide social support (e.g., from friends, relatives, colleagues, buddies, or staff) or noncontingent praise or reward for performance of the behavior.	"Counseling to cope with lack of motivation will focus on exploring the patients' concerns and necessity beliefs. This method is called motivational interviewing." (Alfian et al., 2021)
5.1 Information about health consequences	Provide information (e.g., written, verbal, visual) about health consequences of performing the behavior	"The research fellow also provided information on the likelihood of experiencing any side effects mentioned." (O'Carroll et al., 2013)

Note. BCT = behavior change technique.

Sensitivity analysis was also conducted to investigate whether the outcome measure influenced the results. When the BMQ-Necessity outcome was removed, 17 studies remained, Hedges' $g = .307$, $p < .001$, 95% CI [0.228, 0.386], $I^2 = 0$. When the DAI outcome was removed, 26 studies remained, Hedges' $g = .387$, $p < .01$, 95% CI [0.176, 0.599], $I^2 = 87.76$. When other outcome measures were removed (retaining the most frequently used measures, BMQ and DAI), 29 studies remained. Hedges' $g = .366$, $p < .001$, 95% CI [0.172, 0.561], $I^2 = 87.21$. The results were similar, suggesting no significant difference in the psychometric measures.

Publication Bias

Publication bias analysis was mixed. For necessity beliefs, while Egger's statistic was nonsignificant suggesting no publication bias, $t(36) = -0.02$, $p = .99$, 95% CI [−1.79, 1.76], trim and fill analysis imputed 11 studies to the right of the mean, increasing the overall effect size ($g = .555$, 95% CI [0.397, 0.713]). Similarly for concern beliefs, Egger's statistic was also nonsignificant suggesting no publication bias, $t(21) = 1.09$, $p = .29$, 95% CI [−1.34, 4.23], whereas trim and fill analysis imputed four studies to the left of the mean, $g = -.581$ (95% CI [−0.863, −0.299]) (see online supplemental material 6 for funnel plots).

Subgroup Analysis—Adherence

Studies which reported a significant improvement in adherence for the intervention group ($n = 16$) had larger effects on beliefs for necessity ($g = .48$, $p < .001$, 95% CI [0.25, 0.71]), $Q(15) = 146.22$, $I^2 = 88.32$, relative to those that did not ($n = 11$, $g = .04$, $p = .104$, 95% CI [−0.15, 0.22]), $Q(10) = 15.85$, $I^2 = 30.77$. The difference between the two groups was significant, $Q(1) = 9.95$, $p < .001$. Similarly, where there was a significant improvement in adherence in the intervention group there was a larger reduction in concerns ($n = 10$, $g = -.52$, $p < .001$, 95% CI [−0.99, −0.5]), $Q(9) = 168.14$, $I^2 = 92.38$, than when there was no significant difference in adherence ($n = 6$, $g = -.04$, $p = .237$, 95% CI [−0.31, 0.24]), $Q(5) = 6.79$, $I^2 = 1.69$. The difference between these two groups was significant, $Q(1) = 4.82$, $p < .05$.

Moderator Analysis—BCTs

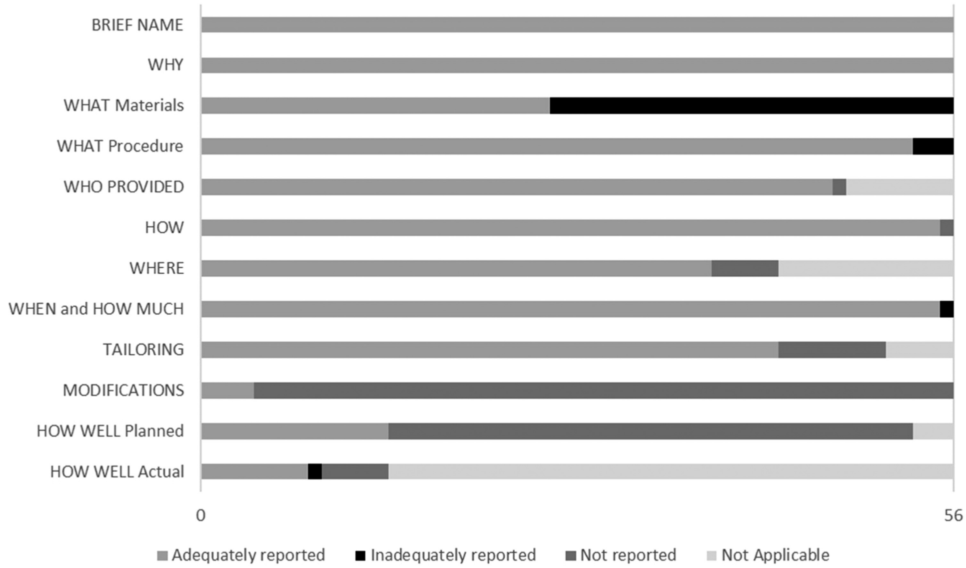
Moderator analyses were conducted for the 33 studies in which BCTs were coded to test for the univariate effect of individual BCTs on beliefs. Fourteen BCTs were associated with significant increases in medication need beliefs (goal setting, action planning, social support [unspecified], social support [practical], information about health consequences, social comparison, pros and cons, comparative imagining future outcomes). The largest effect sizes were seen for interventions including comparative imagining future outcomes ($g = .610$), goal setting behavior ($g = .531$), and action planning ($g = .541$). Four BCTs were associated with a significant reduction in concern/worry beliefs related to medication: action planning ($g = -.679$), problem solving ($g = -.498$), social support (unspecified; $g = -.571$), and information about health consequences ($g = -.510$). Of the BCTs identified, two were associated with nonsignificant increases in medication need beliefs, credible source and incompatible beliefs. Five BCTs were associated with a nonsignificant reduction in concern/worry beliefs related to medication: framing and reframing, social support (practical), salience of consequences, prompts and cues, and credible source. Only one BCT, credible source, was found to be nonsignificant for both necessity and concern beliefs. Interventions did not have significantly larger effects when including any individual BCT than without it (nearly all comparisons between interventions including a BCT vs. interventions not including it were nonsignificant [all p values $> .05$]; see Figure 5).

Discussion

This systematic review and meta-analysis identified RCTs which measured medication-related beliefs and assessed BCTs within interventions that measured medication-related beliefs in individuals prescribed medication/s for a chronic health condition. We found a heterogeneous set of interventions which had been offered to a wide variety of patient groups across different settings. Meta-analysis revealed a small-to-medium effect of the interventions on both need and concern/worry medication-related beliefs. A wide variety of BCTs were identified within the interventions with the most common being providing information about health consequences, problem solving, and social support (unspecified). These effects were larger for studies that reported that the intervention improved adherence. Interventions including these three BCTs significantly increased necessity beliefs and reduced concerns. These three BCTs were amongst the most prevalent in a recent meta-analysis exploring telecommunication interventions aimed at promoting adherence to cardiometabolic medication (Kassavou & Sutton, 2018). There was

Figure 3

Summary of TIDieR Checklist for Included Studies (n = 56)



Note. TIDieR = template for intervention description and replication.

some evidence that "credible source" was not associated with significant changes in either necessity or concern beliefs. However, including any individual BCT did not result in a significantly larger effect on medication-related beliefs relative to interventions without these BCTs. There was evidence of potential gaps in intervention reporting, bias in study design, and publication bias.

To our knowledge this is the first systematic review and meta-analysis to use the behavior change taxonomy to synthesize RCTs measuring of medicated-related beliefs. A wide range of physical and mental health conditions were included, with an equally broad range of interventions. Similar to previous reviews focusing on improving adherence (Horne et al., 2019; Nieuwlaat et al., 2014) the included studies were largely heterogeneous with differences in condition, intervention, timescales, and medication, thus making it challenging to reach definitive conclusions.

What Techniques Are Used in Interventions Which Measured Medication-Related Beliefs?

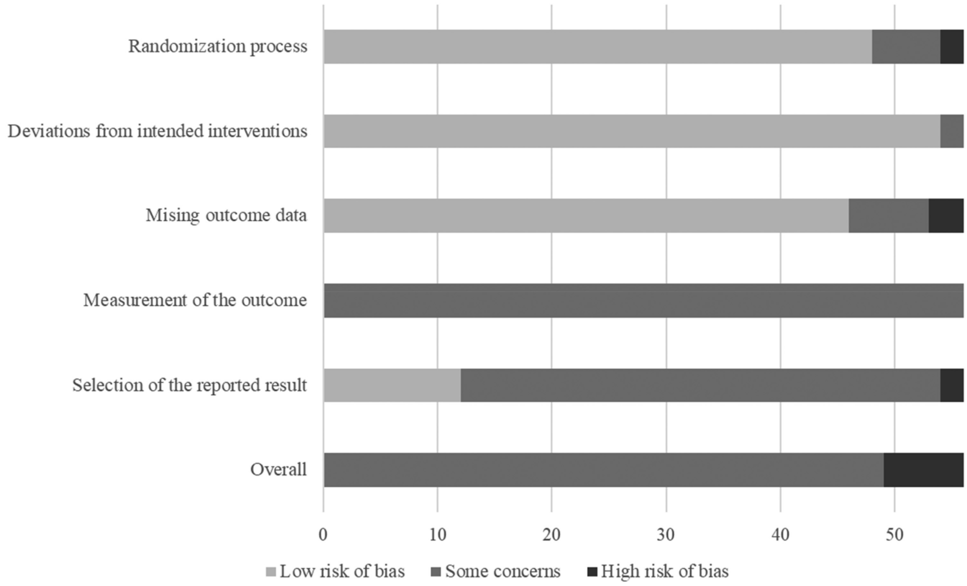
Rather than looking at groups of interventions, this study's first aim was to identify the active components of the interventions using the BCTT (Michie et al., 2013). Both the interventions with a primary outcome related to a specific behavior, for example, adherence, as well as interventions that had beliefs/attitudes as the primary outcome were captured by the BCTT. A range of BCTs were identified. Of the 93 possible BCTs, 36.6% were identified amongst the included studies covering 87.5% of the taxonomy domains. The top five coded BCTs were problem solving, information about health consequences, social support (unspecified), credible source, and pros and cons. Problem solving and pros and cons were operationalized similarly across studies, frequently "structured" or "guided" where individuals looked at medication problems or cons and then discussed potential solutions or pros. Information about health consequences, social support (unspecified), and credible source were all operationalized differently. Information and support were provided in several different ways and the term credible source captured a number of different HCPs.

There may be "untapped" potential in a range of BCTs which were not included in many interventions or identified as included in very few interventions in the current review. While many of these may not be relevant to medication-related beliefs and behaviors, there are certainly some which were not identified which might be interesting candidates for future intervention research. Many of the untested BCTs would be predicted by theory to be potentially effective in changing medication beliefs. For example, biofeedback, where feedback about the body is provided using an external monitoring device was not identified in any interventions but would seem relevant for addressing doubts about medication efficacy for example, address doubts that antihypertensive medications are affecting blood pressure (McManus et al., 2018). Reattribution was also untested despite theories pointing to the role of misattribution of symptoms as adverse effects in increasing their medication concerns (Petrie & Rief, 2019). Anticipated regret around the consequences of not taking medication was unused, although it has been found to motivate uptake of Human Papillomavirus vaccination (Caso et al., 2019) and taking the contraceptive pill (Molloy et al., 2012). Other BCTs commonly used and known to be effective in interventions focused on changing beliefs linked to behaviors such as cognitive behavioral therapy (Bennett-Levy et al., 2004), for example, behavioral experiments were also not identified in any of the included studies. Future research exploring a broader range of BCTs may identify techniques which could increase the effect of interventions on medication beliefs.

How Effective Were Interventions in Changing Medication-Related Beliefs?

Our meta-analyses found that interventions had significant small-to-moderate effects on perceived need for treatment and concerns relative to control groups. Small-to-moderate effects may be

Figure 4
Risk of Bias v2 Assessment (n = 56)



expected to have meaningful clinical impacts on patients. In the current review, studies which were effective for changing medication-related beliefs, the majority noted an improvement in adherence. However, it is unclear whether outcomes that might be viewed as the most important by patients and clinicians (for example, reductions in mortality, complications, and hospitalizations) would be achieved by these interventions given that the beliefs have small-to-moderate effects on behaviors, which, in turn, have small effects on clinical outcomes. Given these relatively small effect sizes, there is potentially a need for more effective methods to modify beliefs and maximize benefits to patients. This is particularly true given the intensive nature of some of the interventions, requiring high levels of commitment and time from both patients and HCPs. The costs of providing these interventions may therefore need to be balanced against their benefits in clinical practice.

Do Specific Techniques Increase the Effectiveness of Interventions?

The three most prevalent effective BCTs were problem solving, information about health consequences, and social support (unspecified). The most frequent BCT was problem solving. Problem solving was mainly operationalized in the included studies by providing participants with “structured problem solving” (identifying barriers and facilitators to taking medication). On first look, it is surprising that this BCT was the most frequent in effective interventions which changed medication beliefs given that it is usually thought of as addressing practical barriers to medication-taking rather than perceptual. Possibly, participants who undertook problem solving addressed barriers and facilitators that impacted on their beliefs, for example, a patient may have explored ways of better coping with adverse effects and therefore reduced their medication concerns. Alternatively, problem solving was always delivered in combination with other BCTs so these other codelivered BCTs may have contributed to this effect.

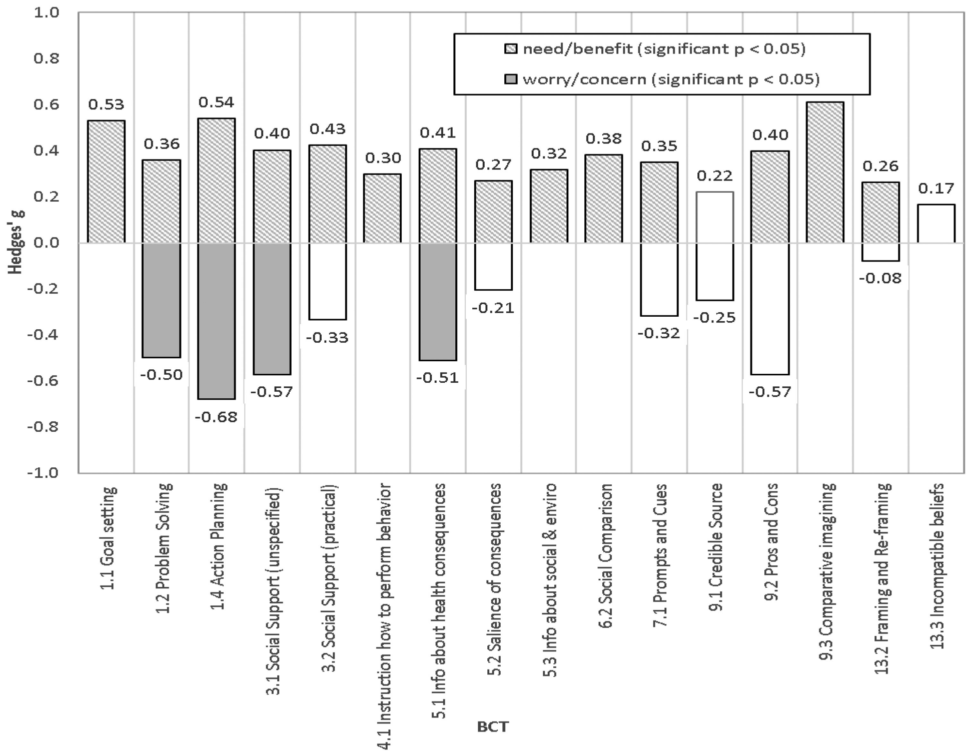
Providing information about health consequences was the next most common effective BCT, this may be an important tool in educating patients about the role of medication in their long-term condition. Previous literature has highlighted that individuals with higher concern beliefs and lower necessity are less likely to adhere (Foot et al., 2016; Horne et al., 2013) and more likely to misattribute symptoms as side effects of medication (Heller et al., 2015). Thus, being provided with information about health consequences of taking versus not taking medication may directly address certain medication-related beliefs.

The third most prevalent BCT was social support (unspecified) which was provided in a range of methods including counseling, a free telephone support line, and cognitive behavioral therapy. Therapies which frequently involve changing beliefs, for example cognitive–behavioral therapy to explore depressive thinking patterns, are grounded in a supportive setting. Results from 16 meta-analyses exploring psychotherapy outcomes, concluded that the therapeutic relationship was as important, if not more so, than the treatment method itself (Norcross & Lambert, 2018). An increasing literature also speaks to the importance of trust for medication-related beliefs. With research suggesting, a patient’s trust in their doctor improved knowledge about medication and adherence (AlRuthia et al., 2019). Perhaps interventions where participants received support resulted in greater trust in healthcare systems and medication and therefore influenced medication beliefs.

The three aforementioned BCTs can be operationalized in different ways which is advantageous given the range in healthcare resources throughout the world and the variability in patients preferences, for example, support could be provided via telephone or face-to-face counseling.

Only one BCT, credible source ($n = 13$), was found to be in more “noneffective” studies for both necessity and concern beliefs. A wide range of interventions were utilized amongst these thirteen studies. One potential difference noticed amongst the studies was training; 60% of the “effective” studies involved training (manuals

Figure 5
Hedges' g for BCTs



Note. BCT = behavior change technique.

and face-to-face training, with some studies mentioning training in communication). Whereas only 38% of "noneffective" studies mentioned specific training. A growing evidence base suggests that the interaction and relationship with a credible source (or physician) can influence health outcomes. Cross-sectional research found the quality of physician–doctor relationship influenced treatment recommendation adherence, with individuals reporting better relationships with their physician perceiving treatment recommendations as more influential (Orom et al., 2018). Therefore, credentials of a credible source may be insufficient alone to change medication-related beliefs.

Quality of Reporting, Risk of Bias, and Publication Bias

All included studies had either some concern or high risk of bias, this was expected due to the nature of the interventions. However, sensitivity analysis in the meta-analysis suggested the studies rated as "high risk of bias" did not have an impact on the overall findings. Within behavioral interventions blinding is not possible since it was clear whether a participant was receiving the intervention or control and the outcome was assessed using self-report, leading to the studies being rated as having "some concerns." Few studies reported on the fidelity of intervention delivery adequately, meaning that interventions may have been modified when delivered. Additionally, interventions and control conditions were often inadequately described. While all papers had some details of their interventions, the exact content of the materials (such as medication review script) was unavailable, and so the active components may not be correctly, or fully, identified (Hoffmann et al., 2014; Horne et al., 2005). The results of the publication bias test were mixed: Egger's test for small study bias was nonsignificant suggesting no publication bias, however Trim and Fill methods imputed several studies, increasing the overall estimated effect size. The high levels of heterogeneity (I^2) may cause funnel plot asymmetry despite absence of bias (Terrin et al., 2003). The systematic relationships between study precision and effect size may underpin the heterogeneity (Ioannidis & Trikalinos, 2007), for example if reporting of clinical outcomes/adherence was prioritized over belief outcomes. However, this is highly speculative and evaluation of publication bias can only be performed by comparing published literature to a robust trial register.

Strengths and Limitations

The review was conducted systematically, and a robust approach was adopted, adhering to the latest PRISMA guidance. A second coder was used for a proportion of studies to assess bias and quality, to maximize rigor. This is the first systematic review and meta-analysis of its kind to examine intervention content using the BCT taxonomy to identify effective interventions measuring medication-related beliefs. Additionally, bias related to interpretating the BCTv1 taxonomy were minimized by having two researchers independently extract available BCTs from all 56 included papers and meet to discuss interpretations. There are limitations to this review, data were extracted by one researcher. However significant effort was taken to ensure the accuracy of the data by the study team overseeing data extraction, discussing effect size calculations, and returning to the dataset at a different timepoint to check. There were also limitations arising from reporting quality and potential publication bias meaning that our findings might not accurately represent the full range of interventions tested. The underreporting of active ingredients is a significant challenge to behavioral research synthesis (de Bruin et al., 2021). Finally, the search was conducted in November 2020 and keyword searches in PubMed found approximately six potentially relevant articles for inclusion from that date. However it is unlikely that all would have sufficient information for BCT coding or meta-analysis. It is possible that reports may change the results for some of the BCTs which have been less tested, but it is unlikely that the findings would change for the most frequently identified BCTs. An updated review would benefit from utilizing the latest behavior change taxonomy, outlined below in future research.

Future Research

Future research would benefit from identifying how to maximize the effectiveness of interventions. For example, interviewing patients and HCPs to understand the best ways of operationalizing BCTs within their specific health condition. Additionally, future research could examine which BCTs work for which medication-related beliefs, to enable brief personalized intervention development, explore some of the undertested techniques, and explore whether BCTs work best in combination or whether they are sufficient by themselves. Furthermore, with the advent of the behavior change intervention ontology (Marques et al., 2023), a new dawn arises in our capacity to develop shared understanding of behavior change theories, intervention techniques, target behaviors, and contextual factors that influence behavior change. Training materials in how to code according to this revised framework are yet to be released, once these are available a new systematic review and meta-analysis could apply the ontology to medication-related beliefs.

Implications for Practice

The current review addresses beliefs about medications and informs the field about change in those beliefs. Meta-analysis indicates that beliefs regarding the necessity and concerns about medication are modifiable. Importantly, the beliefs are strongly associated with medication adherence. Specific BCTs associated with mediation-related change are identified. There was strongest evidence for the importance of problem solving, information about health consequences, and social support (unspecified), in changing medication beliefs. Those looking to design adherence interventions that change medication-related beliefs could explore these BCTs. There are numerous ways to provide problem solving, information, and social support. Interventionists could interview patients and HCP in specific health conditions to investigate the best method to utilize the BCTs within the health condition and resources. We found that many BCTs had not been included, suggesting there may be untapped potential. Interviews could therefore also provide an opportunity for patients and HCPs to explain "what else" is important for medication-related beliefs. Outside of formal interventions, these BCTs could potentially be operationalized in routine clinical practice to support patients. Given the importance of medication beliefs for adherence, perceptions of adverse effects, and satisfaction with treatment, more empirical research testing interventions specifically focused on beliefs may benefit patients and the HCPs who treat them.

Resumen

Objetivo: Las creencias relacionadas con los medicamentos, por ejemplo, las creencias de que los medicamentos son innecesarios o que es probable que se produzcan efectos secundarios, pueden influir en las conductas y experiencias con los medicamentos, lo que podría afectar la calidad de vida y la mortalidad. En ocasiones, puede resultar útil cambiar las creencias relacionadas con los medicamentos, por ejemplo, para reducir las preocupaciones de los pacientes sobre los efectos secundarios cuando la evidencia extensa sugiere que los efectos secundarios son raros. Actualmente no conocemos los métodos más eficaces para abordar las creencias sobre la medicación. ***Métodos:*** Revisión sistemática y metaanálisis de pruebas controladas aleatorizadas que midieron las creencias relacionadas con la medicación en personas a las que se les recetaron medicamentos para afecciones a largo plazo. Extrajimos datos sobre Técnicas de Cambio de Comportamiento (BCT, por sus siglas en ingles), medidas de creencias, características del estudio y del paciente, riesgo de sesgo y calidad de la descripción. ***Resultados:*** Identificamos 56 pruebas que asignaron al azar a 8,714 participantes. En el metaanálisis, las intervenciones produjeron efectos de pequeños a medianos ($n = 36$, g de Hedges $= .362$, IC [Intervalo de Confianza] del 95% [0.20, 0.52], $p < .001$) en el aumento de las creencias sobre la necesidad/beneficio de la medicación y reducir las preocupaciones sobre la medicación ($n = 21$, g de Hedges $= -.435$, IC del 95% [−0.72, −0.15], $p < .01$). Los tamaños del efecto fueron mayores para las intervenciones que informaron un efecto significativo sobre la adherencia. La resolución de problemas, la información sobre las consecuencias para la salud y el apoyo social (sin especificar) fueron los BCTs más prevalentes. Catorce BCTs se asociaron con efectos significativos sobre las creencias de necesidad/beneficio y cuatro BCTs se asociaron con efectos significativos sobre las creencias de preocupación. ***Conclusión:*** Es posible modificar las creencias relacionadas con la medicación utilizando una variedad de intervenciones y técnicas. Las investigaciones futuras deberían explorar las mejores formas de poner en práctica estos BCTs para condiciones de salud específicas para respaldar las creencias sobre la medicación y mejorar la adherencia.

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