Routledge
Taylor & Francis Group

Health Psychology Review

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/rhpr20

A machine-learning assisted review of the use of habit formation in medication adherence interventions for long-term conditions

L. Robinson, M. A. Arden, S. Dawson, S. J. Walters, M. J. Wildman & M. Stevenson

To cite this article: L. Robinson, M. A. Arden, S. Dawson, S. J. Walters, M. J. Wildman & M. Stevenson (2022): A machine-learning assisted review of the use of habit formation in medication adherence interventions for long-term conditions, Health Psychology Review, DOI: 10.1080/17437199.2022.2034516

To link to this article: https://doi.org/10.1080/17437199.2022.2034516

Published online: 14 Feb 2022.

HEALTH PSYCHOLOGY REVIEW
https://doi.org/10.1080/17437199.2022.2034516

Routledge
Taylor & Francis Group

A machine-learning assisted review of the use of habit formation in medication adherence interventions for long-term conditions

L. Robinson[a], M. A. Arden[b], S. Dawson[c], S. J. Walters[a], M. J. Wildman[d] and M. Stevenson[e]

[a]School of Health and Related Research, The University of Sheffield, Sheffield, UK; [b]Centre for Behavioural Science and Applied Psychology, Sheffield Hallam University, Sheffield, UK; [c]Wolfson Adult Cystic Fibrosis Centre, Nottingham University Hospitals NHS Trust, City Hospital, Nottingham, UK; [d]Sheffield Adult Cystic Fibrosis Centre, Sheffield Teaching Hospitals NHS Foundation Trust, Northern General Hospital, Sheffield, UK; [e]Department of Computer Science, The University of Sheffield, Sheffield, UK

ABSTRACT

Adherence to medication in long-term conditions is around 50%. The key components of successful interventions to improve medication adherence remain unclear, particularly when examined over prolonged follow-up periods. Behaviour change theories are increasingly interested in the utility of habit formation for the maintenance of health behaviour change, but there is no documentation on how habit has been conceptualised in the medication adherence intervention literature, or what effect the key technique identified in habit formation theory (context dependent repetition) has in these studies. To examine this, a machine-learning assisted review was conducted. Searches of MEDLINE, EMBASE and PSYCInfo and the reference list of a comprehensive systematic review of medication adherence interventions yielded 5973 articles. Machine learning-assisted title and abstract screening identified 15 independent RCTs published between 1976 and 2021, including 18 intervention comparisons of interest. Key findings indicate that conceptualisations of habit in the medication adherence literature are varied and behaviour change technique coding identified only six studies which explicitly described using habit formation. Future work should aim to develop this evidence base, drawing on contemporary habit theory and with explicit demonstration of what techniques have been used to promote habit formation.

ARTICLE HISTORY
Received 6 October 2021
Accepted 21 January 2022

KEYWORDS
Habit; medication adherence; behaviour change; maintenance; machine-learning assisted review

Background

Adherence to medication is a cornerstone of medical prescribing in long-term conditions but is frequently estimated to be in the region of 50% (Osterberg & Blaschke, 2005; Sabate, 2003). Adherence to medication describes the degree to which a person takes medication as agreed with a healthcare provider (Osterberg & Blaschke, 2005). There are a wide range of methods to measure and quantify adherence (Lehmann et al., 2013; Vrijens et al., 2012) but evidence from large studies of people with long-term conditions demonstrates that adherence is consistently below the minimally accepted standard of 80% (Briesacher et al., 2008; Sabate, 2003; Yeaw et al., 2009).

CONTACT L. Robinson lkrobinson1@sheffield.ac.uk
Supplemental data for this article can be accessed https://doi.org/10.1080/17437199.2022.2034516.

Non-adherence incurs huge costs to both economic and health domains. The economic impact of non-adherence was recently estimated to cost between $949 and $44,190 per person, per year (Cutler et al., 2018). The implications of non-adherence on health outcomes are numerous, including worsening of disease and increased hospitalisations and mortality, and this is evidenced across a wide-range of long-term conditions (Asche et al., 2011; Bangsberg et al., 2001; Chowdhury et al., 2013; Mäkelä et al., 2013). There is widespread consensus on the negative impact of non-adherence to medication, and this was acknowledged by the World Health Organisation with the publication of the 'Adherence to Long Term Therapies' reports (Sabate, 2001, 2003).

The development of interventions to support people with a range of chronic health conditions to improve their adherence to medication stands as one of the most important factors in improving outcomes to prescribed medications (Brown et al., 2016; Saag et al., 2018; Sabate, 2003). Despite this, the 'active ingredients' of effective medication adherence interventions remain unclear (Anderson et al., 2020; Nieuwlaat et al., 2014). In a Cochrane review of medication adherence interventions, authors were prevented from drawing conclusions as to the effectiveness of adherence interventions due to the range of different conceptualisations and measurements of adherence, studied in an array of disease areas, and using a multitude of intervention types (Nieuwlaat et al., 2014). Even within systematic reviews focusing on specific intervention types (e.g., Conn et al., 2016; Conn & Ruppar, 2017; Demonceau et al., 2013; Edmondson et al., 2018), there appears to be a diverse range of methods to implement seemingly similar intervention types (e.g., digital interventions, reminder-based interventions), with varied outcomes. The study of medication adherence interventions could benefit from the use of standardised taxonomies of intervention types and behaviour change techniques (BCTs; Michie et al., 2013) to examine intervention effectiveness.

In addition to the limited understanding of the 'active ingredients' of medication adherence interventions, even less is known about how to maintain adherence to medication in the long-term. Evidence has shown reduced effectiveness of medication adherence interventions with longer follow-up periods (Wiecek et al., 2019). This effect is not unique to medication adherence; failure to maintain health behaviour change effects in the long-term has been identified as a key research priority (Nilsen et al., 2010; Ory et al., 2010) and is gaining increasing attention in the context of social cognitive models of health behaviour (Norman & Connor, 2015). In a systematic review of over 100 theories describing maintenance of behaviour change, Kwasnicka et al. (2016) identified five key themes that theorists place at the core of maintenance theory, including maintenance motives, self-regulation, psychological and physical resources, the physical and social environment, and habit.

Habits have been hypothesised to facilitate maintenance of behaviour by bypassing reflective decision-making processes and enabling people to engage in behaviours as they have in the past, with minimal cognitive expense (Gardner et al., 2020; Gardner & Lally, 2018). Whilst the exact definition of habit is widely disputed, contemporary habit theory definitions, including modern, interdisciplinary accounts of habit (see Fleetwood, 2019) converge on the idea that habitual behaviour (e.g., brushing teeth) is initiated by a stable contextual cue (e.g., getting out of the shower) which is associated with that behaviour (Gardner, 2015; Gardner et al., 2021). The acquisition of a habit for a specific behaviour relies on repetition of the behaviour in response to a stable contextual cue, as this facilitates learning of cue-response associations over time (Lally et al., 2010).

Medication adherence can encompass different behaviours which may vary in complexity, for example, swallowing a pill, to preparing several medications to be administered via a medical device (e.g., a nebuliser). Contemporary habit theory places emphasis on the importance of the habitual instigation of the behaviour, whereby a contextual cue can habitually trigger the initiation of the first sub-action, among a potential sequence of sub-actions which constitute a behaviour (Gardner et al., 2016). Through this lens, techniques required to support the habitual instigation of behaviour should theoretically translate across the range of medication adherence behaviours.

Identifying which BCTs are required to target specific 'mechanisms of action' (MoAs) in behaviour change interventions is challenging (Hagger et al., 2020), but there is a growing evidence base to support researchers in the context of habit formation. Recent research has emphasised that

context-dependent repetition (equivalent to Michie et al.'s (2013) 'Habit formation' BCT) is the principal technique by which habits can form (Gardner et al., 2020; Gardner & Lally, 2018) and thereby any intervention reporting to utilise contemporary habit theory in its design should at least demonstrate use of this technique. However, whilst context dependent repetition is minimally required, growing consensus indicates that self-regulatory BCTs (e.g., action planning, prompts and cues, self-monitoring) may support the individual through the period of effortful repetition in the path to habit formation (Gardner et al., 2020; see also Carey et al., 2018; Connell et al., 2018). In a recent review, Gardner and Rebar (2019) searched for studies utilising context-dependent repetition and identified which *other* BCTs were used in combination to facilitate the formation of health behaviour habits. All included interventions combined context-dependent repetition with some other motivation or action control techniques, such as 'Action planning', 'Goal setting (behaviour)', 'Prompts and cues' and 'Problem solving' (see Michie et al., 2013 BCT taxonomy). This is unsurprising as both theoretical models of habit formation (Gardner et al., 2020; Gardner & Lally, 2018) and lay understandings of how habits are acquired (Brown et al., 2019) implicate a period during which the behaviour must be effortfully repeated before it becomes habitual.

Notably however, no studies included in Gardner and Rebar's review examined habit formation in a medication adherence intervention, yet in the largest synthesis of medication adherence interventions to date, Conn and Ruppar (2017) concluded that 'habit formation' interventions were likely to hold the most promise for facilitating changes in medication adherence. This disparity in findings indicates there may be differences in conceptualisations of what a habit is, and ideas about how it can be targeted, between the medication adherence and contemporary habit theory literatures. The extent to which the existing medication adherence intervention literature aligns with recommendations from contemporary habit theory has not yet been documented. An exploration, through the lens of contemporary habit theory, of how habit has been conceptualised, whether context-dependent repetition was used and which BCTs have been used alongside it could usefully draw attention to discrepancies between these two literatures. Furthermore, examination of the effectiveness of 'context dependent repetition' as a BCT in the context of these medication adherence interventions could provide a useful addition to the growing evidence base for the utility of this technique for supporting long-term behaviour change.

A machine-learning assisted review of randomised controlled trials (RCTs) examining the effectiveness of 'habit' interventions in maintaining adherence was conducted to address these issues.

The specific research objectives of this review are:

(1) To describe how habit has been conceptualised, and whether theory has been applied (i.e., evidence of the requirement for the behaviour to be repeated in the same context to acquire associations between cues and behaviour), in interventions designed to improve medication adherence in long-term conditions;
(2) To describe specific behaviour change techniques (BCTs) that have been used to target habit in interventions to improve adherence to medication in long-term conditions;
(3) To examine the effectiveness of interventions identified as using context-dependent repetition in improving adherence to medication in people with long-term conditions.

Materials and methods

The review was preregistered on PROSPERO, available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020187890

The scope of the review was extensive and inclusive across Population, Intervention type, Comparison, Outcome, Timeline and Study (PICOTS) domains. The scope covered individual and cluster randomised controlled trials (S) of habit-related adherence interventions (I) compared to usual care

or control interventions (C). These had to be conducted in adults with long term conditions (P) and measure effects on adherence(O) at a minimum of 6-months post-randomisation follow-up (T).

Search strategy

The search strategy was implemented in two stages.

Stage 1: identification of studies published prior to 2015

Conn and Ruppar (2017) published a large-scale systematic review of interventions designed to improve medication adherence. The final searches conducted for their review, as reported by Conn and Ruppar, were in 2015. The strategy used was assessed and it was understood that the search conducted by Conn and Ruppar (2017) would be both comprehensive and inclusive enough for the present review. A list of the included studies was retrieved and screened for eligible studies against the inclusion criteria for the present review.

Stage 2: identification of studies published after 2015

Electronic database searches were conducted on 13th May 2020: MEDLINE (1946 to May 12, 2020), PSYCInfo (1806 to May Week 2, 2020) and EMBASE (1974 to 2020 May 13) were searched. Key search terms included medication adherence (MeSH), randomised controlled trials, habit and behavioural or complex interventions. The full MEDLINE, PSYCInfo and EMBASE search strategies are available in Supplementary material 1.

Reference lists of included studies were also screened for eligible studies.

Inclusion criteria

Texts reporting RCTs of interventions designed to improve medication adherence in adults living with long-term conditions were the focus of this review. Eligible studies had to use the term 'habit', or 'automaticity' with reference to the SRBAI, in either the introduction, methods or associated documentation describing the intervention in more detail. Studies examining intervention effects in health conditions for which there is no cure and which is managed with a regimen of medication were eligible for this review. This specific criterion, used by the department of health (Department of Health, 2012), was chosen because: (i) this definition excludes disease groups such as tuberculosis, which is sometimes considered a long-term condition but can be cured with a 6-month prescription of antibiotics. The present review is concerned with long term (>6month) effects of interventions and therefore inclusion of diseases of this nature would be inappropriate; (ii) this definition excludes conditions such as sleep apnoea; whilst sleep apnoea is also sometimes considered to be a long term condition, it is primarily treated using mechanical devices worn overnight, rather than medicines taken in discrete episodes.

The focus of the review is to examine how the development of habits in the context of medication adherence facilitates long-term maintenance of medication-taking behaviour. This extends beyond initiation of the behaviour and requires evidence over prolonged periods. In line with the Transtheoretical model's conceptualisation of maintenance (Prochaska & Di Clemente, 1982), studies with a minimum follow-up of 6-months only were eligible for inclusion in this review.

All studies reporting full-scale RCTs published in peer reviewed journals were eligible for inclusion. Any number or type of comparison intervention was acceptable. Studies reporting adherence as a primary or secondary outcome variable were included.

Exclusion criteria

Studies of intervention effects on people who were in prison or people with substance abuse and/or psychological disorders were excluded. This is in line with Conn and Ruppar's (2017) exclusion

criteria and avoids inclusion of populations requiring specialist intervention design to support additional complexities in the self-management of disease.

Studies published as conference abstracts and journal supplements were excluded due to insufficient detail to code BCTs. Pilot and feasibility studies and studies not available in English or in full-text were excluded.

Study selection and data extraction

Title and abstract screening

Title and abstract screening was conducted using an active learning approach (see O'Mara-Eves et al., 2015), in which a portion of studies were manually labelled (include/exclude) and used to train a machine learning text-classification algorithm. The algorithm outputs the remaining, unlabelled studies in rank order of likelihood of inclusion, which the reviewer then continues to manually label. This process is iterated until the likelihood of identification of additional studies for inclusion is deemed low enough to cease screening (see O'Mara-Eves et al., 2015). Application of machine learning techniques for text classification is gaining increasing popularity in health science reviews (e.g., Currie et al., 2019; Shemilt et al., 2021; Shemilt et al., 2021) and a detailed description of the methods applied here are available in Supplementary Material 2 (see also Marshall & Wallace, 2019; O'Mara-Eves et al., 2015).

Full-text screening

All abstracts identified in the title and abstract screening process were manually screened. Due to the nature of the interventions of interest, a large number of articles were expected to be eligible for the full-text screening stage. In anticipation of this, a two-stage full-text screening process was planned and implemented.

In the first stage, full-texts were searched for keywords in either the introduction, methods or associated documentation (referenced in the methods) which detailed intervention content. Key words were 'habit(s/ual)' and/or 'automatic(ity)', used specifically in relation to medication adherence behaviours. The protocol states that the keyword 'Routine(s)' would also be searched at this stage but further experience from piloting this stage of the screening revealed that whilst some studies were using the keyword routine, it was unclear if they were using this in reference to habit formation and therefore this was excluded from the search process at this stage (see *Discussion* for more detail on this decision). If identified as potentially relevant in this stage, texts progressed to the second stage in which they were screened against the remaining inclusion and exclusion criteria.

Conference abstracts and journal supplement abstracts reporting potentially relevant studies were followed up to identify any journal articles which reported the study in full. The authors of protocols detailing relevant interventions were emailed to request trial results if available,[1] and full-texts of articles that could not be accessed by other means were requested from authors.

Data extraction

Study characteristics (design, recruitment, retention, population details, sample characteristics, study setting, follow-up), intervention features (including detailed coding of BCTs – see below), description of comparison groups, and adherence and habit outcomes were extracted using a data extraction form. Conceptualisations of habit were derived by reading descriptions around the location of keywords ('habit(s/ual)' and/or 'automatic(ity)') in the full-texts or (associated documentation which were referenced in the methods) and detailed intervention content.

Intervention BCT coding

Two reviewers (LR, SD) independently coded intervention BCTs using Michie and colleagues' taxonomy of 93 BCTs v1 (Michie et al., 2013). Intervention descriptions were extracted; if protocols or

methodology papers were available, these were also examined for additional details on intervention content. Differences were then discussed and a third expert reviewer (MA) was included to resolve any outstanding discrepancies. Some studies described some or all intervention features using Michie et al.'s (2013) taxonomy (indicated in Table 2 and supplementary material). In these instances, BCTs were extracted directly and the remaining text was checked for any additional BCTs that could be coded.

Adherence data extraction

The majority of studies included more than one summary of adherence, and/or at more than one time-point. 'Primary' outcomes for the purposes of principle comparisons in this review were selected in the following order of priority: outcomes nearest 6 months; stated as the primary outcome/power calculations based on expected effect size of this outcome; objective measurement tool; taking adherence (i.e., the proportion of medications taken relative to those prescribed). This was favoured over scheduling adherence (i.e., the proportion of doses taken within a specified time period relative to those prescribed), as taking adherence is most similar to other primarily extracted outcome measures, compared to scheduling adherence which is more stringent. Adherence outcomes summarised at time-points < 6 months, for within-group analyses or for sub-groups of participants were not extracted.

Quality assessment

The Cochrane revised risk of bias tool and variant for cluster RCTs (Higgins et al., 2019) was used to conduct quality appraisals. One reviewer (LR) conducted quality assessments. The primary extracted outcome was assessed for each study. Protocols and/or trial registry records were used to support assessment, when available. All five domains were assessed but items relating to blinding of participants and interventionists to treatment allocation were not assessed, due to the nature of behaviour change interventions being inevitably unblinded. To enable algorithm calculation, these items were scored as low risk for all studies. The cluster randomised trial tool includes two assessments for domain 1. In order to compare assessment of bias across individual and cluster randomised studies, assessments were combined on this domain: studies assessed as low risk on both items of this domain were given an overall summary of low; studies with at least one assessment of 'some concerns' or 'high risk' were summarised as 'some concerns' or 'high risk' overall, respectively. This is in line with overall summaries as described in the Cochrane RoB handbook (Sterne et al., 2019).

Data analysis

An assessment was conducted to determine the appropriateness of meta-analysis of findings from studies eligible for inclusion. The homogeneity of populations, intervention types, intervention content, adherence measurement tools and summary measures and timepoints at which participants were followed-up across all studies was considered. Owing primarily to between-study variation in conceptualisations and use of 'habit' as a construct in this review (*see Results*), and due to insufficient data available, a meta-analysis to determine the effectiveness of habit-based interventions would not be appropriate or achievable with this pool of studies. A planned, narrative review of conceptualisations of habit and the intervention BCTs was conducted. Following this, studies which explicitly used 'context-dependent repetition' (i.e., the principal BCT required to form a habit) were carried forward for examination of intervention effects. Effect sizes were calculated for adherence outcomes for each RCT based on the raw observed data; if this was not available this was calculated on the adjusted difference. Adherence outcomes were synthesised following the Cochrane Handbook 'Vote counting based on the direction of effect' method, as planned (McKenzie & Brennan, 2019). Probability of observing the overall direction of effect was assessed using a binomial probability test and confidence intervals calculated using the Wilson interval method (Brown et al., 2001).

Results

Searches yielded a total of 5973 studies of which, 17 articles were included (Figure 1). Two of these were protocols for studies for which the main articles were also included, thus screening identified 15 independent studies, including 18 intervention comparisons.

Overview of included studies

Characteristics of the 15 included studies are given in Table 1.

Interventions were designed for a variety of target populations, including people with cardiovascular disease and/or high cholesterol ($n = 5$ studies), human immunodeficiency virus (HIV; $n = 3$),

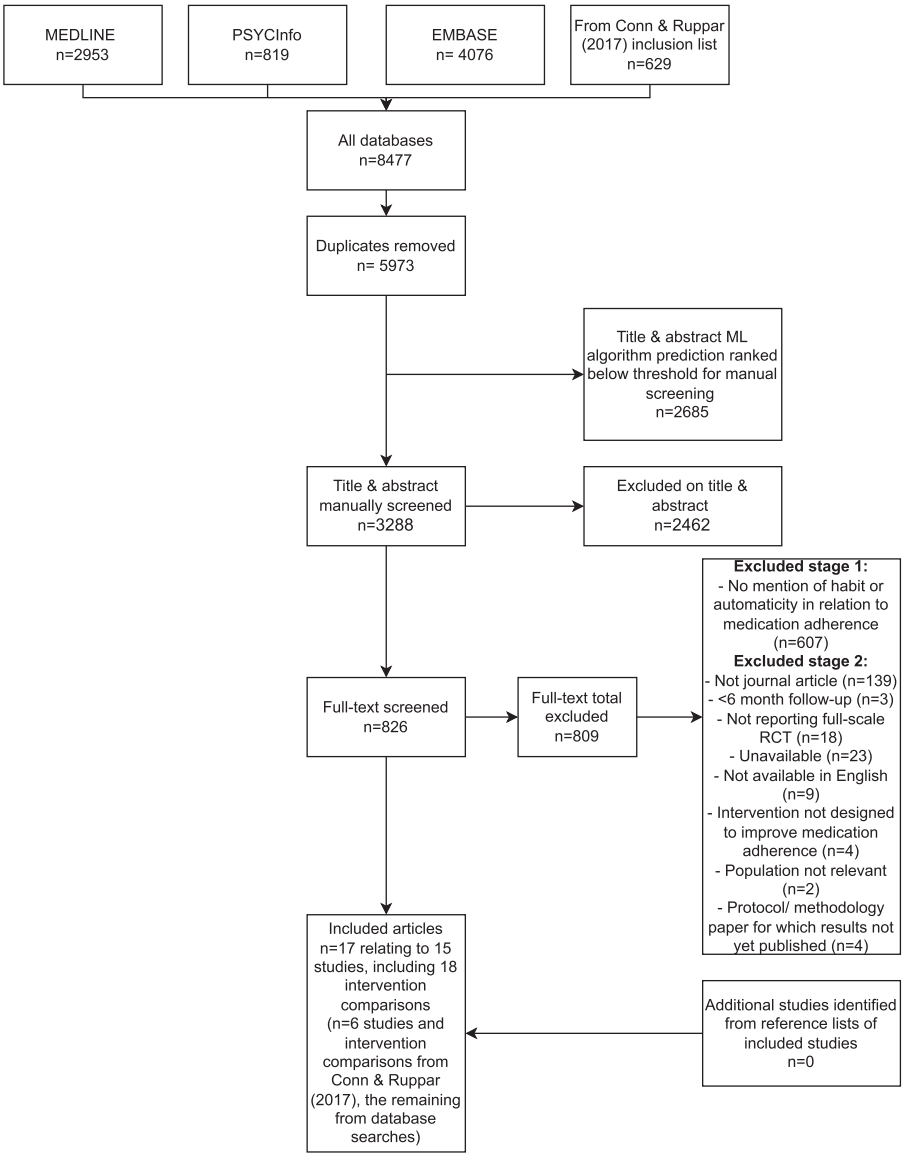

Figure 1. Screening flow-diagram.

Table 1. Study characteristics.

First author (Year)	Disease group and characteristics	Description of medication and dosage	Participant characteristics	*n* per group randomized	Intervention and comparator	Maximum follow-up period
Barankay (2020)	Statin prescription; self-reported non-adherence; LDL-C level > 100 mg/dL and diagnosed ASCVD /10-year CVD risk score > 7.5% OR LDL-C > 190 mg/dL and no other risk factors OR both	Pills; One pill bottle opening per day expected	Mean age (SD) = 58.5 (10.3); female = 519 (64.5%)	Simple daily sweepstakes: *n* = 199; Deadline sweepstakes: *n* = 204; Sweepstakes plus deposit contract: *n* = 201; Control: *n* = 201	Simple daily sweepstakes; Deadline sweepstakes; Sweepstakes plus deposit contract; vs Control	6 months
De Bruin (2010)	Diagnosis of HIV; ≥6 months on HAART; ≥18 years old	Pills; Majority of participants (90% +) on polytherapy	Mean age (SD): intervention = 47.3 (9.8); control = 48.7(9.8); Male %: intervention = 92%, control = 90%	Intervention *n* = 66; control *n* = 67	Electronic Monitoring-Based Counselling vs usual care	8–9 months
Farmer (2016)	Diagnosis of type-2 diabetes for ≥3 months; ≥18 years old; no known CVD events	Pills; One medication session daily	Mean age (SD): Action planning = 61.5(11.1), usual care = 63.9 (12); Male%: Action planning = 54, usual care = 59	Intervention *n* clusters = 30, *n* participants = 265; Control: n clusters = 29, n participants = 378	Brief action planning intervention vs usual care	12 months
Gregoriano (2019)	Diagnosis of asthma and/or COPD; prescribed daily inhaled medication and at least one exacerbation in the previous 12 months	Puff inhaled/dry powders; Intervention mean medications prescribed daily (SD) = 1.9 (0.8); Control mean (SD) = 2.0 (0.8)	Mean age (SD): Intervention = 64.7(12.4); Control = 69.0 (8.8); Male(%): Intervention = 61%; Control(%) = 69%	Total *n* randomised (*n*) = 169; Total entering baseline visit (*n*) = 165: Intervention = 84; Control *n* = 81	Daily alarm clock and support phone calls vs control	6 months
Haynes (1976)	Cardiovascular medication pill-count < 80% and high blood pressure (≥90 mm Hg); Dominion Foundries employees	Pills; dosage not stated	Mean age (SD) not reported. Male %: intervention = 100%, control = 100%	Intervention *n* = 20; control *n* = 19	Behavioural intervention vs usual care	6 months
Lin (2017)	People with CAD that had undergone CABG; responsible for self-administration of medications; not meeting criteria for other pre-specified comorbid diseases or health problems	Pills; Prescriptions across the sample: > 90% aspirin, 80% + beta blockers, 60% + ACE inhibitors, 70% + lipid lowering drugs	Mean age (SD): Intervention = 74.32 (5.26), control = 75.23 (5.82); Male%: intervention = 67.4%, control = 65.3%	Intervention: *n* centres = 6, *n* participants = 144; Control: *n* = 6 centres, n participants = 144	Multifaceted intervention including motivational interviewing vs usual care	18 months
Milam (2005)	Diagnosis of HIV for ≥3 months; attending participating HIV clinic; sexually active in past 3 months; ≥18 years old	Pills; Mean number of pills per day (SD) = 4.39 (1.8)	Mean age (SD): adherence intervention = 39(8.1); safer sex group = 39(7.8); Male %: adherence intervention = 87.9%; safer sex arm = 89.2%	Adherence arm: *n* clusters = 2, *n* participants = 149; safe sex intervention: *n* clusters = 4, *n* participants = 288	Brief adherence intervention vs safe sex intervention (no adherence component)	17–18 months
O'Dwyer (2020)	People prescribed salmeterol/fluticasone Diskus inhaler for asthma, COPD, or other (3-6% unknown diagnosis); filled ≥3 prescriptions in past 6 months	Inhaled medications; dosage not stated for this sample	Mean age (SD): Biofeedback group = 54(15), demonstration group = 53(15); control = 55 (13); Male %: Biofeedback group = 42%; demonstration group = 57%; control = 50%	Biofeedback group: n clusters = 27, n participants = 74; Demonstration group: n clusters = 37, n participants = 56; Control group: n clusters = 10, n participants = 22	Biofeedback or demonstration vs usual care	6 months

Pakpour (2015)	Diagnosis of epilepsy; ≥18 years old; independently responsible for medication taking; prescribed AEDs	Pills; Majority of participants (~70%) on monotherapy[a]	Mean age (SD): intervention = 41.37 (16.25), comparator = 39.86(15.01); Female %: intervention = 32.8%; control = 35.5%	Intervention *n* = 137; control *n* = 138	Multimodal behavioural intervention vs usual care	6 months
Reddy (2017)	Veterans with diagnosis of CAD; 30–75 years old; <80% adherence at entry to study	Pills; 1 session daily	Mean age (SD): Individual feedback = 65.6(4.1), partner feedback = 64.9(6.2), usual care = 64.1(6.6); Male %: Individual feedback = 100%, partner feedback = 96.3%, control = 91.7%	Individual feedback *n* = 36; partner feedback *n* = 54; control *n* = 36	Individual feedback or partner feedback vs usual care	26 weeks
Russell (2020)	People prescribed ≥1 twice-daily immunosuppressive medication following kidney transplant; ≥18 years old; functioning kidney transplant; no other life-shortening diagnosis	Pills; At least 1 medication, administered twice daily	Mean age (SD): SystemCHANGE = 53(11.2), Attention control = 50.7(9.7); Male%: SystemCHANGE = 66.7%; attention control = 50%	Intervention *n* = 45; control *n* = 44	SystemCHANGE intervention vs attention control	12 months
Stacy (2009)	Dyslipidaemia; ≥21 years; enrolled in pharmacy plan and placed claim for a statin prescription	Pills; 57.8% prescribed 3 + medications	Mean age: intervention = 54.6, control = 54.2; Females: intervention = 62.1%; control = 62.7%	Intervention: *n* = 298; Enhanced care control *n* = 280	Interactive voice response technology intervention vs enhanced care control	6 months
Tang (2014)	Diagnosis of epilepsy; ≥16 years old; AEDs prescribed ≥6 months; non-adherence occurred in the last 6 months	Pills; Not stated	Mean age (SD): Education and behavioural intervention = 30.8(11.6), Education only = 31.6(13); male%: Education and behavioural intervention = 58.9%; education only = 49.1%	Education and behavioural intervention *n* = 65, Education only *n* = 59,	Education plus behavioural intervention vs education only	6 months
Tuldrà (2000)	Attending HIV-outpatient clinic; initiating first or second line HAART	Pills; Mean (SD) doses per day = 3(2)	Mean age (SD): intervention = 39 (10), control = 38(7); male%: intervention = 73%; control = 79%	Intervention: *n* = 55; Control *n* = 61	Psychoeducative intervention vs usual care	48 weeks
Wildman (2021)	Diagnosis of CF; ≥16 years old	Nebulised; dosage not stated for this sample	Mean age (SD): Intervention = 31.1(10.6), control = 30.3(10.8); Female%: intervention = 51.3%, control = 50.8%	Intervention *n* = 305; control *n* = 303	CFHealthHub intervention vs usual care	12 months

CAD = Coronary artery disease; AED = anti-epileptic drug; ASCVD = Atherosclerotic cardiovascular disease; LDL-C = Low density lipoprotein cholesterol; HIV = Human immunodeficiency virus; HAART = Highly active anti-retroviral therapy; COPD = Chronic obstructive pulmonary disease; CVD = cardiovascular disease; CABG = coronary artery bypass graft; CF = cystic fibrosis; SD = standard deviation.

[a]Based on *n* in Table 1 of (Pakpour et al., 2015).

Table 2. 'Habit formation' intervention content and findings.

First author (Year)	Intervention name	BCTs coded[a]	Intervention duration to assessment timepoint details	Data collection	Adherence summary and timepoint measured	Adjustments to estimates	n (I,C) analysed	Effect on adherence (nearest 6 months)	Direction of effect and effect size (nearest 6 months)[b]	Effect on adherence > 6 months	Effect on habit
Gregoriano (2019)	Daily alarm clock and support phone calls vs control	1.2 Problem solving; 2.2 Feedback on behaviour; 7.1 Prompts/cues; 8.1 Behavioural practice/ rehearsal; 8.3 Habit formation	Intervention delivered over 6 months	Electronic device or POEMs where appropriate for dry powder medications	Mean number of days (max 200) that taking-adherence was in target adherence range (80-100%)	n/a	I (Puff inhaler) = 57, I (Dry powders) = 41 C (Puff inhaler) = 60, C (Dry powders) = 49	Significant difference for puff inhalers and dry powder capsules: Puff inhalers, Intervention mean(SD) = 81.6 (14.2), control mean (SD) = 60.1(30.3), $p < .001$; Dry powders Intervention mean (SD) = 89.6(9.8), Control mean(SD) = 80.2(21.3), $p = .01$	Favours intervention **Puff inhalers: Unadjusted d (95%CI) = 0.90 (0.52, 1.28)** **Dry powders: Unadjusted d (95%CI) = 0.55 (0.13, 0.97)**	n/a	Not measured
Haynes (1976)	Behavioural intervention vs usual care	1.2 Problem solving; 1.3 Goal setting (outcome); 1.4 Action planning; 1.6 Discrepancy between current behaviour and goal; 2.2 Feedback on behaviour; 2.3 Self-monitoring of behaviour; 2.4 Self-monitoring of outcome of behaviour; 2.6 Biofeedback; 3.1 Social support (unspecified); 7.1 Prompts/cues; 8.1 Behavioural practice/ rehearsal; 8.3 Habit formation; 10.4 Social reward; 10.10 Reward (outcome); 12.1 Restructuring	Intervention delivered over full 6 months	Unused pill count	Change in adherence at 6-months, adherence calculated as proportion of pills prescribed that are taken in the month of follow-up	n/a	I = 20 C = 18	Significant difference: Intervention mean (SE) = 65.8(8.2) vs control mean(SE) = 43.2 (10.1), Baseline adjusted difference = 22.8, $p = .025$	Favours intervention **Unadjusted Hedges g (95% CI) = 0.56 (−0.09, 1.21)**	n/a	Not measured

		the physical environment									
Milam (2005)	Brief adherence intervention vs safe sex intervention (no adherence component)	1.2 Problem solving 1.4 Action planning 7.1 Prompts/cues 8.1 Behavioural practice/ rehearsal 8.3 Habit formation	Intervention delivered until month 10–11	Self-report of number of pills taken over past 7 days	Percent of patients whose 7-day adherence > 95% measured at 17–18 months	Income, ethnicity, employment status, AIDS diagnosis, HAART regimen (vs. non-HAART), and number of pills per day, adherence at baseline and clustering	I = 149 C = 288	No significant effect: Intervention n(%) = 128 (85.9%) vs control n(%) = 201(69.8%). Adjusted OR = 2.05, [95% CI: 0.92 to 4.56], $p = .077$	Favours intervention **(Unadjusted) RR (95% CI) = 1.23 (1.11, 1.36)**	(Outcome measured at 17–18 months)	Not measured
Russell (2020)	SystemChange™ vs attention control	1.1 Goal setting (behaviour) 1.4 Action planning 1.5 Review behaviour goals 1.6 Discrepancy between current behaviour and goal 2.2 Feedback on behaviour 4.4 Behavioural experiments 15.3 Focus on past success	Intervention delivered over 6 months	MEMS-cap	Adherence rate defined as doses taken on time/ total doses at 6 months	Ethnicity, marital status, perceived health score, and perceived social support	I = 45 C = 44	Significant difference: Intervention mean (SD) = 0.81(0.25) vs control mean(SD) = 0.64(0.24), $p < .001$. Adjusted difference B = 0.2 (95% CI = 0.12 to 0.27; SE = 0.039, $p < .001$)	Favours intervention **Unadjusted d (95%CI) = 0.69 (0.27, 1.12)**	Significant difference at 12 months: Intervention mean (SD) = 0.65(0.37) vs control mean(SD) = 0.53(0.29), $p = .004$. Adjusted B = 0.16 (95% CI = 0.06 to 0.26; SE = 0.05) $p < .001$. Favours intervention. **Unadjusted d (95% CI) = 0.36 (−0.06, 0.78)**	Not measured
Tang (2014)	Education plus behavioural intervention vs education only	1.4 Action planning 7.1 Prompts/cues 8.1 Behavioural practice/ rehearsal 8.3 Habit formation 9.1 Credible source	Intervention delivered over full 6 months	Morisky Medication Adherence Scale (MMAS-4)	Number of individuals whose self-report adherence improved at 6-months.	n/a	I = 56 C = 53	Favours intervention. No significant effect: Intervention n improved (%) = 36 (64.3%) vs Control n improved (%) = 33 (62.3%), $p = 0.827$	Favours intervention **RR(95% CI) = 1.03 (0.78, 1.37)**	n/a	Not measured
Wildman (2021)	CFHealthHub intervention vs usual care	1.1 Goal setting (behaviour) 1.2 Problem solving 1.4 Action planning 1.5 Review behavioural goals 1.6 Discrepancy between current behaviour and goal 2.2 Feedback on behaviour 2.3 Self-monitoring	Intervention delivered over 12-month period	PARI eTrack™ electronic device	Normative adherence (adjustments made for ideal treatment for effectiveness) at 12 months	Treatment arm, time in weeks, baseline adherence (first two weeks), and past-year IV days	I = 295 C = 293	Favours intervention. Significant effect: intervention mean (SD) = 52.9%(31.4) vs control mean(SD) = 34.9%(31.7), adjusted mean difference = 9.5% (95%CI, 8.6-10.4)	Favours intervention **Adjusted d (95% CI) = 1.71 (1.52, 1.90)**	(Outcome measured at 12 months)	Favours intervention

(*Continued*)

Table 2. Continued.

First author (Year)	Intervention name	BCTs coded[a]	Intervention duration to assessment timepoint details	Data collection	Adherence summary and timepoint measured	Adjustments to estimates	n (I,C) analysed	Effect on adherence (nearest 6 months)	Direction of effect and effect size (nearest 6 months)[b]	Effect on adherence > 6 months	Effect on habit
		of behaviour 3.2 Social support (practical) 4.1 Instruction on how to perform the behaviour 5.1 Information about health consequences 5.2 Salience of consequences 6.1 Demonstration of the behaviour 7.1 Prompts/cues 8.1 Behavioural practice/ rehearsal 8.3 Habit formation 8.7 Graded tasks 9.1 Credible source 10.4 Social reward 12.1 Restructure the physical environment 12.5 Adding objects to the environment 15.3 Focus on past success 15.4 Self-talk 16.3 Vicarious consequences									

I = Intervention; C = Control; MEMS = Medication event monitoring system; POEMs = Polymedication Electronic Monitoring System; HAART = Highly active anti-retroviral therapy; SE = standard error; SD = standard deviation; CI = confidence interval.

[a]BCTs in bold represent BCTs coded by the study authors directly, using Michie et al.'s (2013) taxonomy.

[b]The effect size was estimated for each RCT based on the raw observed data; if this was not available on the adjusted difference.

respiratory disease ($n = 3$), epilepsy ($n = 2$), diabetes ($n = 1$) and for people prescribed immunosuppressants following kidney transplantation ($n = 1$).

Few details on the regimen prescribed for the included samples were given but likely ranged from requiring one opening of a pill bottle per day (e.g., Barankay et al., 2020) to a mean of 4.39 (SD = 1.8) doses of medication prescribed per day (Milam et al., 2005).

Conceptualisations of 'habit', intervention characteristics and 'habit formation' interventions

Conceptualisation of habit

Conceptualisations of what a habit is, references to key habit literature and provision of detail on how habits were targeted with specific intervention content varied greatly between studies.

Descriptions of habit in two studies closely aligned with contemporary habit theory, indicating both that habits arise from context-dependent repetition and that the development of habits reduces the need for effortful self-regulation of medication-taking behaviour (de Bruin et al., 2020; Wildman et al., 2021). Seminal literature on modern habit theory was referenced in both studies (e.g., Gardner & Rebar, 2019; Ouelette & Wood, 1998).

Barankay et al. (2020) dissociate three perspectives on habit from the psychological, economic and management literatures and apply these ideas to each of three intervention arms respectively, and examine their effects in maintaining the behaviour after withdrawal of incentives. In all three arms, including the control arm, a daily reminder was sent out. Whilst this could potentially act as a cue for the behaviour, this does not appear to be the active ingredient of their habit intervention arms, and whilst participants could choose the time at which this was received, the participants were not explicitly asked to link medication with the reminder. In the second arm, the authors state they draw on management theory in that 'habits arise as a consequence of newly established routines'. To encourage routines, participants in this arm were told they will only be entered into a sweepstake if they take their medications before they receive their reminder. The potential for reward was removed if behaviour was performed after the reminder each day. The idea of building medication-taking routines aligns more closely with contemporary habit theory in that existing routines could be used as a consistent cue to trigger performance of the new behaviour. However, there was no indication that the participant was supported to identify a cue or daily routine to enable repeated performance of the behaviour prior to their deadline, just that the behaviour itself was to become a routine. Other than specifying that the routine had to occur before the alarm, it is unclear what strategies were used to support this.

Reddy et al. (2017) designed their study to last 13 weeks, referencing key habit literature which demonstrated the average time for habits to form is 66 days (Lally et al., 2010). Reddy et al. (2017) stated that their aim was to create a '3-step habit loop' (referencing a book by Duhigg, 2012) but habit was here defined as medication-taking behaviour that is demonstrated by 'persistent adherence once the intervention is complete'. Reddy et al. (2017) referenced Context-dependent repetition was not indicated as a feature of habit formation in this study. Similarly, O'Dwyer et al. (2020) described habit as a behaviour which occurs regularly or routinely, but did not state that performance of the behaviour in a consistent context is also key to habit formation. Habitual performance of medication-taking in this intervention referred to both frequency with which the behaviour occurred but also in the way the medication was administered. This distinction, regarding habitual 'instigation' vs habitual 'execution' has been the topic of discussion in the wider habit literature (e.g., Gardner et al., 2016).

Six studies refer to habit as a behaviour that can be achieved by linking or performing medication-taking behaviours with other routines or 'habits' (Farmer et al., 2016; Gregoriano et al., 2019; Haynes et al., 1976; Milam et al., 2005; Russell et al., 2019; Tang et al., 2014). Whilst the need to link medication-taking behaviour with an existing routine was clearly indicated in the intervention description as well as in the background and rationale for most of these studies, the action planning intervention described by Farmer et al. (2016) did not explicitly mention that it was a routine (i.e., repeated

behaviour or cue) which was to be linked with medication-taking. This was important for coding habit formation as a BCT (see below).

Conceptualisation and implementation of habit remains unclear in two studies (Stacy, Schwartz, Ershoff, & Shreve, 2009; Tuldrà et al., 2000). Both studies explicitly link medication adherence to 'developing a habit', 'habit formation' or supporting participants in the 'acquisition of habits', but provide no elaboration on how this was achieved, and made no reference to other publications, studies or theoretical descriptions of habit.

Two interventions conceptualised habit as automaticity, using the Self-Report Behavioural Automaticity Index (SRBAI; Gardner et al., 2012), a widely used measure of habit and behavioural automaticity (Lin et al., 2017; Pakpour et al., 2015). Pakpour et al. (2015) first mention behavioural automaticity in the methods when describing the SRBAI and is only discussed thereafter in terms of change in behavioural automaticity; no explicit explanation as to the purpose or value in increasing automaticity (or habit) is given. Lin et al. (2017) state the rationale for measurement of behavioural automaticity: 'Behavioral automaticity reflects whether a patient engages in a behavior (e.g., taking medication) relatively automatically; that is, quickly, easily, and without the need for conscious thought'. Neither intervention states that a key mechanism to achieve behavioural automaticity is through context-dependent repetition.

Intervention content and techniques

Behaviour change techniques are presented in Supplementary Material 3. The most frequently coded technique was 'Feedback on behaviour' ($n = 11$ interventions), followed by 'Prompts/cues' ($n = 10$), 'Problem solving' and 'Action planning' (both $n = 8$) and 'Behavioural practice/rehearsal ($n = 6$)'. Thereafter, all other identified intervention techniques ($n = 34$) were coded for five or fewer interventions.

Only two studies used a BCT taxonomy to describe intervention content; both used Michie et al.'s (2013) taxonomy. The number of intervention techniques coded within a study varied from two to 15. Whilst for some studies this is likely an accurate reflection of the BCTs actually implemented in the interventions, some BCTs were precluded from being coded in some studies due to lack of detail.

'Context-dependent repetition' was coded for six interventions (see below).

Interventions utilising 'context-dependent repetition' and effects on adherence

Context-dependent repetition was identifiable in six of the 18 interventions (33%; Table 2), despite this being the primary mechanism by which theory predicts new habits will form (Gardner et al., 2020; Gardner & Lally, 2018). One study self-coded habit formation using Michie et al. (2013) taxonomy (Wildman et al., 2021). For some studies, absence of this BCT could be due to a lack of clarity in intervention descriptions leading to inability to definitively code it. For example, some studies described enough to code action planning, but context-dependent repetition could not be coded because there was not a clear indication that the details of the action plan involved *repetition* of the action plan in a specific context (e.g., Farmer et al., 2016). Stacy et al. (2009) included a figure to describe their intervention content which only contained the phrase 'Developing a habit' but with no reference to a taxonomy or with any additional description to contextualise exactly what was meant by this, and therefore context-dependent repetition could not be definitively coded for this study. Generally, context-dependent repetition was coded when authors described linking medication-taking behaviour with a routine or cue which occurred on a *daily* basis, therefore implying repetition.

Habit formation was never used as a standalone technique. Coding of Michie et al.'s (2013) 'Habit formation' BCT necessarily requires coding of 'Behavioural practice'. Five of the six interventions also used 'Prompts/cues', 'Action planning' and 'Problem solving'.

All six interventions indicated that an interventionist helped the participant to identify a consistent cue or daily routine which was to be linked with the behaviour. One study utilised an alarm

reminder and allowed the participant to choose the time of the alarm to coincide with their daily habits. Unlike the four other interventions, the alarm reminder itself was the intended cue in this intervention rather than the daily routine. Some interventions also described that the cue and behaviour were explicitly linked by writing them down on a dedicated action planning form which was designed to help with this task (Milam et al., 2005; Tang et al., 2014; Wildman et al., 2021).

Intervention effects on adherence

The present review aimed to examine the effectiveness of habit-based interventions. As identified by Michie and Prestwich (2010), referencing habit theories does not equate to an intervention being theory-based. For the present review, intervention effects were summarised for all included interventions (Supplementary material 4) but more utility can be gained from focusing on only the studies which used context-dependent repetition. Use of context-dependent repetition as a BCT was minimally required for an intervention to be described as 'habit-based' in line with contemporary habit theory and therefore detailed examination of intervention effects has been limited to these studies.

Findings from all six of these interventions showed positive effects on adherence (100%, 95%CI = [61–100%], $p = 0.03$), but effect sizes ranged from small (RR = 1.03, Tang et al., 2014) to very large (adjusted $d = 1.71$, Wildman et al., 2021; see Table 2). Interventions were implemented in diverse study contexts, used a range of outcome measures and were conducted across a number of disease groups (cardiovascular disease, COPD, epilepsy, HIV, kidney transplant and cystic fibrosis); some delivered multiple, relatively frequent face-to-face sessions, whilst others appeared to deliver the intervention in a single clinic visit. The small effects found by Tang et al. (2014) related to 'improvements in adherence'; this was a dichotomous outcome (improvement/no improvement) indicated by the score on a self-report measure of adherence. Comparatively, more objective measures of adherence were used by Gregoriano et al. (2019), Haynes et al. (1976), Wildman et al. (2021) and Russell et al. (2020); these studies found medium to very large effects. The largest effect (adjusted $d = 1.71$; Wildman et al., 2021) was also the study with the most BCTs coded, although this is likely attributable to the authors coding the intervention BCTs themselves, using Michie et al. (2013) taxonomy. In addition, some of these interventions ranged from simplistic interventions (e.g., completion of an action planning form; Tang et al., 2014) to complex interventions (e.g., Russell et al., 2020; Wildman et al., 2021) designed to improve adherence by targeting issues across Capability, Opportunity and Motivation (Michie et al., 2013).

Intervention effects on habit strength

Three studies (Lin et al., 2017; Pakpour et al., 2015; Wildman et al., 2021) measured change in habit strength and all used the SRBAI (Gardner et al., 2012), but Wildman et al.'s (2021) study was the only intervention of the three in which context-dependent repetition' was identified as a BCT. A small effect of the intervention on habitual automaticity was observed in this study, with an adjusted difference of 1.2 points on the SRBAI (scale range 4–20, 95% CI = 0.5–1.8, adjusted $d = 0.31$).

Both Pakpour et al. (2015) and Lin et al. (2017) rescaled the SRBAI to give an outcome measure scale of 1–5. A significantly greater increase in habit strength was observed by Pakpour et al. (2015) in the intervention group at 6-months compared to usual care (Intervention mean (SD) = 1.64(0.56); control mean (SD) = 1.35(0.49); Beta(SE) = 0.49(0.09), $p < 0.001$) with a medium effect size (unadjusted $d = 0.55$). Similar effects were observed by Lin et al. (2017) at six-months (B(SE) = 0.57(0.05), $p < .01$, unadjusted $d = 0.59$) and were maintained at 12 months (B(SE) = 0.47(0.05), $p < .01$, unadjusted $d = 0.55$), and 18 months (B(SE) = 0.5(0.06), $p < .01$, unadjusted $d = 0.53$).

Risk of bias

All included studies were assessed to have at least some quality concerns. Most studies scored high in risk of bias overall ($n = 12$), mostly triggered by high risk of bias in domains relating to the randomisation process, missing outcome data and risk of bias in measurement of the outcome when

Table 3. Quality assessment.

Study	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall summary
Barankay (2020)	Low	High	High	Low	Some concerns	High
De Bruin (2010)	Low	Low	High	Low	Some concerns	High
Farmer (2016)	Low	Some concerns	High	Low	Some concerns	High
Gregoriano (2019)[a]	Low	High	High	Low	Some concerns	High
Haynes (1976)[a]	Some concerns	Low	Low	Low	Some concerns	Some concerns
Lin (2017)[b]	Low	Low	High	High	Some concerns	High
Milam (2005)[a]	High	Some concerns	High	High	Some concerns	High
O'Dwyer (2020)	High	Low	High	Low	Some concerns	High
Pakpour (2015)[b]	Low	Low	Low	High	Some concerns	High
Reddy (2017)	Low	Low	Low	Low	Some concerns	Some concerns
Russell (2020)[a]	High	Low	Some concerns	Low	Some concerns	High
Stacy (2009)	Low	High	Low	Low	Some concerns	High
Tang (2014)[a]	High	High	High	High	Some concerns	High
Tuldrà (2000)	Some concerns	Low	High	High	Some concerns	High
Wildman (2021)[a,b]	Low	Low	Low	Low	Some concerns	Some concerns

Domain 1: risk of bias arising from the randomisation process; Domain 2: risk of bias due to deviations from the intended intervention (effect of assignment to intervention); Domain 3: risk of bias due to missing outcome data; Domain 4: risk of bias in measurement of an outcome; Domain 5: risk of bias in selection of reported result. 'High' refers to high risk of bias and 'low' refers to low risk of bias in the respective domain.

[a]Studies coded to have used context-dependent repetition in the intervention content.

[b]Studies which measured change in habit strength.

participants self-reported adherence and were aware of their intervention assignment. Least concerns were expressed with risk of bias caused by intervention assignment, although all studies were coded low by default on items assessing blinding of allocation and blinding of interventionists in this domain. Four of the six interventions that were coded as including context-dependent repetition as a BCT, and for which intervention effects on adherence has been discussed, were coded as having high risk of bias and two with some concerns. Two of three interventions which measured change in habit were coded as having high risk of bias and one with some concerns. Risk of bias assessments are summarised in Table 3.

Discussion

Summary of findings

This machine-learning assisted review of RCTs aimed to explore conceptualisations of habit and examine the effectiveness of habit interventions in maintaining adherence to medication in people with long term conditions. The review identified 15 RCTs, published between 1976 and 2021.

The findings indicate that a broad range of definitions, intervention characteristics and BCTs have been used to promote maintained adherence to medication and medication-taking 'habits'. Conceptualisation and use of the term 'habit' often did not align with contemporary habit theory in medication adherence interventions, and with a few exceptions, many of the interventions that were identified do not explicitly include context-dependent repetition as a BCT.

Conceptualisations of habit in adherence interventions

The findings of this review highlight the need to reserve the use of the term 'habit' to cue-dependent automaticity, acquired through repetition of behaviour in a stable context. One study drew on ideas about habit from three older literatures to develop three different intervention arms and examined effects against one another (Barankay et al., 2020). However, recent opinions demonstrate an appetite to aggregate interdisciplinary ideas on habit into a unified concept and theory, for consistency of application (Fleetwood, 2019; Gardner et al., 2021). Only two studies in this review made reference to seminal habit theory and literature (e.g., Gardner & Rebar, 2019; Ouelette & Wood, 1998), and

emphasised that both repetition and context stability of the behaviour are necessary components. Other studies described definitions more aligned with lay conceptualisations of habit (see Brown et al., 2019), with focus only on the importance of repetition, but little or no explicit reference to the importance of a stable contextual cue. The remaining studies made reference to habits, or habitual/automaticity of behaviours but gave no elaboration on how this was to be established. This finding is echoed in a systematic review by Rebar et al. (2016), examining habit formation in physical activity and we reiterate the importance of Rebar and colleagues' recommendations that, in scientific contexts, the term 'habit' should only be used in line with contemporary habit theory.

Among the six interventions in which context-dependent repetition of behaviour was identified as a BCT, all used it in combination with other BCTs. Most frequently combined were: 'Behavioural practice/rehearsal'; 'Prompts /cues'; 'Action planning' and 'Problem solving'. Some interventions included habit as one of a combination of mechanisms of action, but Gardner and Rebar (2019) presented similar findings in a review of habit formation across a range of health behaviours. However, Gardner and Rebar's (2019) study did not include any medication adherence interventions. The replication of this observation in medication adherence interventions suggests that, whilst 'Habit formation' (i.e., context-dependent repetition) is labelled as a single intervention technique in the BCT taxonomy (Michie et al., 2013, although see other taxonomies – Kok et al., 2016), a number of techniques might be used in combination with it to facilitate self-regulation and action control in the period whilst habits are forming. This aligns with expert consensus on the function of habit formation (behavioural cueing, behavioural regulation) with which other self-regulatory techniques have been associated, as well as with theoretical models of habit formation (Gardner et al., 2020; Gardner & Lally, 2018).

Only one study utilised incentives (Barankay et al., 2020); this study explicitly drew on economic theories of habit formation for this feature, but the importance of reward also relates to early behaviourist work on habit (e.g., Hull, 1943) in which external reward was thought to facilitate repetition of behaviour. The role of reward is heavily implicated in neurological models of habit formation (see Wood & Rünger, 2016). However use of material (financial) incentives alone is unlikely to have long-term effectiveness for maintaining behaviour beyond termination of their receipt (Mantzari et al., 2015). Barankay et al. (2020) combined incentives with other intervention content but did not emphasise the need to repeat adherence with a contextually stable cue. This therefore precluded coding of context-dependent repetition. Nevertheless, the use of external reward, rather than assuming the presence of an intrinsic reward when a goal is achieved during habit formation, is a theoretical concept which is seldom addressed in habit interventions. There is some evidence to suggest that people who find a behaviour more intrinsically rewarding are more likely to repeat behaviours during habit formation and achieve greater habitual automaticity (Gardner & Lally, 2013). This in turn has been evidenced to predict the maintenance of behaviour, via habit strength (Phillips, 2020; Phillips et al., 2016). However, this evidence base is mostly gleaned from physical activity interventions, not medication adherence interventions. It is both intuitive and scientifically evidenced that physical activity improves mood and mental health and therefore is likely to relate to the degree to which a person experiences reward. It is unclear if the same degree of intrinsic reward can be achieved through adhering to medication. Therefore, the form which 'reward' takes in habit interventions for medication adherence may require some more careful consideration.

Overall effectiveness of the included interventions

The primary motivation to synthesise results among interventions was to understand the effects of habit interventions on medication adherence. However, conceptualisations of what a habit is and the BCTs used in these interventions were diverse. This, along with various different intervention types, various methods to capture and summarise adherence data, and the fact that only six of 18 interventions appeared to use the principal BCT required to facilitate habit formation, prevented meaningful meta-analysis of intervention effects. The focus of the synthesis was therefore on a

detailed description of differences in conceptualisations of 'habit interventions' and comparisons of effectiveness among the six interventions which used context-dependent repetition.

The observed positive effects of these six interventions on adherence to medication indicate that context-dependent repetition in combination with other behavioural regulation techniques could be effective in sustaining improvements in medication adherence, for at least six months. This finding must be interpreted with caution as no studies made direct comparisons between interventions with and without habit formation as a BCT, and only one of these studies examined the effects of the intervention on habit strength (Wildman et al., 2021). Small positive effects on habit were found, but findings cannot be generalised beyond this study.

Strengths and limitations

A change was made to the inclusion and exclusion criteria in a deviation from the original review protocol, in order to facilitate a more refined and targeted synthesis of the use and conceptualisation of 'habit' in the existing medication adherence literature. The decision to exclude studies only making reference to 'routines' rather than explicitly using the keywords 'habit(ual)' or 'automatic (ity)' facilitated a detailed analysis of how habit had been conceptualised within this literature, without projecting theory and assumptions of the authors' intentions to build habits for their intervention in the absence of these keywords. Inclusion of studies which intended to form medication-taking routines, without further extension of the language screened for in the full-text screening stage, such as 'action planning' or description of linking medication-taking behaviours to other existing routines would have led to only a partial inclusion of this group of studies. The alternative, to expand the inclusion criteria to include studies describing this, would have been beyond the scope of the primary research objectives of this review. Furthermore, this expansion would involve some pre-specification of the BCTs which would likely lead to habit formation. This approach, whilst valid, is opposite to the objectives of this review, which aimed to identify which BCTs were being used in interventions with the intention to form medication-taking habits.

The heterogeneity in conceptualisations and implementations of habit formation interventions in this review meant that a meta-analysis could not be conducted. However, valuable insights were gained by turning attention to a narrative characterisation of the differences in conceptualisations of habit. In the opinion of the reviewers, the most important finding from this study is the need to reserve the term 'habit' for instances in which a behaviour is automatically cued by a stimulus. Use of modern theories of habit will support the development of medication adherence interventions.

Quality assessments of the included studies led to the judgement that 12 of the 15 studies presented evidence with a high risk of bias; the remaining two studies presented with at least some concerns. Four of the six studies included in the discussion of intervention effectiveness were coded as high risk of bias. However, given the focus of the review, confidence in the bias of effect sizes was less important than the confidence in determining all of the components of the included interventions. Insufficient detail may have meant that fewer BCTs were coded than were actually present in some interventions. This finding is not unique to this review (Michie & Johnston, 2012), and is echoed across reviews which have attempted to code interventions, across a range of fields (e.g., de Bruin et al., 2010; Candy et al., 2018).

An adaptive learning method utilising machine learning classifier was used to assist with title and abstract screening. This is a novel approach which is under rapid development in the interdisciplinary field of computer science applications to text mining for reviewing (O'Mara-Eves et al., 2015). A key success of this approach was the reduction in workload for the reviewers. The iterative approach, combining the speed and power of the text classifier with the conceptual input of the reviewer in steering the learning of the classifier, enabled title and abstract screening completion when 55% of the titles and abstracts retrieved from database searches had been manually labelled. Fewer relevant articles were identified with each 5% increment in screening, with only an additional 8 articles

found in the final 299 studies screened. This technique could be powerfully implemented in future reviews, especially when a large number of records are identified in the database search stage.

Implications and recommendations

The key finding of this review is that there are a limited number of theory-informed habit-based interventions, designed to enable sustained adherence to medications in long-term conditions. Interventions that utilise context-dependent repetition as a BCT, in combination with other behavioural regulation techniques, show promising outcomes for eliciting sustained improvements in medication adherence for at least six months. However, few interventions of this nature have been tested in RCTs in the medication adherence literature, and the existing evidence is mostly low in quality. For a number of interventions included in this review, 'context-dependent repetition' (equivalent to Michie et al.'s (2013) 'Habit formation BCT) was coded because the repetition of a behaviour was tied to another daily routine. Authors' explicit use of taxonomies to code this BCT will facilitate future syntheses which aim to aggregate the findings of habit intervention studies in medication adherence. Only three studies in this review included a measure of habit, and few studies evidenced the use of contemporary habit theory to support the identification of relevant BCTs. Recently, literature has been produced specifically to facilitate the design of interventions and studies of habit formation in health behaviours (e.g., Gardner et al., 2020, 2021). Recommendations from these sources should facilitate this process, even among intervention designers unfamiliar with this rapidly growing literature, or from other disciplines.

Note

1. This led papers being included that were published after the end date of the searches but for which results were provided prior to completion of data extraction (Barankay et al., 2020; Wildman et al, 2021).

Data availability

Python source code available from Github: https://github.com/lkrobinson/active_learning_systematic_review/blob/main/README.md.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

References

Anderson, L. J., Nuckols, T. K., Coles, C., Le, M. M., Schnipper, J. L., Shane, R., Jackevicius, C., Lee, J., Pevnick, J. M., Choudhry, N. K., O'Mahony, D., & Sarkisian, C. (2020). A systematic overview of systematic reviews evaluating medication adherence interventions. *American Journal of Health-System Pharmacy*, *77*(2), 138–147. https://doi.org/10.1093/ajhp/zxz284

Asche, C., LaFleur, J., & Conner, C. (2011). A review of diabetes treatment adherence and the association with clinical and economic outcomes. *Clinical Therapeutics*, *33*(1), 74–109. https://doi.org/10.1016/j.clinthera.2011.01.019

Bangsberg, D., Perry, S., Charlebois, E., Clark, R., Robertson, M., Zolopa, A., & Moss, A. (2001). Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS*, *15*(9), 1181–1183. https://doi.org/10.1097/00002030-200106150-00015

Barankay, I., Reese, P. P., Putt, M. E., Russell, L. B., Loewenstein, G., Pagnotti, D., Yan, J., Zhu, J., McGilloway, R., Brennan, T., Finnerty, D., Hoffer, K., Chadha, S., & Volpp, K. G. (2020). Effect of patient financial incentives on statin adherence and lipid control. *JAMA Network Open*, *3*(*10*), e2019429. http://doi.org/10.1001/jamanetworkopen.2020.19429

Briesacher, B. A., Andrade, S. E., Fouayzi, H., & Chan, K. A. (2008). Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy*, *28*(4), 437–443. https://doi.org/10.1592/phco.28.4.437

Brown, D., Morrissey, S., Hagger, M., & Hamilton, K. (2019). A qualitative investigation into the representations of habit by lay people. *Preprint*, https://doi.org/10.31234/osf.io/wf4ah

Brown, L. D., Cai, T. T., & DasGupta, A. (2001). Interval estimation for a binomial proportion. *Statistical Science*, *16*(2), 110–117. https://doi.org/10.1214/ss/1009213286

Brown, M. T., Bussell, J., Dutta, S., Davis, K., Strong, S., & Mathew, S. (2016). Medication adherence: Truth and consequences. *The American Journal of the Medical Sciences*, *351*(4), 387–399. https://doi.org/10.1016/j.amjms.2016.01.010

Candy, B., Vickerstaff, V., Jones, L., & King, M. (2018). Description of complex interventions: Analysis of changes in reporting in randomised trials since 2002. *Trials*, *19*(1), 110. https://doi.org/10.1186/S13063-018-2503-0

Carey, R. N., Connell, L. E., Johnston, M., Rothman, A. J., De Bruin, M., Kelly, M. P., & Michie, S. (2018). Behavior change techniques and their mechanisms of action: A synthesis of links described in published intervention literature. *Annals of Behavioral Medicine*, *53*(8), 693–707. https://doi.org/10.1093/abm/kay078

Chowdhury, R., Khan, H., Heydon, E., Shroufi, A., Fahimi, S., Moore, C., Stricker, B., Mendis, S., Hofman, A., Mant, J., & Franco, O. H. (2013). Adherence to cardiovascular therapy: A meta-analysis of prevalence and clinical consequences. *European Heart Journal*, *34*(38), 2940–2948. https://doi.org/10.1093/eurheartj/eht295

Conn, V. S., & Ruppar, T. M. (2017). Medication adherence outcomes of 771 intervention trials: Systematic review and meta-analysis. *Preventive Medicine*, *99*, 269–276. https://doi.org/10.1016/j.ypmed.2017.03.008

Conn, V. S., Ruppar, T. M., Enriquez, M., & Cooper, P. (2016). Medication adherence interventions that target subjects with adherence problems: Systematic review and meta-analysis. *Research in Social and Administrative Pharmacy*, *12*(2), 218–246. https://doi.org/10.1016/j.sapharm.2015.06.001

Connell, L. E., Carey, R. N., De Bruin, M., Rothman, A. J., Johnston, M., Kelly, M. P., & Michie, S. (2018). Links between behavior change techniques and mechanisms of action: An expert consensus study. *Annals of Behavioral Medicine*, *53*(8), 708–720. https://doi.org/10.1093/abm/kay082

Currie, G. L., Angel-Scott, H. N., Colvin, L., Cramond, F., Hair, K., Khandoker, L., Liao, J., Macleod, M., McCann, S. K., Morland, R., Sherratt, N., Stewart, R., Tanriver-Ayder, E., Thomas, J., Wang, Q., Wodarski, R., Xiong, R., Rice, A. S. C., Sena, E. S., & Lalu, M. (2019). Animal models of chemotherapy-induced peripheral neuropathy: A machine-assisted systematic review and meta-analysis. *PLOS Biology*, *17*(5), e3000243. https://doi.org/10.1371/JOURNAL.PBIO.3000243

Cutler, R. L., Fernandez-Llimos, F., Frommer, M., Benrimoj, C., & Garcia-Cardenas, V. (2018). Economic impact of medication non-adherence by disease groups: A systematic review. *BMJ Open*, *8*(1), e016982–e016982. https://doi.org/10.1136/bmjopen-2017-016982

de Bruin, M., Black, N., Javornik, N., Viechtbauer, W., Eisma, M. C., Hartman-Boyce, J., Williams, A. J., West, R., Michie, S., & Johnston, M. (2020). Underreporting of the active content of behavioural interventions: A systematic review and meta-analysis of randomised trials of smoking cessation interventions. *Health Psychology Review*, *15*(2), 195–213. https://doi.org/10.1080/17437199.2019.1709098

de Bruin, M., Hospers, H. J., van Breukelen, G. J. P., Kok, G., Koevoets, W. M., & Prins, J. M. (2010). Electronic monitoring-based counseling to enhance adherence among HIV-infected patients: A randomized controlled trial. *Health Psychology*, *29*(*4*), 421–428. http://doi.org/10.1037/a0020335

Demonceau, J., Ruppar, T., Kristanto, P., Hughes, D. A., Fargher, E., Kardas, P., De Geest, S., Dobbels, F., Lewek, P., Urquhart, J., & Vrijens, B. (2013). Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: A systematic literature review and meta-analysis. *Drugs*, *73*(6), 545–562. https://doi.org/10.1007/s40265-013-0041-3

Department of Health. (2012). *Long term conditions compendium of information: Third edition*. http://www.dh.gov.uk/publications.

Duhigg, C. (2012). *The power of habit: Why we do what we do and how to change*. Random House.

Edmondson, D., Falzon, L., Sundquist, K. J., Julian, J., Meli, L., Sumner, J. A., & Kronish, I. M. (2018). A systematic review of the inclusion of mechanisms of action in NIH-funded intervention trials to improve medication adherence. *Behaviour Research and Therapy*, *101*, 12–19. https://doi.org/10.1016/j.brat.2017.10.001

Farmer, A. J., Oke, J., Hardeman, W., Tucker, L., Sutton, S., Kinmonth, A.-L., Griffin, S., & Holman, R. R. (2016). The effect of a brief action planning intervention on adherence to double-blind study medication, compared to a standard trial protocol, in the Atorvastatin in Factorial with Omega EE90 Risk Reduction in Diabetes (AFORRD) clinical trial: A cluster randomised sub-study. *Diabetes Research and Clinical Practice*, *120*, 56–64. http://doi.org/10.1016/j.diabres.2016.07.004

Fleetwood, S. (2019). A definition of habit for socio-economics. *Review of Social Economy*, *79*(2), 131–165. https://doi.org/10.1080/00346764.2019.1630668

Gardner, B. (2015). A review and analysis of the use of 'habit' in understanding, predicting and influencing health-related behaviour. *Health Psychology Review*, *9*(3), 277–295. https://doi.org/10.1080/17437199.2013.876238

Gardner, B., Abraham, C., Lally, P., & de Bruijn, G.-J. (2012). Towards parsimony in habit measurement: Testing the convergent and predictive validity of an automaticity subscale of the self-report habit index. *The International Journal of Behavioral Nutrition and Physical Activity*, *9*(1), 102. https://doi.org/10.1186/1479-5868-9-102

Gardner, B., & Lally, P. (2013). Does intrinsic motivation strengthen physical activity habit? Modeling relationships between self-determination, past behaviour, and habit strength. *Journal of Behavioral Medicine*, *36*(5), 488–497. https://doi.org/10.1007/s10865-

Gardner, B., & Lally, P. (2018). Modelling habit formation and its determinants. In B. Verplanken (Ed.), *The psychology of habit* (pp. 207–230). Springer Nature Switzerland AG.

Gardner, B., Phillips, L. A., & Judah, G. (2016). Habitual instigation and habitual execution: Definition, measurement, and effects on behaviour frequency. *British Journal of Health Psychology*, *21*(3), 613–630. https://doi.org/10.1111/BJHP.12189

Gardner, B., Rebar, A., & Lally, P. (2020). Habit interventions. In M. S. Hagger, L. Cameron, K. Hamilton, N. Hankonen, & T. Lintunen (Eds.), *The handbook of behaviour change* (pp. 599–616). Cambridge University Press.

Gardner, B., Rebar, A., & Lally, P. (2021). How does habit form? Guidelines for tracking real-world habit formation. *Preprint*.

Gardner, B., & Rebar, A. L. (2019). *Habit formation and behaviour change. Oxford Research Encyclopedia of Psychology*. Oxford University Press.

Gregoriano, C., Dieterle, T., Breitenstein, A.-L., Dürr, S., Baum, A., Giezendanner, S., Maier, S., Leuppi-Taegtmeyer, A., Arnet, I., Hersberger, K. E., & Leuppi, J. D. (2019). Does a tailored intervention to promote adherence in patients with chronic lung disease affect exacerbations? A randomized controlled trial. *Respiratory Research*, *20*(*1*). http://doi.org/10.1186/s12931-019-1219-3

Hagger, M. S., Moyers, S., McAnally, K., & McKinley, L. E. (2020). Known knowns and known unknowns on behavior change interventions and mechanisms of action. *Health Psychology Review*, *14*(1), 199–212. https://doi.org/10.1080/17437199.2020.1719184

Haynes, R. B., Gibson, E. S., Hackett, B. C., Sackett, D. L., Taylor, D. W., Roberts, R. S., & Johnson, A. L. (1976). Improvement of medication compliance in uncontrolled hypertension. *The Lancet*, *307*(7972), 1265–1268. https://doi.org/10.1016/S0140-6736(76)91737-2

Higgins, J. P., Savovic, J., Page, M., Sterne, J. A., & RoB2 Development Group. (2019). *Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)*. https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool/current-version-of-rob-2

Hull, C. (1943). *Principles of behavior: An introduction to behavior theory*. Appleton-Century.

Kok, G., Gottlieb, N. H., Peters, G.-J. Y., Mullen, P. D., Parcel, G. S., Ruiter, R. A. C., Fernández, M. E., Markham, C., & Bartholomew, L. K. (2016). A taxonomy of behaviour change methods: An intervention mapping approach. *Health Psychology Review*, *10*(3), 297–312. https://doi.org/10.1080/17437199.2015.1077155

Kwasnicka, D., Dombrowski, S. U., White, M., & Sniehotta, F. (2016). Theoretical explanations for maintenance of behaviour change: A systematic review of behaviour theories. *Health Psychology Review*, *10*(3), 277–296. https://doi.org/10.1080/17437199.2016.1151372

Lally, P., van Jaarsveld, C. H. M., Potts, H. W. W., & Wardle, J. (2010). How are habits formed: Modelling habit formation in the real world. *European Journal of Social Psychology*, *40*(6), 998–1009. https://doi.org/10.1002/ejsp.674

Lehmann, A., Aslani, P., Ahmed, R., Celio, J., Gauchet, A., Bedouch, P., Bugnon, O., Allenet, B., & Schneider, M. P. (2013). Assessing medication adherence: Options to consider. *International Journal of Clinical Pharmacy*, *36*(1), 55–69. https://doi.org/10.1007/s11096-013-9865-x

Lin, C.-Y., Yaseri, M., Pakpour, A. H., Malm, D., Broström, A., Fridlund, B., Burri, A., & Webb, T. L. (2017). Can a multifaceted intervention including motivational interviewing improve medication adherence, quality of life, and mortality rates in older patients undergoing coronary artery bypass surgery? A multicenter, randomized controlled trial with 18-month follow-up. *Drugs & Aging*, *34*(*2*), 143–156. http://doi.org/10.1007/s40266-016-0429-3

Mäkelä, M. J., Backer, V., Hedegaard, M., & Larsson, K. (2013). Adherence to inhaled therapies, health outcomes and costs in patients with asthma and COPD. *Respiratory Medicine*, *107*(10), 1481–1490. https://doi.org/10.1016/j.rmed.2013.04.005

Mantzari, E., Vogt, F., Shemilt, I., Wei, Y., Higgins, J. P. T., & Marteau, T. M. (2015). Personal financial incentives for changing habitual health-related behaviors: A systematic review and meta-analysis. *Preventive Medicine*, *75*, 75–85. https://doi.org/10.1016/j.ypmed.2015.03.001

Marshall, I. J., & Wallace, B. C. (2019). Toward systematic review automation: A practical guide to using machine learning tools in research synthesis. *Systematic Reviews*, *8*(1), 163. https://doi.org/10.1186/s13643-019-1074-9

McKenzie, J. E., & Brennan, S. E. (2019). Synthesizing and presenting findings using other methods. *Cochrane Handbook for Systematic Reviews of Interventions*, 321–347. https://doi.org/10.1002/9781119536604.ch12

Michie, S., & Johnston, M. (2012). Theories and techniques of behaviour change: Developing a cumulative science of behaviour change. *Health Psychology Review*, *6*(1), 1–6. https://doi.org/10.1080/17437199.2012.654964

Michie, S., & Prestwich, A. (2010). Are interventions theory-based? Development of a theory coding scheme. *Health Psychology*, *29*(1), 1–8. https://doi.org/10.1037/a0016939

Michie, S., Richardson, M., Johnston, M., Abraham, C., Francis, J., Hardeman, W., Eccles, M. P., Cane, J., & Wood, C. E. (2013). The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: Building an international consensus for the reporting of behavior change interventions. *Annals of Behavioral Medicine*, *46*(1), 81–95. https://doi.org/10.1007/s12160-013-9486-6

Milam, J., Richardson, J. L., McCutchan, A., Stoyanoff, S., Weiss, J., Kemper, C., Larsen, R. A., Hollander, H., Weismuller, P., & Bolan, R. (2005). Effect of a brief antiretroviral adherence intervention delivered by HIV care providers. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *40*(*3*), 356–363. http://doi.org/10.1097/01.qai.0000159710.98960.81

Nieuwlaat, R., Wilczynski, N., Navarro, T., Hobson, N., Jeffery, R., Keepanasseril, A., Agoritsas, T., Mistry, N., Iorio, A., Jack, S., Sivaramalingam, B., Iserman, E., Mustafa, R. A., Jedraszewski, D., Cotoi, C., & Haynes, R. B. (2014). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews*, *11*. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000011.pub4/full

Nilsen, W. J., Haverkos, L., Nebeling, L., & Taylor, M. V. (2010). Maintenance of long-term behavior change. *American Journal of Health Behavior*, *34*(6), 643–646. https://doi.org/10.5993/AJHB.34.6.1

Norman, P., & Connor, M. (2015). Predicting and changing health behaviour: Future directions. In P. Norman & M. Connor (Eds.), *Predicting and changing health behaviour: Research and practice with social cognition models* (3rd ed., pp. 390–430). Open University Press.

O'Mara-Eves, A., Thomas, J., McNaught, J., Miwa, M., & Ananiadou, S. (2015). Using text mining for study identification in systematic reviews: A systematic review of current approaches. *Systematic Reviews*, *4*(1), 1. https://doi.org/10.1186/s13643-015-0031-5

Ory, M. G., Smith, M. L., Mier, N., & Wernicke, M. M. (2010). The science of sustaining health behavior change: The health maintenance consortium. *American Journal of Health Behavior*, *34*(6), 647–659. https://doi.org/10.5993/AJHB.34.6.2

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine*, *353*(5), 487–497. https://doi.org/10.1056/nejmra050100

Ouellette, J. A., & Wood, W. (1998). Habit and intention in everyday life: The multiple processes by which past behavior predicts future behavior. *Psychological Bulletin*, *124*(*1*), 54–74. http://doi.org/10.1037/0033-2909.124.1.54

Pakpour, A. H., Gholami, M., Esmaeili, R., Naghibi, S. A., Updegraff, J. A., Molloy, G. J., & Dombrowski, S. U. (2015). A randomized controlled multimodal behavioral intervention trial for improving antiepileptic drug adherence. *Epilepsy & Behavior*, *52*, 133–142. http://doi.org/10.1016/j.yebeh.2015.08.036

Phillips, L. A. (2020). Challenging assumptions about habit: A response to Hagger (2019). *Psychology of Sport and Exercise*, *47*, 101502. https://doi.org/10.1016/j.psychsport.2019.03.005

Phillips, L. A., Chamberland, P. É., Hekler, E. B., Abrams, J., & Eisenberg, M. H. (2016). Intrinsic rewards predict exercise via behavioral intentions for initiators but via habit strength for maintainers. *Sport, Exercise, and Performance Psychology*, *5*(4), 352–364. https://doi.org/10.1037/spy0000071

Prochaska, J. O., & Di Clemente, C. C. (1982). Transtheoretical therapy: Toward a more integrative model of change. *Psychotherapy: Theory, Research & Practice*, *19*(3), 276–288. https://doi.org/10.1037/h0088437

Rebar, A. L., Dimmock, J. A., Jackson, B., Rhodes, R. E., Kates, A., Starling, J., & Vandelanotte, C. (2016). A systematic review of the effects of non-conscious regulatory processes in physical activity. *Health Psychology Review*, *10*(4), 395–407. https://doi.org/10.1080/17437199.2016.1183505

Reddy, A., Huseman, T. L., Canamucio, A., Marcus, S. C., Asch, D. A., Volpp, K., & Long, J. A. (2017). Patient and partner feedback reports to improve statin medication adherence: A randomized control trial. *Journal of General Internal Medicine*, *32*(*3*), 256–261. http://doi.org/10.1007/s11606-016-3858-0

Russell, C. L., Hathaway, D., Remy, L. M., Aholt, D., Clark, D., Miller, C., Ashbaugh, C., Wakefield, M., Ye, S., Staggs, V. S., Ellis, R. J., & Goggin, K. (2019). Improving medication adherence and outcomes in adult kidney transplant patients using a personal systems approach: SystemCHANGE™ results of the MAGIC randomized clinical trial. *American Journal of Transplantation*, *20*(*1*), 125–136. http://doi.org/10.1111/ajt.v20.1

Saag, K. G., Bhatia, S., Mugavero, M. J., & Singh, J. A. (2018). Taking an interdisciplinary approach to understanding and improving medication adherence. *Journal of General Internal Medicine*, *33*(2), 136–138. https://doi.org/10.1007/s11606-017-4215-7

Sabate, E. (2001). *Adherence to long term therapies: Policy for action*. World Health Organization. https://apps.who.int/iris/handle/10665/66984

Sabate, E. (2003). *Adherence to long-term therapies: Evidence for action*. World Health Organization. https://apps.who.int/iris/handle/10665/42682

Shemilt, I., Arno, A., Thomas, J., Lorenc, T., Khouja, C. C., Raine, G., Sutcliffe, K., D'Souza, P., Wright, K., & Sowden, A. (2021). Using automation to produce a 'living map' of the COVID-19 research literature. *Journal of EAHIL*, *17*(2), 11–15. https://doi.org/10.32384/jeahil17469

Shemilt, I., Noel-Storr, A., Thomas, J., Featherstone, R., & Mavergames, C. (2021). *Machine learning reduced workload for the Cochrane COVID-19 study register: Development and evaluation of the Cochrane COVID-19 study classifier*. https://assets.researchsquare.com/files/rs-689189/v1/789144f5-66e5-4303-81af-63f1c45bd793.pdf?c=1626298662

Stacy, J. N., Schwartz, S. M., Ershoff, D., & Shreve, M. S. (2009). Incorporating tailored interactive patient solutions using interactive voice response technology to improve statin adherence: Results of a randomized clinical trial in a managed care setting. *Population Health Management*, *12*(*5*), 241–254. http://doi.org/10.1089/pop.2008.0046

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H.-Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., … Higgins, J. P. T. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*, *366*, l4898. http://dx.doi.org/10.1136/bmj.l4898

Tang, F., Zhu, G., Jiao, Z., Ma, C., Chen, N., & Wang, B. (2014). The effects of medication education and behavioral intervention on Chinese patients with epilepsy. *Epilepsy & Behavior*, *37*, 157–164. http://doi.org/10.1016/j.yebeh.2014.05.017

Tuldrà, A., Fumaz, C. R., Ferrer, M. J., Bayés, R., Arnó, A., Balagué, M., Bonjoch, A., Jou, A., Negredo, E., Paredes, R., Ruiz, L., Romeu, J., Sirera, G., Tural, C., Burger, D., & Clotet, B. (2000). Prospective randomized two-arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *25*(*3*), 221–228. http://doi.org/10.1097/00126334-200011010-00003

Vrijens, B., De Geest, S., Hughes, D. A., Przemyslaw, K., Demonceau, J., Ruppar, T., Dobbels, F., Fargher, E., Morrison, V., Lewek, P., Matyjaszczyk, M., Mshelia, C., Clyne, W., Aronson, J. K., & Urquhart, J. (2012). A new taxonomy for describing and defining adherence to medications. *British Journal of Clinical Pharmacology*, *73*(5), 691–705. https://doi.org/10.1111/j.1365-2125.2012.04167.x

Wiecek, E., Tonin, F. S., Torres-Robles, A., Benrimoj, S. I., Fernandez-Llimos, F., & Garcia-Cardenas, V. (2019). Temporal effectiveness of interventions to improve medication adherence: A network meta-analysis. *PLoS ONE*, *14*(3), e0213432. https://doi.org/10.1371/journal.pone.0213432

Wildman, M. J., O'Cathain, A., Maguire, C., Arden, M. A., Hutchings, M., Bradley, J., Walters, S. J., Whelan, P., Ainsworth, J., Buchan, I., Mandefield, L., Sutton, L., Tappenden, P., Elliott, R. A., Hoo, Z. H., Drabble, S. J., & Beever, D. (2021). Self-management intervention to reduce pulmonary exacerbations by supporting treatment adherence in adults with cystic fibrosis: a randomised controlled trial. *Thorax*, *9*. http://doi.org/10.1136/thoraxjnl-2021-217594

Wood, W., & Rünger, D. (2016). Psychology of habit. *Annual Review of Psychology*, *67*(1), 289–314. https://doi.org/10.1146/annurev-psych-122414-033417

Yeaw, J., Benner, J. S., Walt, J. G., Sian, S., & Smith, D. B. (2009). Comparing adherence and persistence across 6 chronic medication classes. *Journal of Managed Care Pharmacy*, *15*(9), 728–740. https://doi.org/10.18553/jmcp.2009.15.9.728