NICE National Institute for Health and Care Excellence

Appendix A1: Summary of evidence from surveillance

2019 surveillance of medicines adherence (2009) NICE guideline CG76

Patient involvement in decisions about medicines

Recommendations in this section of the guideline

Preamble to the recommendations

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the guidance.

Recommendation 1.4.2 has been replaced by recommendations in the NICE guideline on medicines optimisation.

These recommendations apply to all healthcare professionals who prescribe, dispense or review medicines or who have a role in making decisions about medicines with patients. Healthcare professionals are reminded of their duty under the Disability Discrimination Act (2005) to make reasonable adjustments to ensure that all people have the same opportunity for health.

Communication

Good communication between healthcare professionals and patients is needed for involvement of patients in decisions about medicines and for supporting adherence. Some patients may find it easier to communicate with their healthcare professional than others.

1.1.1 Healthcare professionals should adapt their consultation style to the needs of individual patients so that all patients have the opportunity to be involved in decisions about their medicines at the level they wish.

1.1.2 Consider any factors such as physical or learning disabilities, sight or hearing problems and difficulties with reading or speaking English, which may affect the patient's involvement in the consultation.

1.1.3 Establish the most effective way of communicating with each patient and, if necessary, consider ways of making information accessible and understandable (for example, using pictures, symbols, large print, different languages, an interpreter or a patient advocate).

1.1.4 Encourage patients to ask about their condition and treatment.

1.1.5 Ask patients open-ended questions because these are more likely to uncover patients' concerns.

1.1.6 Be aware that the consultation skills needed for increasing patient involvement can be improved.

Increasing patient involvement

Patient involvement in the decision-making process requires that healthcare professionals acknowledge patients' views about their condition and its treatment, and that both healthcare professional and patient have a role in making decisions about treatment. Simple interventions to increase patient involvement do not necessarily increase the overall length of consultation and may be justified by benefits, particularly over the course of a long-term condition.

1.1.7 Offer all patients the opportunity to be involved in making decisions about prescribed medicines. Establish what level of involvement in decision-making the patient would like.

1.1.8 Discuss with the patient why they might benefit from the treatment. Clearly explain the disease or condition and how the medicine will influence this.

1.1.9 Explain the medical aims of the treatment to patients and openly discuss the pros and cons of proposed medicines. The discussion should be at the level preferred by the patient.

1.1.10 Clarify what the patient hopes the treatment will achieve.

1.1.11 Avoid making assumptions about patient preferences about treatment. Talk to the patient to find out their preferences, and note any non-verbal cues that may indicate you need to explore the patient's perspective further.

1.1.12 Healthcare professionals have a duty to help patients to make decisions about their treatment based on an understanding of the likely benefits and risks rather than on misconceptions.

1.1.13 Accept that patients may have different views from healthcare professionals about the balance of risks, benefits and side effects of medicines.

1.1.14 Be aware that increasing patient involvement may mean that the patient decides not to take or to stop taking a medicine. If in the healthcare professional's view this could have an adverse effect, then the information provided to the patient on risks and benefits and the patient's decision should be recorded.

1.1.15 Accept that the patient has the right to decide not to take a medicine, even if you do not agree with the decision, as long as the patient has the capacity to make an informed decision and has been provided with the information needed to make such a decision.

1.1.16 Assess the patient's capacity to make each decision using the principles in the Mental Capacity Act (2005). To lack capacity patients must: (a) have an impairment of or disturbance or malfunction of brain and mind, and (b) demonstrate lack of capacity to:

- understand the information relevant to the decision
- retain information for long enough to use it in the decision
- use or weigh information as part of the process of making the decision
- communicate the decision (whether by talking, using sign language or any other means).

1.1.17 If the patient has specific concerns, record a summary of the discussion, because this may be helpful in future consultations.

1.1.18 Encourage and support patients, families and carers to keep an up-to-date list of all medicines the patient is taking. The list should include the names and dosages of prescription and non-prescription medicines and herbal and nutritional supplements. If the patient has any allergic or adverse reactions to medicines, these should be noted.

Understanding the patient's knowledge, beliefs and concerns about medicines

There is evidence that patients make decisions about medicines based on their understanding of their condition and the possible treatments, their view of their own need for the medicine and their concerns about the medicine.

1.1.19 Be aware that patients' concerns about medicines, and whether they believe they need them, affect how and whether they take their prescribed medicines.

1.1.20 Ask patients what they know, believe and understand about medicines before prescribing new treatments and when reviewing medicines.

1.1.21 Ask if the patient has any specific concerns about their medicines, whenever you prescribe, dispense or review medicines. These may include concerns about becoming dependent on medicines and concerns about adverse effects. Address these concerns.

1.1.22 Be aware that patients may wish to minimise how much medicine they take.

1.1.23 Be aware that patients may wish to discuss:

- what will happen if they do not take the medicine suggested by their healthcare professional
- non-pharmacological alternatives to medicines
- how to reduce and stop medicines they may have been taking for a long time, particularly those known to be associated with withdrawal symptoms
- how to fit taking the medicine into their daily routine
- how to make a choice between medicines if they believe they are taking too many medicines.

Providing information

Patients need information about their condition and possible treatments if they are to be involved in making informed decisions about medicines. The format and content of the information provided should meet the needs of individual patients.

1.1.24 Offer patients information about medicines before the medicines are prescribed.

1.1.25 Offer patients information that is relevant to their condition, possible treatments and personal circumstances, and that is easy to understand and free from jargon.

1.1.26 Check that patients have any information they wish about medicines when the medicines are dispensed.

1.1.27 Discuss information on medicines with the patient rather than just presenting it. The discussion should take into account what the patient understands and believes about the condition and treatment.

1.1.28 Do not assume that the patient information leaflets (PILs)* that patients receive with their medicines will meet each patient's needs. Address concerns that patients may have after reading the standard PILs.

* Patient information leaflets (PILs) contain information for patients on how medicines should be used. It is a legal requirement that this information is included on the label or within the packaging of a medicine.

1.1.29 Patients differ in the type and amount of information they need and want. Therefore the provision of information should be individualised and is likely to include, but not be limited to:

- what the medicine is
- how the medicine is likely to affect their condition (that is, its benefits)
- likely or significant adverse effects and what to do if they think they are experiencing them
- how to use the medicine
- what to do if they miss a dose
- whether further courses of the medicine will be needed after the first prescription
- how to get further supplies of medicines.

1.1.30 Be careful not to make assumptions about a patient's ability to understand the information provided. Check with the patient that they have understood the information. Information for patients should be clear and logical and, if possible, tailored to the needs of the individual patient.

1.1.31 Suggest where patients might find reliable information and support after the consultation: for example, by providing written information or directing them to other resources (for example, NHS Choices).

1.1.32 Provide inpatients with the same information as patients in other settings. Information should include:

- what the medicine is
- how the medicine is likely to affect their condition (that is, its benefits)
- likely or significant adverse effects and what to do if they think they are experiencing them
- how to use the medicine
- what to do if they miss a dose
- whether further courses of the medicine will be needed after the first prescription
- how to get further supply after discharge.

Surveillance proposal

This section of the guideline should not be updated.

Editorial amendments

The reference to the Disability Discrimination Act (2005) in the preamble to the recommendations in NICE CG76 should be updated to refer to the Equalities Act (2010).

In recommendation 1.1.31, the reference to 'NHS Choices' should be updated to 'the NHS website'.

In recommendation 1.1.16, a cross reference should be added to Decision-making and mental capacity (NICE NG108).

2019 surveillance summary

Tools to identify people at risk of non-adherence

A validation study(1) examined a tool to identify people at risk of non-adherence to medicines for long-term conditions and included people prescribed medicines for prevention of cardiovascular disease. The sample was noted to consist of 'generally high adherers'. As part of this study, the tool was reduced from 30 questions to 10 and further work to validate the amended tool is needed.

Interventions to help patients to make decisions

We identified 2 studies that assessed whether interventions to help patients to make decisions improves medicines adherence.

A Cochrane review(2) assessed 4 studies (n=1,342) of shared decision-making in adults or children with asthma compared with control (usual care or

multicomponent interventions excluding the shared decision-making component). Although meta-analysis was not possible because of heterogeneity, shared decision-making appeared to improve medicines adherence, asthma-related outcomes and quality of life.

A Cochrane review(3) assessed 10 studies (n=492,000) of shared decision-making interventions for people with infections. Shared decision-making reduced antimicrobial prescribing but had no effects on health service resource use or patients' satisfaction with the consultation.

Intelligence gathering

Topic experts indicated that the nature of the guideline meant that recommendations were durable, but that they may not be well implemented in the health system. However, there was interest in assessing digital technologies.

We received feedback that there has been progress in aspects of care covered by the guidelines, including shared decision-making.

Impact statement

The finding that shared decision-making may improve medicines adherence and reduce potentially inappropriate antimicrobial prescribing is consistent with current recommendations in this section of the guideline, which support such an approach.

New evidence is unlikely to change guideline recommendations.

Supporting adherence

Recommendations in this section of the guideline

Assessing adherence

Patients do not always take their medicines exactly as prescribed, and healthcare professionals are often unaware of how patients take their medicines. The purpose of assessing adherence is not to monitor patients but rather to find out whether patients need more information and support.

1.2.1 Recognise that non-adherence is common and that most patients are non-adherent sometimes. Routinely assess adherence in a non-judgemental way whenever you prescribe, dispense and review medicines.

1.2.2 Consider assessing non-adherence by asking the patient if they have missed any doses of medicine recently. Make it easier for them to report non-adherence by:

- asking the question in a way that does not apportion blame
- explaining why you are asking the question
- mentioning a specific time period such as 'in the past week'

- asking about medicine-taking behaviours such as reducing the dose, stopping and starting medicines.

1.2.3 Consider using records of prescription re-ordering, pharmacy patient medication records and return of unused medicines to identify potential non-adherence and patients needing additional support.

Interventions to increase adherence

Patients may need support to help them make the most effective use of their medicines. This support may take the form of further information and discussion, or involve practical changes to the type of medicine or the regimen. Any interventions to support adherence should be considered on a case-by-case basis and should address the concerns and needs of individual patients.

1.2.4 If a patient is not taking their medicines, discuss with them whether this is because of beliefs and concerns or problems about the medicines (intentional non-adherence) or because of practical problems (unintentional non-adherence).

1.2.5 Be aware that although adherence can be improved, no specific intervention can be recommended for all patients. Tailor any intervention to increase adherence to the specific difficulties with adherence the patient is experiencing.

1.2.6 Find out what form of support the patient would prefer to increase their adherence to medicines. Together, you and your patient should consider options for support.

1.2.7 Address any beliefs and concerns that patients have that result in reduced adherence.

1.2.8 Because evidence supporting interventions to increase adherence is inconclusive, only use interventions to overcome practical problems associated with non-adherence if a specific need is identified. Target the intervention to the need. Interventions might include:

- suggesting that patients record their medicine-taking
- encouraging patients to monitor their condition
- simplifying the dosing regimen
- using alternative packaging for the medicine
- using a multi-compartment medicines system.

1.2.9 Side effects can be a problem for some patients. If this is the case you should:

- discuss how the patient would like to deal with side effects
- discuss the benefits, side effects and long-term effects with the patient to allow them to make an informed choice
- consider adjusting the dosage
- consider switching to another medicine with a different risk of side effects

- consider what other strategies might be used (for example, timing of medicines).

1.2.10 Ask patients if prescriptions charges are a problem for them. If they are, consider possible options to reduce costs.

Surveillance proposal

This section of the guideline should not be updated.

2019 surveillance summary

Methods of reminding patients to take medicines

We identified 47 studies assessing interventions that included a method of reminding patients to take medicines, including text messages, mobile or online apps, or telehealth interventions involving reminders or alerts (see Table 1).

The studies were primarily randomised controlled trials (RCTs; 35 studies), with 4 Cochrane reviews, 1 systematic review with network meta-analysis and 6 standard systematic reviews also identified. These studies reported on 45 analyses looking at the outcome of adherence, and 62 analyses related to clinical and patient-oriented outcomes or healthcare resource use.

Overall, methods of reminding patients to take medicines appear to be effective for improving adherence (effective in 37 of 45 analyses, 82%) and improving clinical, patient-oriented, or healthcare resource use outcomes (41 of 62 analyses, 66%) such as improved blood lipid profile in cardiovascular disease, reduced viral load in people with HIV and attending appointments with healthcare professionals.

The studies included a variety of different populations, with the most common populations analysed being cardiometabolic conditions, infections, and respiratory disorders. There was no indication that effects of reminding patients to take medicines were restricted to specific populations.

Mobile health interventions and telehealth interventions without use of reminders

We identified 34 studies assessing mobile or telehealth interventions that did not appear to include a component for reminding patients to take their medicines (see

Table 2 below). This included 21 RCTs, 2 Cochrane reviews, 9 other systematic reviews and 1 cost-effectiveness analysis. These studies reported on 24 analyses looking at the outcomes of adherence, and 71 analyses related to clinical and patient-oriented outcomes or healthcare resource use.

Mobile and telehealth interventions without reminders appeared to be effective for improving adherence in around half of the analyses (14 of 23, 61%) and improving clinical, patient-oriented, or healthcare resource use outcomes (44 of 71 analyses, 62%) such as improved blood lipid profile in cardiovascular disease, patient satisfaction and quality of life.

Most of these studies were in people with cardiometabolic conditions but there was no indication that effects of mobile and telehealth interventions without reminders were restricted to this population.

Other interventions aiming to improve medicines adherence

We identified 33 studies of interventions aiming to improve medicines adherence that did not include reminders or use of mobile or telehealth interventions (see Table 3 below). This included 6 Cochrane reviews, 1 NIHR-funded Health Technology Assessment, 1 systematic review with network meta-analysis, 6 standard systematic reviews, and 18 RCTs, including 2 NIHR-funded studies.

Overall, interventions aiming to improve medicines adherence appear to be effective for adherence (effective in 29 of 47 analyses, 62%) and improving clinical, patient-oriented, or healthcare resource use outcomes (26 of 44 analyses, 61%) such as improved blood glucose in diabetes, reduced viral load in people with HIV and or successful treatment of tuberculosis.

The interventions that showed no effect on adherence tended to be simple interventions and included having a medicines adherence partner, a video intervention (no further details reported in the abstract), cognitive behavioural therapy, and motivational interviewing. Electronic pill bottles or pill storage devices had no effect on adherence in 4 of 5 analyses.

However, several simple interventions did show an effect on adherence, including payment of £15 for having long-acting antipsychotic injections and simplified drug regimens in asthma and cardiovascular disease.

Multi-compartment medicines systems

An NIHR-funded Health Technology Assessment(4) assessed the feasibility of determining the effectiveness and cost-effectiveness of multi-compartment medicines systems. This work consisted of a systematic review, stakeholder focus groups and a feasibility RCT. The systematic review noted: 'Of the eight studies, four suggested improved adherence in the MOD [multicompartment medicines device] group. Owing to overall heterogeneity, a meta-analysis was not possible.' The 3-week feasibility RCT had 4 arms: weekly medication organisation device; monthly medication organisation device; weekly usual packaging; monthly usual packaging. Overall 29 participants were included (7–8 people per arm). The adherence rates in all arms during the study were high (95–97%) and did not differ between groups. Five adverse events occurred in people using

medication organisation devices. This is a notable number in a small study of short duration. For all 5 people who had adverse events, the authors concluded 'It is a possibility that study participation improved medication adherence…' However, for 2 of these patients, adherence was lower during the study than before the intervention, which contradicts the authors' conclusion on the cause of the adverse event. Additionally, the suggestion that adverse events were caused by the multi-compartment medicines systems is contradicted by the finding that these systems did not affect adherence.

Intelligence gathering

Topic expert feedback that the recommendations were durable, but may not be well implemented and interest in new technology was applicable to this section of the guideline.

We received feedback on concerns about multi-compartment medicines systems, which are used to aid adherence; however no additional studies eligible for consideration in surveillance were identified. Observational studies of this issue are limited by the inability to determine whether multi-compartment medicines systems are themselves problematic, or if they are a marker of polypharmacy and possible inappropriate prescribing. The guideline suggests these systems as one of several options to overcome practical problems associated with non-adherence if a specific need is identified.

Impact statement

Overall, interventions making use of digital technologies appear to improve adherence to treatments and may improve clinical outcomes. No single component or activity appeared to be driving the effects of interventions.

However, drawing robust conclusions from the evidence is difficult.

First, interventions, such as text messaging, were studied alone and as part of a complex intervention across studies. Text messaging appeared to have beneficial effects on adherence and some clinical outcomes. However, no effect was seen in a substantial proportion of analyses. It is unclear what may be driving effects in some studies but not others. There was no indication that text messaging was more effective or less effective in specific populations, such as cardiovascular conditions or infectious disease. NICE recommends the use of text messaging as a form of communicating with patients in several guidelines, including reducing the differences in uptake of immunisations in under 19s, and sunlight exposure: risks and benefits.

Additionally, the evidence does not address contextual issues around data protection and whether patients are willing to receive text messages from their doctors, the optimum content and frequency of text messaging, and whether findings in specific populations are transferable to less studied populations.

These issues were common across the evidence identified in surveillance.

Second, interventions may not be appropriately classified in surveillance. The surveillance process is an abstract-level assessment of the evidence looking for indicators that a guideline should be updated. Detailed information about the

interventions was often absent from the abstract. Studies describing their interventions as mobile interventions or telehealth interventions may be describing highly similar approaches, or may be vastly different.

Nevertheless, the interventions are complementary to and support established and recognised good practice around medicines adherence. Most of the evidence comes from specific populations such as cardiometabolic conditions and infectious diseases. Although the principles behind interventions for improving medicines adherence may have broad similarities across populations, technologies programmed for specific populations may not be easily reconfigured for other populations.

Therefore, the evidence is insufficient to indicate a need to update the guideline on medicines adherence. However, the evidence identified in this surveillance review will also be considered in the context of the relevant disease-specific guidelines during scheduled surveillance of the relevant guidelines.

New evidence is unlikely to change guideline recommendations.

Reviewing medicines

Recommendations in this section of the guideline

Patients may use medicines long term. The initial decision to prescribe medicines, the patient's experience of using the medicines and the patient's needs for adherence support should be reviewed regularly. The patient's own list of medicines may be a useful aid in a medicines review.

1.3.1 Review patient knowledge, understanding and concerns about medicines, and a patient's view of their need for medicine at intervals agreed with the patient, because these may change over time. Offer repeat information and review to patients, especially when treating long-term conditions with multiple medicines.

1.3.2 Review at regular intervals the decision to prescribe medicines, according to patient choice and need.

1.3.3 Enquire about adherence when reviewing medicines. If non-adherence is identified, clarify possible causes and agree any action with the patient. Any plan should include a date for a follow-up review.

1.3.4 Be aware that patients sometimes evaluate prescribed medicines using their own criteria such as their understanding of their condition or the symptoms most troubling to them. They may, for example, stop and start the medicine or alter the dose and check how this affects their symptoms. Ask the patient whether they have done this.

Surveillance proposal

No new information was identified.

This section of the guideline should not be updated.

Communication between healthcare professionals

Recommendations in this section of the guideline

Patients may be under the care of healthcare professionals from different disciplines and specialties at the same time; responsibility for patients' care may be transferred between healthcare professionals, and medicines reviews may be carried out by healthcare professionals other than the prescriber. Therefore good communication between healthcare professionals is required to ensure that fragmentation of care does not occur.

1.4.1 Healthcare professionals involved in prescribing, dispensing or reviewing medicines should ensure that there are robust processes for communicating with other healthcare professionals involved in the patient's care.

1.4.2 This recommendation has been replaced by recommendations in section 1.2 in the NICE guideline on medicines optimisation.

1.4.3 Healthcare professionals involved in reviewing medicines should inform the prescriber of the review and its outcome. This is particularly important if the review involves discussion of difficulties with adherence and further review is necessary.

Surveillance proposal

No new information was identified.

This section of the guideline should not be updated.

Research recommendations

What are the most clinically effective and cost-effective methods for identifying and addressing the perceptual barriers (such as beliefs and concerns about medicines) that influence motivation to start and continue with treatment, and the practical barriers (such as limitations in personal capacity and resources) that limit an individual's ability to implement intentions to adhere to medicines?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

What are the most clinically effective and cost-effective ways of communicating the potential benefits and risks of medicines to promote informed choice and optimal adherence?

Summary of findings

This research recommendation relates to shared decision-making, which will be covered by the in-development guideline on shared decision-making.

How can practitioners and patients be supported to improve the quality of prescribing-related consultations and medicines reviews so that they facilitate informed choice and optimal adherence to medicines?

Summary of findings

This research recommendation covers issues that have since been addressed in NICE's guideline on medicines optimisation (NICE guideline NG5).

What are the effects of medicines reviews by healthcare professionals other than the prescriber on patients, prescribers and outcomes? How can the process of medicines review be enhanced or improved to address issues of informed choice and adherence?

Summary of findings

This research recommendation covers issues that have since been addressed in NICE's guideline on medicines optimisation (NICE guideline NG5).

How can we facilitate the open disclosure of medicine-taking behaviours within consultations relating to medicines prescribing and review? How can we equip health practitioners to respond appropriately and effectively?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

What are the effects of non-prescriber medicine reviews (e.g. by pharmacists) on patients, prescribers and outcomes? How can the process of medicine review be enhanced or improved to address issues of informed choice and adherence?

Summary of findings

This research recommendation covers issues that have since been addressed in NICE's guideline on medicines optimisation (NICE guideline NG5).

What are the effects of social disadvantage and ethnicity on informed choice, shared decision-making and adherence to prescribed medicines?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

How do the perceptions and life circumstances of different age groups (children, young adults, elderly people) influence informed choice, shared decision-making and adherence. What are the implications for interventions to support these?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

What are the particular barriers to medicines use for people with multiple pathologies (and their informal carers) and what interventions are required?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Evidence tables

Key to the tables

Type of study: SR = systematic review; SR-C = Cochrane review; SR-HTA = NIHR-funded systematic review (Health Technology Assessment); SR-NMA = systematic review with network meta-analysis; RCT = randomised controlled trial; RCT-NIHR = NIHR-funded randomised controlled trial; CE = cost-effectiveness study.

Studies = the number of studies in a systematic review or the specified analysis from the systematic review.

n = number of participants. The number of participants was not always reported in the abstract.

The outcome adherence means adherence to medicines, unless otherwise specified.

This information and any table-specific footnotes can be found in the last row of each table.

Table 1 Methods of reminding patients to take medicines

Study	Type*	Studies	n	Population	Intervention	Comparator	Outcome	Result
Hui et al. 2017(5)	SR	12		Asthma	Mobile health apps (with education, monitoring, electronic diary, action plans, medication reminders, professional support, decision support)	Unspecified control	Asthma control	Improved with intervention
Pool et al. 2017(6)	RCT		408	Asthma	Online questionnaire on symptoms, medication, and health care service use, with tailored feedback and reminders	Active control of similar structure but focused on preventive medicine for conditions other than asthma	Adherence	No significant effect with intervention
							Asthma control	Improved with intervention
							Health service resource use	No significant effect with intervention
							Number of asthma medicines used	No significant effect with intervention
Johnson et al. 2016(7)	RCT		89	Asthma (adolescents)	Text messaging plus website	Usual care	Adherence	Improved with intervention
							Quality of life	Improved with intervention
							Self-efficacy	Improved with intervention
Normansell et al. 2017(8)	SR-C	6		Asthma (inhaled corticosteroids)	Electronic trackers or reminders	Usual care or other intervention	Adherence	Improved with intervention
		5			Education interventions	Usual care or other intervention	Adherence	Improved with intervention

		3			Simplified regimen	Usual care or other intervention	Adherence	Improved with intervention
		39			Any intervention‡ aimed at increasing adherence	Usual care or other intervention	Asthma control	No significant effect with intervention
		39			Any intervention‡ aimed at increasing adherence	Usual care or other intervention	Exacerbations	No significant effect with intervention
Graetz et al. 2018(9)	RCT		44	Cancer (breast, hormone receptor positive taking aromatase inhibitors)	Internet-based app with reminders	Internet-based app without reminders	Adherence	Improved with intervention
							Use of app	Improved with intervention
Choudhry et al. 2018(10)	RCT		4,078	Cardiometabolic conditions (uncontrolled diabetes, hypertension, or hyperlipidaemia with poor adherence)	Telehealth intervention (text messages, pillboxes, mailed progress reports, motivational interviewing)	Usual care	Adherence	Improved with intervention
							Admission to hospital	No significant effect with intervention
							Disease control rated as good	No significant effect with intervention
							Doctor's appointments	No significant effect with intervention
							Emergency department use	Improved with intervention
Pandey et al. 2017(11)	RCT		34	Cardiovascular disease	Text messaging	Usual care	Adherence	Improved with intervention
Lin et al. 2017(12)	RCT		288	Cardiovascular disease (after coronary artery bypass grafting)	Text messaging, psychoeducation, motivational interviewing	Usual care	Adherence	Improved with intervention
							Blood lipid profile	Improved with intervention
							Mortality (at 18 months)	Improved with intervention
							Quality of life	Improved with intervention
Maslakpak et al. 2016(13)	RCT		123	Cardiovascular disease (antihypertensives)	Text messaging reminders	Reminder cards	Adherence	No significant effect with intervention
					Text messaging reminders or reminder cards	Usual care	Adherence	Improved with intervention
Varleta et al. 2017(14)	RCT		314	Cardiovascular disease (antihypertensives)	Text messaging education on adherence and healthy lifestyle	Usual care	Adherence	Improved with intervention

Morawski et al. 2018(15)	RCT		411	Cardiovascular disease (hypertension, uncontrolled on up to 3 medications)	Mobile health app (reminder alerts, adherence reports, optional peer support)	Usual care	Adherence	Improved with intervention
							Blood pressure (systolic)	No significant effect with intervention
van Driel et al. 2016(16)	SR-C	3	663	Cardiovascular disease (lipid lowering)	Intensive patient care (for example electronic reminders, pharmacist-led interventions, patient education)	Usual care	Adherence	Improved with intervention
		7	11,204	Cardiovascular disease (lipid lowering)	Intensive patient care (for example electronic reminders, pharmacist-led interventions, patient education)	Usual care	Adherence	Improved with intervention
		3	333	Cardiovascular disease (lipid lowering)	Intensive patient care (for example electronic reminders, pharmacist-led interventions, patient education)	Usual care	Cholesterol (low-density lipoprotein [LDL]; short term)	Improved with intervention
		2	127	Cardiovascular disease (lipid lowering)	Intensive patient care (for example electronic reminders, pharmacist-led interventions, patient education)	Usual care	Cholesterol (total)	Improved with intervention
		4	430	Cardiovascular disease (lipid lowering)	Intensive patient care (for example electronic reminders, pharmacist-led interventions, patient education)	Usual care	Cholesterol (total; short term)	Improved with intervention
Kessler et al. 2018(17)	RCT		179	Cardiovascular disease (lipid lowering; with medicine possession lower than 80%)	Alerts on missed doses (emails, text messaging, or automated phone calls)	Usual care	Adherence	Improved with intervention
					Alerts on missed doses (emails, text messaging, or automated phone calls) plus medication adherence partner (social support)	Usual care	Adherence	Improved with intervention
					Medicines adherence partner (social support)	Usual care	Adherence	No significant effect with intervention

Adler et al. 2017(18)	SR-C	6	1,310	Cardiovascular disease (secondary prevention)	Text messaging or multimedia messaging	No intervention or other modes of communication	Adherence	Improved with intervention (meta-analysis not possible because of heterogeneity)
Fuller et al. 2018(19)	SR	17	17,448	Cardiovascular disease (secondary prevention)	Text messaging	Unspecified control	Adherence	Improved with intervention (but statistical data not reported in abstract)
					Fixed-dose combination pill	Unspecified control	Adherence	Improved with intervention
					Community health intervention	Unspecified control	Adherence	Improved with intervention
Chen et al. 2018(20)	RCT		100	Cardiovascular disease (secondary prevention)	Mobile health app (physicians prescribe and record patient information; patients receive text messages or automated voice calls)	Usual care	Adherence	Improved with intervention
							Smoking cessation	Improved with intervention
							Vegetable consumption	Improved with intervention
Buis et al. 2017(21)	RCT		123	Cardiovascular disease (uncontrolled hypertension, Black participants only)	Text messaging	Usual care	Adherence	No significant effect with intervention
							Blood pressure (diastolic)	No significant effect with intervention
							Blood pressure (systolic)	No significant effect with intervention
							Blood pressure (systolic; subgroup with higher levels at baseline)	Improved with intervention
Kimmel et al. 2016(22)	RCT		270	Cardiovascular disease (warfarin)	Daily reminder	Usual care	Time in target international normalised ratio (INR) range	Improved with intervention
					Lottery incentive**	Usual care	Adherence	Improved with intervention
							Anticoagulation	No significant effect with intervention
Broadbent et al. 2018(23)	RCT		60	Chronic obstructive pulmonary disease	Robot assistant (measured physiological data, reminded patients to take medicines,	Usual care	Quality of life	No significant effect with intervention
							Rehabilitation exercise frequency	Improved with intervention

					recorded adherence, provide education, allow patients to report feeling unwell, show health status and adherence over time)		Adherence	Improved with intervention
Adikusuma et al. 2018(24)	RCT		40	Diabetes (type 2)	Text messaging, counselling, pharmacist motivation	Usual care	Adherence	Improved with intervention
							Glycated haemoglobin	Improved with intervention
Sugita et al. 2017(25)	RCT		41	Diabetes (type 2)	Text messaging health education	Text messaging reminders	Adherence	No significant effect with intervention
Feng et al. 2017(26)	RCT			Endoscopic sinus surgery (post-surgical intranasal corticosteroids)	Mobile health app reminders	Usual care	Adherence	Improved with intervention
							Endoscopic scores	No significant effect with intervention
							Sino-nasal outcome	No significant effect with intervention
Al-Aqeel et al. 2017(27)	SR-C	12	1,642	Epilepsy	Behavioural interventions (such as intensive reminders)	Unspecified control	Adherence	Improved with intervention (meta-analysis not possible because of heterogeneity)
Cook et al. 2017(28)	RCT		201	Glaucoma	Telephone reminders	Usual care	Adherence	Improved with intervention
Olives et al. 2016(29)	RCT		2,521	Infection (antibiotics)	Text messaging or voicemail instructions	Usual care	Antibiotic prescriptions filled	No significant effect with intervention
					Text messaging instructions	Voicemail instructions	Antibiotic prescriptions filled	Improved with intervention
Kanters et al. 2017(30)	SR-NMA	85	16,271	Infection (HIV)	Text messaging	Usual care	Adherence	Improved with intervention
Amankwaa et al. 2018(31)	SR	11		Infection (HIV)	Text messaging	Unspecified control	Adherence	Improved with intervention
		20					Adherence	Improved with intervention
		7					Appointment attendance	Improved with intervention
		11					CD4 cell count or viral load	Improved with intervention
	RCT		242	Infection (HIV)	Text messaging and telephone reminders	Usual care	Adherence†	Improved with intervention

Abdulrahman et al. 2017(32)					plus adherence counselling during clinic visits		Adherence	Improved with intervention
							Attending appointments	Improved with intervention
							CD4 cell count	Improved with intervention
							Incidence of tuberculosis	Improved with intervention
							Viral load	Improved with intervention
Ruan et al. 2017(33)	RCT		100	Infection (HIV)	Text messaging	Usual care	Adherence	Improved with intervention
							CD4 cell count	No significant effect with intervention
							Knowledge	Improved with intervention
Linnemayr et al. 2017(34)	RCT		332	Infection (HIV, antiretrovirals and antimicrobial prophylaxis in adolescents and young adults with poor adherence)	Text messaging (2-way)	Usual care	Adherence	No significant effect with intervention
					Text messaging (1-way)	Usual care	Adherence	No significant effect with intervention
Garofalo et al. 2016(35)	RCT		105	Infection (HIV, antiretrovirals in adolescents and young adults with poor adherence)	Text messaging (2-way; tailored)	Usual care	Adherence‡	Improved with intervention
Moore et al. 2018(36)	RCT		75	Infection (HIV, methamphetamine users)	Text message reminders plus medication event monitoring system	Medication event monitoring system	Adherence	No significant effect with intervention
							Methamphetamine use	Improved with intervention
Morillo-Verdugo et al. 2018(37)	RCT		53	Infection (HIV, plus high or very high cardiovascular risk)	Telehealth intervention (adherence monitoring, advice on diet, exercise and smoking cessation, text messaging, motivational interviewing)	Usual care	Adherence	Improved with intervention
							Blood pressure (controlled)	Improved with intervention
							Cardiovascular risk (reduced from high or very high to moderate or low)	Improved with intervention
							Smoking cessation	Improved with intervention

Kempe et al. 2016(38)	RCT		867	Infection (human papillomavirus vaccination)	Preference-based recall for parents or adolescents (text message, email, automatic telephone dialler, or 2 of those methods)	Usual care	Completed vaccination series	Improved with intervention
							Late completion of vaccination series	Improved with intervention
Alipanah et al. 2018(39)	SR	129		Infection (tuberculosis)	Digital interventions (medication monitoring, text message reminders)	Unspecified control	Adherence	Improved with intervention (meta-analysis not possible because of heterogeneity)
							Treatment success	Improved with intervention (meta-analysis not possible because of heterogeneity)
Fang et al. 2017(40)	RCT		350	Infection (tuberculosis)	Text messaging plus education	Usual care (directly observed therapy)	Interrupted treatment	Improved with intervention
							Missing doses	Improved with intervention
							Adherence (treatment completion)	Improved with intervention
Johnston et al. 2018(41)	RCT		358	Infection (tuberculosis, latent, treatment completion)	Text messaging (2-way)	Usual care	Adherence	No significant effect with intervention
Huang et al. 2017(42)	RCT		90	Kidney disease (on haemodialysis with uncontrolled hypertension)	Text messaging	Usual care	Blood pressure (systolic)	No significant effect with intervention
							Health behaviours (adherence, lower salt intake, consistency of home blood pressure monitoring)	Improved with intervention
Kashgary et al. 2017(43)	SR	23		Mixed	Appointment reminders from mobile technologies	Unspecified control	Missed appointments	Improved with intervention
		19			Mobile interventions	Unspecified control	Adherence	Improved with intervention
Dai et al. 2017(44)	RCT		46,581	Mixed	Reminders (to take target medication or to predict 30-day adherence or commit to self-determined level of adherence for	Standard mailings	Adherence (at 3 months)	Improved with intervention
							Adherence (at 6 months)	Improved with intervention

					30 days) plus standard mailings			
Kravitz et al. 2018(45)	RCT		215	Musculoskeletal pain (chronic)	Mobile health intervention (patient reminders, responding to questions about pain and adverse events)	Usual care	Pain interference	No significant effect with intervention
							Shared decision-making	Improved with intervention
Reich et al. 2017(46)	RCT		1,790	Psoriasis (mild to moderate; topical therapy)	Treatment optimisation tool (telephone and email helpdesks, treatment reminders, patient information materials, guidance for dermatologists and nurses)	Usual care	Quality of life (dermatology-related)	No significant effect with intervention
							Response to treatment (physician's global assessment of clear or almost clear)	Improved with intervention
Valimaki et al. 2017(47)	RCT		1,139	Psychosis	Text messaging (tailored for patients to encourage adherence to medicines)	Unspecified control	Costs of treatment to patient	Worse with intervention
							Disability at time of psychiatric hospital admission (reduction)	Improved with intervention
							Duration of stay in psychiatric hospital	No significant effect with intervention
							Readmission to psychiatric hospital	No significant effect with intervention
							Time between psychiatric hospital admissions	No significant effect with intervention
Mary et al. 2018(48)	RCT		96	Rheumatoid arthritis (methotrexate)	Text messaging reminders	Usual care or pharmacist-led counselling	Adherence	Improved with intervention
						Usual care	Patient satisfaction	Improved with intervention
Reese et al. 2017(49)	RCT		120	Transplant recipients (kidney)	Electronic pill bottles with customised reminders (alarms, text messaging, telephone calls, emails) with or without healthcare professional notification	Electronic pill bottle without reminders or healthcare professional notification	Adherence	Improved with intervention
							Blood concentration of tacrolimus	No significant effect with intervention
Foster et al. 2018(50)	RCT		169	Transplant recipients (kidney;	Preference-based reminders (text	Electronic medication	Adherence	Improved with intervention

				adolescent and young adults)	messaging, email, visual cues) plus electronic adherence monitoring, plus 3-monthly coaching with adherence feedback	monitoring plus 3-monthly coaching without adherence feedback	Taking medication on time	Improved with intervention

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†Outcome = adherence rated as good. ‡ Outcome = adherence of 90% or more **No further details on intervention in abstract

Table 2 Mobile and telehealth interventions

Study	Type*	Studies	n	Population	Intervention	Comparator	Outcome	Result
Merchant et al. 2016(51)	RCT		495	Asthma (short-acting beta agonists)	Telemonitoring	Usual care	Asthma control	Improved with intervention
							Days without use of short-acting beta agonists	Improved with intervention
							Doses of short-acting beta agonist (reduction)	Improved with intervention
Kassavou et al. 2018(52)	SR	17		Cardiometabolic conditions	Automated telecommunication interventions	Unspecified control	Adherence	Improved with intervention
Frias et al. 2017(53)	RCT		109	Cardiometabolic conditions (diabetes type 2 plus hypertension)	Digital medicine (adherence monitoring by ingestible sensor, physical activity monitoring, plus mobile health app)	Usual care	Blood pressure (systolic)	Improved with intervention
Crawshaw et al. 2017(54)	SR	23	9,735	Cardiovascular disease (acute coronary syndromes)	Healthcare provider-led interventions** (with telephone contact)	Healthcare provider-led interventions (in-person contact only)	Adherence	Improved with intervention
					Healthcare provider-led interventions**	Unspecified control	Adherence	Improved with intervention
Desteghe et al. 2018(55)	RCT		48	Cardiovascular disease (atrial fibrillation)	Telemonitoring	Observation	Adherence	Improved with intervention
					Telemonitoring with immediate feedback on medication intake errors	Observation	Adherence	Improved with intervention
Guo et al. 2017(56)	RCT		113	Cardiovascular disease (atrial fibrillation)	Mobile health intervention (educational materials, decision support tools, self-care protocols, structured follow-up)	Usual care	Adherence	Improved with intervention
							Anxiety	Improved with intervention
							Depression	Improved with intervention
							Patient satisfaction (with anticoagulation)	Improved with intervention
							Quality of life	Improved with intervention

Gallagher et al. 2017(57)	RCT		40	Cardiovascular disease (heart failure, admitted to hospital)	Telemonitoring of adherence with telephone support	Passive adherence monitoring	Adherence	No significant effect with intervention
				Cardiovascular disease (heart failure, admitted to hospital)	Electronic adherence with telephone support	Passive adherence monitoring	Readmission to hospital	No significant effect with intervention
Duan et al. 2017(58)	SR	46	13,875	Cardiovascular disease (hypertension)	Telemonitoring	Unspecified control	Blood pressure (controlled)	Improved with intervention
							Blood pressure (diastolic)	Improved with intervention
							Blood pressure (systolic)	Improved with intervention
Palmer et al. 2018(59)	SR-C	4	2,429	Cardiovascular disease (primary prevention)	Mobile phone interventions aiming to improve adherence	Usual care or interevention without mobile phone component	Blood pressure	Improved with intervention (meta-analysis not possible because of heterogeneity)
							Cholesterol levels	Improved with intervention (meta-analysis not possible because of heterogeneity)
Salisbury et al. 2017(60)	RCT-NIHR		641	Cardiovascular disease (primary prevention)	Telehealth service (telephone calls from health information advisers encouraging behaviour change and use of online resources)	Usual care	Response to treatment	No significant effect with intervention
Salisbury et al. 2016a(61)	RCT		641	Cardiovascular disease (primary prevention)	Telephone calls from trained lay health advisers (promote online resources for risk reduction, optimising medicines)	Usual care	Blood pressure (diastolic)	Improved with intervention
							Blood pressure (systolic)	Improved with intervention
							BMI	No significant effect with intervention
							Cardiovascular risk (reduction)	No significant effect with intervention
							Cholesterol	No significant effect with intervention
							Weight	Improved with intervention

Dixon et al. 2016(62)	CE		641	Cardiovascular disease (primary prevention)	Telephone calls from trained lay health advisers (promote online resources for risk reduction, optimising medicines)	Usual care	Cost-effectiveness	Intervention was cost effective (ICER=£10,859)
Kraft et al. 2017(63)	SR	1		Cardiovascular disease (secondary prevention of stroke or transient ischaemic attack)	Telehealth intervention	Usual care	Adherence	No significant effect with intervention
		4			Telehealth intervention	Usual care	Blood pressure	Improved with intervention
		1			Telehealth intervention	Usual care	Mortality	Worse with intervention
Gandhi et al. 2017(64)	SR	27	5,165	Cardiovascular disease (secondary prevention)	Mobile health technology (unspecified)	Usual care	Adherence	Improved with intervention
							Admission to hospital	No significant effect with intervention
							Angina	Improved with intervention
							Blood pressure	Improved with intervention
							Exercise goals	No significant effect with intervention
							Mortality	No significant effect with intervention
							Recurrent stroke or transient ischaemic attack	Improved with intervention
							Smoking cessation	No significant effect with intervention
Santo et al. 2018(65)	RCT		163	Cardiovascular disease (secondary prevention)	Mobile health app (interactive customisable)	Mobile health app (basic)	Adherence	No significant effect with intervention
					Mobile health app (basic app or interactive customisable app)	Usual care	Adherence	Improved with intervention
							Blood pressure	No significant effect with intervention
							Cholesterol	No significant effect with intervention
Salisbury et al. 2017(60)	RCT-NIHR		609	Depression	Telehealth service (telephone calls from health information advisers encouraging	Usual care	Response to treatment	Improved with intervention

					behaviour change and use of online resources)			
Salisbury et al. 2016b(66)	RCT		609	Depression	Telephone calls from trained lay health advisers (assessment and goal setting, promoting online resources including cCBT, optimising medicines)	Usual care	Anxiety	Improved with intervention
							Patient health	Improved with intervention
							Patient satisfaction (with access to services)	Improved with intervention
							Patient satisfaction (with support)	Improved with intervention
							Self-management and health literacy	Improved with intervention
Miremberg et al. 2018(67)	RCT		120	Diabetes (gestational)	Mobile health app (feedback on adherence and blood glucose control)	Unspecified control	Adherence	Improved with intervention
							Blood glucose	Improved with intervention
							Insulin treatment needed	Improved with intervention
							Neonatal complications	No significant effect with intervention
Grady et al. 2017(68)	RCT		137	Diabetes (type 1 or 2, uncontrolled)	Mobile health app plus blood glucose meter	Blood glucose meter	Glycated haemoglobin	No significant effect with intervention
Viana et al. 2016(69)	SR	6	494	Diabetes (type 1)	Telemonitoring	Unspecified control	Glycated haemoglobin†	No significant effect with intervention
Di Bartolo et al. 2017(70)	RCT		182	Diabetes (type 1, adolescents and young adults)	Telemonitoring of glucose control	Usual care	Glycated haemoglobin	No significant effect with intervention
							Self-monitoring of blood glucose	No significant effect with intervention
Kim et al. 2018(71)	SR	38	6,855	Diabetes (type 2)	Telemonitoring	Unspecified control	Blood pressure (systolic)	Improved with intervention
							Glycated haemoglobin (controlled)	Improved with intervention
Wild et al. 2016(72)	RCT		321	Diabetes (type 2, uncontrolled)	Telemonitoring (online recording of blood glucose measurements with	Usual care	Adherence	No significant effect with intervention
							Blood pressure (diastolic)	Improved with intervention

					general practitioner review)		Blood pressure (systolic)	Improved with intervention
							Frequency of telephone contact with practice nurses (increase)	Improved with intervention
							Glycated haemoglobin	Improved with intervention
							Health service use (other than telephone calls with practice nurses)	No significant effect with intervention
							Quality of life	No significant effect with intervention
							Weight	No significant effect with intervention
Kleinman et al. 2017(73)	RCT		91	Diabetes (type 2; uncontrolled)	Mobile health app	Usual care	Adherence	Improved with intervention
							Blood glucose testing frequency	Improved with intervention
Muller et al. 2017(74)	RCT		402	Headache (non-acute)	Telemonitoring	Usual care	Adherence	No significant effect with intervention
							Health service use (headache-related)	Improved with intervention
							Patient (satisfaction with treatment)	No significant effect with intervention
Himelhoch et al. 2017(75)	RCT		28	HIV (antiretrovirals in people with history of substance use)	Mobile health intervention	Usual care (directly observed therapy plus adherence counselling)	Adherence	No significant effect with intervention
Daher et al. 2017(76)	SR	99		Infection (sexually transmitted, including HIV)	Mobile health intervention or internet health intervention	Unspecified control	Clinic attendance	Improved with intervention
							Adherence	Improved with intervention
Posadzki et al. 2016(77)	SR-C	25		Mixed	Automated telephone communication systems	Control or other type of automated telephone communication system	Adherence	Improved with intervention
							Clinical outcomes	Little or no effect with intervention††
	RCT		158	Parkinson's disease	Mobile health app	Usual care	Adherence	Improved with intervention

Lakshminaraya ana et al. 2017(78)							Motor symptoms (change from baseline)	No significant effect with intervention
							Patients' perception of quality of consultation with doctor	Improved with intervention
Cingi et al. 2015(79)	RCT		327	Respiratory (asthma or allergic rhinitis)	Mobile health app	Unspecified control	Asthma control	Improved with intervention
							Quality of life (rhinitis-related)	Improved with intervention
Beebe et al. 2017(80)	RCT		105	Schizophrenia	Telehealth intervention (weekly problem solving telephone call)	Usual care	Antipsychotic levels in therapeutic range	Improved with intervention
							Adherence	No significant effect with intervention
							Adherence	No significant effect with intervention
McClure et al. 2016(81)	RCT		66	Smokers taking varenicline	Mobile health app with tailored advice plus standard self-help materials	Mobile health app with standard self-help materials	Adherence	No significant effect with intervention
							Smoking cessation	No significant effect with intervention
							Stopping varenicline	No significant effect with intervention
DeVito Dabbs et al. 2016(82)	RCT		201	Transplant recipients (lung)	Mobile health intervention‡	Usual care	Adherence	Improved with intervention
							Mortality	No significant effect with intervention
							Readmission to hospital	No significant effect with intervention
							Reporting abnormal health indicators	Improved with intervention
							Self-monitoring	Improved with intervention

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The outcome adherence means adherence to medicines, unless otherwise specified.

† Glycated haemoglobin was considered an indirect measure of adherence. ‡ Outcome = adherence of 90% or more **No further details on intervention in abstract. ††Meta-analysis not possible because of heterogeneity.

Table 3 Other interventions aiming to improve adherence

Study	Type*	Studies	n	Population	Intervention	Comparator	Outcome	Result
Myhill et al. 2017(83)	RCT		97	Acne (mild to moderate, taking adapalene plus benzoyl peroxide)	Education (video, information card, internet-based information)	Usual care or usual care plus additional clinic visits	Adherence	Improved with intervention
Priebe et al. 2016(84)	RCT-NIHR		131	Antipsychotics (long-term injectables)	Payment (£15)	Usual care	Adherence	Improved with intervention
							Adherence†	Improved with intervention
							Quality of life	Improved with intervention
Kew et al. 2016(85)	SR-C	1	23	Asthma	Cognitive behavioural therapy	Usual care	Adherence	No significant effect with intervention
		3	95				Asthma control	Improved with intervention
		6	214				Quality of life	Improved with intervention
Julious et al. 2016(86)	RCT-NIHR		12,179	Asthma (parents of children with asthma)	GP letter before end of school summer holidays	Usual care	Health service resource use (unscheduled)	No significant effect with intervention
							Prescriptions collected	Improved with intervention
							Scheduled health care use	Improved with intervention
Lobban et al. 2017(87)	RCT		96	Bipolar disorder	Online relapse prevention intervention	Usual care	Adherence	No significant effect with intervention
							Monitoring of early warning signs of depressive relapse	Improved with intervention
							Monitoring of early warning signs of hypomania relapse	Improved with intervention
							Positive perceptions of bipolar disorder	Improved with intervention

Al AlShaikh et al. 2016(88)	SR	17		Cardiovascular (stroke secondary prevention, antithrombotics)	Interventions aiming to improve adherence	Unspecified control	Adherence	Improved with intervention
				Cardiovascular (stroke secondary prevention, individual drug classes)			Adherence	Improved with intervention
				Cardiovascular (stroke secondary prevention, lipid lowering)			Adherence	Improved with intervention
				Cardiovascular (stroke secondary prevention, overall regimen)			Adherence	No significant effect with intervention
Reddy et al. 2017(89)	RCT		126	Cardiovascular disease (lipid lowering; veterans with poor adherence)	Electronic adherence monitoring with alarms and feedback	Electronic adherence monitoring without alarms or feedback	Adherence	Improved with intervention (at 3 months)
				Cardiovascular disease (lipid lowering; veterans with poor adherence)	Electronic adherence monitoring with alarms and feedback	Electronic adherence monitoring without alarms or feedback	Adherence	No significant effect with intervention (at 6 months, 3 months after intervention ended)
				Cardiovascular disease (lipid lowering; veterans with poor adherence)	Electronic adherence monitoring with alarms and feedback plus medication adherence partner (social support)	Electronic adherence monitoring without alarms or feedback	Adherence	Improved with intervention (at 3 months)
				Cardiovascular disease (lipid lowering; veterans with poor adherence)	Electronic adherence monitoring with alarms and feedback plus medication adherence partner (social support)	Electronic adherence monitoring without alarms or feedback	Adherence	No significant effect with intervention (at 6 months, 3 months after intervention ended)
Bahiru et al. 2017(90)	SR-C	4	3,835	Cardiovascular disease (primary and secondary prevention)	Fixed-dose combination therapy (at least 1 blood-pressure lowering drug and at least 1 lipid lowering drug)	Usual care, placebo, or active drug comparator	Adherence	Improved with intervention
		11	6,906				Adverse events	Improved with intervention
		13	7,638				Blood pressure (systolic)	Improved with intervention

		6	4,517				Cardiovascular events	No significant effect with intervention
		12	7,153				Cholesterol (LDL)	Improved with intervention
		11	6,565				Cholesterol (total)	Improved with intervention
		5	5,300				Mortality	No significant effect with intervention
Volpp et al. 2017(91)	RCT		1,509	Cardiovascular disease (secondary prevention with at least 2 of: statins, aspirin, beta blocker, antiplatelet agent)	Electronic pill bottle, lottery incentives, social support	Usual care	Adherence	No significant effect with intervention
							Admission to hospital (time to first)	No significant effect with intervention
							Admission to hospital with vascular event or death	No significant effect with intervention
							Admissions to hospital	No significant effect with intervention
							Costs	No significant effect with intervention
Viana et al. 2016(69)	SR	5	349	Diabetes (type 1)	Educational interventions	Unspecified control	Glycated haemoglobin‡	No significant effect with intervention
		7	818		Psychological intervention	Unspecified control	Glycated haemoglobin‡	Improved with intervention
Kim et al. 2016(92)	RCT		182	Diabetes (type 2)	Internet-based glucose monitoring	Usual care	Glycated haemoglobin (at 3 months)	Improved with intervention
							Glycated haemoglobin (at 6 months)	Improved with intervention
Hansen et al. 2017(93)	RCT		165	Diabetes (type 2; uncontrolled)	Video consultation plus online recording of blood glucose, blood pressure and weight	Usual care	Glycated haemoglobin	Improved with intervention
Al-Aqeel et al. 2017(27)	SR-C	12	1,642	Epilepsy	Education and counselling	Unspecified control	Adherence	Mixed success of intervention

								(meta-analysis not possible because of heterogeneity)
					Mixed interventions		Adherence	Improved with intervention (meta-analysis not possible because of heterogeneity)
Cook et al. 2017(28)	RCT		201	Glaucoma	Motivational interviewing	Usual care	Adherence	No significant effect with intervention
						Usual care	Patient satisfaction	Improved with intervention
Kanters et al. 2017(30)	SR-NMA	85	16,271	Infection (HIV)	'Supporter' intervention	Usual care	Viral load	Improved with intervention
					Cognitive behavioural therapy		Viral load	Improved with intervention
Bogart et al. 2017(94)	RCT		215	Infection (HIV, antiretrovirals in Black men)	Electronic adherence monitoring plus culturally adapted counselling	Electronic adherence monitoring	Adherence	Improved with intervention
Kempe et al. 2016(38)	RCT		867	Infection (human papillomavirus vaccination)	Email or phone recall	Other methods of recall	Completed vaccination series	Improved with intervention
					Recall for adolescents	No recall for adolescents		No significant effect with intervention
Alipanah et al. 2018(39)	SR	129		Infection (tuberculosis)	Directly observed therapy (by healthcare professional)	Directly observed therapy (by family member)	Adherence	Improved with intervention
					Directly observed therapy in the community	Directly observed therapy in the clinic	Loss to follow-up	Improved with intervention
							Sputum smear conversion	Improved with intervention
							Treatment success	Improved with intervention
					Directly observed therapy	Self-administered therapy	Adherence	Improved with intervention
							Antibiotic resistance	Improved with intervention

							Sputum smear conversion	Improved with intervention
							Treatment success	Improved with intervention
Miani et al. 2017(95)	SR-HTA	6		Mixed	Short-term prescription (28 days)	Longer-term prescriptions (more than 28 days)	Adherence	Worse with intervention
							Costs (driven by prescriber time)	Worse with intervention
Weeks et al. 2016(96)	SR-C	4	700	Mixed	Non-medical prescribing	Medical prescribing	Adherence	Improved with intervention
Zaugg et al. 2018(97)	SR-C	7	22,924	Mixed	Giving feedback about patients' adherence to physicians	Usual care	Adherence	Little or no effect with intervention
		2	4,181				Health service resource use	Little or no effect with intervention (meta-analysis not possible because of heterogeneity)
		2	1,292				Patient outcomes	Little or no effect with intervention (meta-analysis not possible because of heterogeneity)
Tsoli et al. 2018(98)	SR	15		Mixed	Interactive voice response phone systems	Unspecified control	Adherence	Improved with intervention
Choudhry et al. 2017(99)	RCT		53,480	Mixed (up to 3 medicines for chronic diseases with medication possession of 30–80%)	Digital timer pill bottle cap	Usual care	Adherence	No significant effect with intervention
					Pill bottle strip with toggles	Usual care	Adherence	No significant effect with intervention
					Pill box	Usual care	Adherence	No significant effect with intervention
					Pill box	Pill bottle strip with toggles	Adherence	Improved with intervention
Danila et al. 2018(100)	RCT		2,684	Osteoporosis	Video intervention (tailored)	Usual care	Adherence	No significant effect with intervention

				Osteoporosis			Attendance for bone-mineral density testing	No significant effect with intervention
				Osteoporosis (calcium supplementation)			Adherence	No significant effect with intervention
				Osteoporosis (vitamin D supplementation)			Adherence	No significant effect with intervention
Alinia et al. 2017(101)	RCT		40	Psoriasis (topical therapy)	Internet-based intervention	Usual care	Adherence	Improved with intervention
							Psoriasis area and severity index (at 3 months)	Improved with intervention
							Psoriasis area and severity index (at 3 months)	Improved with intervention
El Miedany et al. 2016(102)	RCT		211	Rheumatoid arthritis	Electronic patient-reported outcome measures	Paper-based patient-reported outcomes measures	Adherence	Improved with intervention
							Arthritis disease activity	No significant effect with intervention
							Stopping medication	Improved with intervention
El Miedany et al. 2017(103)	RCT		147	Systemic lupus erythematosus	Electronic patient-reported outcome measures	Usual care (clinic assessments)	Adherence	Improved with intervention
Dobbels et al. 2017(104)	RCT		205	Transplant recipients (heart, liver, lung; taking tacrolimus)	Electronic adherence monitoring with feedback, motivational interviewing	Electronic adherence monitoring plus usual care	Adherence	Improved with intervention
							Event-free survival	No significant effect with intervention

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