NICE Medicines and prescribing centre

Medicines optimisation

Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes

Clinical Guideline

Methods, evidence and recommendations

October 2014

Commissioned by the National Institute for Health and Care Excellence

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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1 Introduction

1.1 Introduction

Getting the most from medicines for both patients and the NHS is becoming increasingly important as more people are taking more medicines. Medicines prevent, treat or manage many illnesses or conditions and are the most common intervention in healthcare. However, it has been estimated that between 30% and 50% of medicines prescribed for long-term conditions are not taken as intended (World Health Organisation 2003). This issue is exacerbated by the growing number of people with long-term conditions. In 2012, the Department of Health published a report Long term conditions compendium of Information: third edition (2012), which suggested that about 15 million people in England now have a long-term condition and the number of long-term conditions a person may have also increases with age: 14% of people aged under 40 years and 58% of people aged 60 years and over report having a long-term condition. The report defines a long-term condition as 'a condition that cannot, at present, be cured but is controlled by medication and/or other treatment/therapies'. When one or more non-curable long-term conditions are diagnosed, this is termed 'multimorbidity'. The number of people with multimorbidity in 2008 was 1.9 million, but this is expected to rise to 2.9 million by 2018. Twenty-five per cent of people aged over 60 years report having 2 or more long-term conditions.

Data from the Health and Social Care Information Centre (HSCIC) shows that over the last decade the average number of prescription items per year for any one person in England received increased from 13 (in 2003) to 19 (in 2013). The figures for Wales show an increase from 17 (in 2003) to 25 (in 2013). When a patient is taking multiple medicines this is called 'polypharmacy', a term that has been used in health for many years. With an ageing population, polypharmacy has become even more important to consider when making clinical decisions for individual patients.

In 2013, The King's Fund published Polypharmacy and medicines optimisation – making it safe and sound. This paper outlined the historic view that polypharmacy was something to avoid, but proposed an alternative approach to the concept of polypharmacy: that it may have positive (appropriate) or negative (problematic) potential. Reducing the number of medicines a patient is taking may not be the only factor to consider when reviewing polypharmacy.

Table 1 The King's fund definitions of polypharmacy

Appropriate polypharmacy
'Prescribing for an individual for complex conditions or for multiple conditions in circumstances where medicines use has been optimised and where the medicines are prescribed according to best evidence.'
Problematic polypharmacy
'the prescribing of multiple [medicines] inappropriately, or where the intended benefit of the [medicines are] not realised.'

As the population ages and life expectancy increases, more patients are living with several long-term conditions that are being managed with a growing number of medicines. Maintaining this careful balance gets more difficult for patients and health professionals, particularly when also trying to reduce health inequalities of the population.

Optimising a patient's medicines is important to ensure a patient is taking their medicines as intended and can support the management of long-term conditions, multimorbidities and polypharmacy. Medicines optimisation aims to ensure a person-centred approach to safe and effective medicines use, enabling people to obtain the best possible outcomes from their medicines. Shared decision-making is an essential part of evidence-based medicine, seeking

to use the best available evidence to guide decisions about the care of the individual patient, taking into account their needs, preferences and values (Greenhalgh et al. 2014; Sackett et al. 1996).

An important part of shared decision-making is about health professionals understanding the patient's desired level of involvement in decision-making about their medicines. When having these discussions it is often difficult for the patient and the health professional to decide whether the medicines being taken are appropriate and this decision may be different for each individual patient.

Involving patients in decisions about their care and treatment is not a new concept. Over several years the UK government has supported an approach to change how the NHS engages with patients. Equality and excellence: liberating the NHS (2010) outlined the government's vision of putting the public and patients first through shared decision-making. This White paper stressed that this would only happen by 'involving patients fully in their own care, with decisions made in partnership with clinicians, rather than clinicians alone' and would be implemented by making shared decision-making the 'norm'. Subsequent to the government's White paper, the King's Fund published Making shared decision-making a reality: no decision about me without me (2011), which aimed to outline the skills and resources required by health professionals to use shared decision-making, and suggested tools that may help patients in decision-making when implementing this principle throughout the NHS.

Patient experience in adult NHS services (NICE clinical guideline 138, 2012) provides recommendations aiming to improve the experience of care for people using adult NHS services to create sustainable changes that aim to move the NHS towards a truly patient-centred service. In relation to medicines, Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence (NICE clinical guideline 76, 2009) recommends that all patients have the opportunity to be involved in decisions about their medicines at the level they wish, through shared decision-making. Furthermore, Good practice in prescribing and managing medicines and devices (2013) published by the General Medical Council also emphasises the need to take account of the patient's needs, wishes and preferences.

The safety of medicines is another important consideration when optimising medicines and can be a continual challenge. However, effective systems and processes can minimise the risk of preventable medicines-related problems such as side effects, adverse effects or interactions with other medicines or comorbidities. The risk of patients suffering harm from their medicines increases with polypharmacy.

The Francis Report (2013) emphasised the need to put patients first at all times, and that they must be protected from avoidable harm. In addition, the Berwick report (2013) recommended 4 guiding principles for improving patient safety, including:

- placing the quality and safety of patient care above all other aims for the NHS

- engaging, empowering, and hearing patients and carers throughout the entire system, and at all times.

Adverse events of medicines represent a considerable burden on the NHS and have a significant impact on patients. Approximately 5% to 8% of all hospital admissions are due to preventable adverse events of medicines. When patients transfer between different care providers, such as at the time of hospital admission or discharge, there is a greater risk of poor communication and unintended changes to medicines. When patients move from one care setting to another, between 30% and 70% of patients have an error or unintentional change to their medicines.

Patient safety and medicines is not a new issue and several national initiatives exist to help improve patient safety. In 1964, the Medicines and Healthcare products Regulatory Agency (MHRA) and Commission on Human Medicines launched the national yellow card scheme for reporting side effects to medicines. The scheme is still in existence today and over 600,000 UK yellow cards have been received in that time.

The National Reporting and Learning System (NRLS) was introduced in 2010 by the National Patient Safety Agency (NPSA) as a single, national reporting system for patient safety incidents in England and Wales. The NRLS staff reviewed all alerts to help NHS organisations understand patient safety incidents and why and how they happened, learning from these experiences and taking action to prevent future harm to patients. In June 2012, the key functions and expertise for patient safety developed by the NPSA transferred to NHS England.

In 2014, NHS England and the MHRA issued a joint alert 'Patient safety alert improving medication error reporting and learning'. The alerts aim to improve the quality of data reported by providers and introduce national networks to maximise learning and provide guidance on minimising harm relating to medication error reporting. NHS England also launched at this time a new National Patient Safety Alerting System (NPSAS) to strengthen the rapid dissemination of urgent patient safety alerts to healthcare providers via the Central Alerting System (CAS). The new system is a three-stage system to provide 'useful educational and implementation resources to support providers to put appropriate measures in place to prevent harm and encourage and share best practice in patient safety'.

To further support the patient safety agenda, the NHS Safety Thermometer was introduced by the Department of Health as a measurement tool to support an additional programme of work aimed at supporting patient safety and improvement. The tool is accessible to organisations across all healthcare settings, such as hospitals, care homes and community nursing, and allows them to measure, monitor and analyse patient harms and harm-free care at a local level to assess improvement over time.

Medicines use can be complex and how patients can take their medicines safely and effectively has been a challenge for the health service for many years. Liberating the NHS (2010) emphasised the need to improve the outcomes of healthcare for all, to deliver care that is safer, more effective and provides a better experience for patients. Furthermore, the focus of health and social care to become a more integrated service, with person-centred care, has been made a priority after the Health and Social Care Act was passed in 2012. The Act aims to modernise the NHS, putting clinicians at the centre of commissioning and empowering patients. The NHS Constitution – the NHS belongs to us all (2013) outlined the values and principles of the NHS in England and gave people the right to be involved in discussions and decisions about their health and care, and to be given information to enable them to do this. Patients with capacity have the right make an informed decision and can refuse to take their medicines.

In the past, the term 'medicines management' had been defined as 'a system of processes and behaviours that determines how medicines are used by the NHS and patients' (National prescribing centre 2002). Medicines management has primarily been led by pharmacy teams. Medicines management is an important enabler of medicines optimisation. The definition of 'optimise' is to 'make the best or most effective use of (a situation or resource)'. Medicines optimisation focuses on actions taken by all health and social care practitioners and requires greater patient engagement and professional collaboration across health and social care settings.

The Royal Pharmaceutical Society produced a guide Medicines optimisation: helping patients make the most of medicines (2013) to support the medicines optimisation agenda. This guide suggests 4 guiding principles for medicines optimisation, aiming to lead to improved patient outcomes:

- 'Aim to understand the patient's experience
- Evidence based choice of medicines
- Ensure medicines use is as safe as possible
- Make medicines optimisation part of routine practice'.

To further support the implementation of the guiding principles, NHS England launched the prototype medicines optimisation dashboard (2014). The dashboard aims to 'encourage [Clinical Commissioning Groups] CCGs and trusts to think more about how well their patients are supported to use medicines and less about focusing on cost and volume of drugs'. Supporting information outlines the purpose of the dashboard.

Striving towards a person-centred service through joint working across health and social care achieves the best possible outcomes for the patient. This incorporates a patient's values and preferences and minimises harm, supporting effective medicines optimisation. This guideline reviews the evidence available to support health and social care practitioners, and health and social care organisations, in considering the systems and processes required to ensure safe and effective medicines optimisation.

For the purpose of this guideline, when the term 'organisations' is used, this includes all commissioners and providers, unless specified otherwise in the text. Commissioners are those individuals who undertake commissioning, which is 'the process used by health services and local authorities to: identify the need for local services; assess this need against the services and resources available from public, private and voluntary organisations; decide priorities; and set up contracts and service agreements to buy services. As part of the commissioning process, services are regularly evaluated'. Providers are organisations that directly provide health or social care services.

1.2 Patient-centred care

This guideline offers best practice advice on the care of all people who are taking medicines.

Patients and health professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their health professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have capacity to make decisions, health professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards.

NICE has produced guidance on the components of good patient experience in adult NHS services. All health professionals should follow the recommendations in Patient experience in adult NHS services. In addition, all health and social care practitioners working with people using adult NHS mental health services should follow the recommendations in Service user experience in adult mental health. Also if a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's Transition: getting it right for young people. Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people and diagnosis and management should be reviewed throughout the transition process. There should be clarity about who is the lead clinician to ensure continuity of care.

1.3 Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care').

1.3.1 Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

1.3.2 Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that an intervention will not be of benefit for most patients.

1.3.3 Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

2 Development of a NICE clinical guideline

2.1 What is a NICE guideline

NICE guidelines make evidence-based recommendations on a wide range of topics, from preventing and managing specific conditions, improving health and managing medicines in different settings, to providing social care to adults and children, and planning broader services and interventions to improve the health of communities.

NICE guidelines cover health and care in England and use the best available evidence; they involve people affected by the guideline and advance equality of opportunity for people who share characteristics protected under the Equality Act (2010).

In addition to the recommendations, guidelines also summarise the evidence behind the recommendations and explain how the recommendations were derived from the evidence. Many guideline recommendations are for individual health and social care practitioners, who should use them in their work in conjunction with judgement and discussion with people using services. Some recommendations are for local authorities, commissioners and managers, and cover planning, commissioning and improving services. Healthcare professionals should take NICE guidance fully into account when exercising their clinical judgement, but it does not override their responsibility to make decisions appropriate to the circumstances and wishes of the individual patient. The reasons for any differences should be documented.

Predetermined and systematic methods are used to identify and evaluate the evidence relating to specific review questions.

The guidelines are produced using the following steps:
- the guideline topic is referred to NICE from the Department of Health
- stakeholders register an interest in the guideline and are consulted throughout the development process
- the NICE medicines and prescribing centre prepares the scope (stakeholders can comment on the draft at a scoping workshop and through a 4 week consultation)
- the NICE medicines and prescribing centre establishes a Guideline Development Group (GDG) (through a formal application and selection process)
- a draft guideline is produced after the GDG assesses the available evidence and makes recommendations
- there is a consultation on the draft guideline (the full version and the NICE version)
- the final guideline is published.

The NICE medicines and prescribing centre and NICE produce a number of different versions of this guideline the:
- 'full guideline' contains all the recommendations, plus details of the methods used and the underpinning evidence
- 'NICE guideline' lists the recommendations
- 'information for the public' is written using suitable language for people without specialist medical knowledge
- NICE Pathways brings together all related NICE guidance.

This version is the full version. The other versions can be downloaded from NICE at
www.nice.org.uk.

2.2 Remit

NICE received the remit for this guideline from the Department of Health. NICE
commissioned the NICE medicines and prescribing centre to produce the guideline.

2.3 Who developed the guideline

A multidisciplinary Guideline Development Group (GDG) comprising health professionals and
lay members developed this guideline (see the start of the document for the list of Guideline
Development Group members and acknowledgements).

The National Institute for Health and Care Excellence (NICE) supported the development of
this guideline. The GDG was convened by the NICE medicines and prescribing centre and
was chaired by Dr Weeliat Chong in accordance with guidance from NICE.

The group met regularly during the development of the guideline. At the start of the guideline
development process all GDG members declared interests including consultancies, fee-paid
work, share-holdings, fellowships and support from the healthcare industry. At all subsequent
GDG meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their
declared interest made it appropriate. The details of declared interests and the actions taken
are shown in appendix A.

Staff from the NICE medicines and prescribing centre provided methodological support and
guidance for the development process. The team working on the guideline included an
assistant project manager, systematic reviewers (senior advisers), health economists,
information scientists and a project lead. They undertook systematic searches of the
literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis
where appropriate and drafted the guideline in collaboration with the GDG.

2.4 What this guideline covers

The guideline covers all populations:
- All children, young people and adults using medicines.[1]
- All children, young people and adults who are receiving sub-optimal benefit from
  medicines, for example, not receiving a medicine when they should or could benefit from
  medicines.
- All practitioners who prescribe, supply and/or administer medicines.

The guideline covers all settings:
- All publicly-funded health and social care commissioned or provided by NHS
  organisations, local authorities (in England), independent organisations or independent
  contractors.
- The guideline will be relevant to health and social care practitioners, and organisations
  commissioning or providing health and/or social care for children, young people and
  adults that involves medicines use.

For further details please refer to the scope in appendix B and review questions in appendix
C.2.

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[1] The term 'medicines' covers all healthcare treatments, such as oral medicines, topical medicines, inhaled
products, injections, wound care products, appliances and vaccines.

2.5 What this guideline does not cover

This guideline does not exclude any populations or settings.

The guideline does not cover: specific clinical conditions or named medicines, although on occasion the evidence identified to answer a review question was included a patient population who may have had a specific clinical condition for example, patients with asthma or hypertension.

Patient consent and patient and service user experience are not covered although the content of these guidelines were noted in the development of the medicines optimisation guideline.

Patient education and public information campaigns were not covered.

Specific systems and processes of medicines optimisation were excluded from the scope including:
- shared care arrangements for medicines
- repeat dispensing and repeat prescribing systems
- access to medicines
- medicines shortages
- prescription charges
- waste medicines
- education and training of health and social care practitioners.

Medicines adherence was not covered in this guideline as there is already a NICE guideline on Medicines adherence. However, the outcome of medicines adherence was reported in response to the interventions in the review question.

Relationships between the guideline and other NICE guidance

2.6 Related NICE guidance

Medicines optimisation incorporates other NICE guidance, particularly condition specific guidelines. For this reason all related condition specific guidance is not included in this section, however related guidance will be linked to within the NICE pathway.

2.6.1 Published NICE guidance

NICE guidelines
- Medicines adherence. NICE clinical guideline 76 (2009).
- Service user experience in adult mental health. NICE clinical guideline 136 (2011).
- Developing and updating local formularies. NICE medicines practice guidelines 1 (2012).
- Patient experience in adult NHS services. NICE clinical guideline 138 (2012).
- Patient Group Directions. NICE medicines practice guideline 2 (2013).
- Managing medicines in care homes. NICE social care guideline 1 (2014).
- Drug allergy. NICE clinical guideline 183 (2014).
- Atrial fibrillation and heart valve disease: self-monitoring coagulation status using point-of-care coagulometers (the CoaguChek XS system and the INRatio2PT/INR monitor). NICE diagnostics guidance (2014).

Patient safety guidance

- [Technical patient safety solutions for medicines reconciliation on admission of adults to hospital. NICE patient safety guidance 1 (2007).](#)

2.6.2 NICE guidance in development

NICE is currently developing the following related guidance (details available from the NICE website):

- [Social care of older people with multiple long-term conditions](#). Publication expected October 2015.
- [Transition between inpatient hospital settings and community or care home settings for adults with social care needs](#). Publication expected November 2015.
- [The safe use and management of controlled drugs.](#) NICE medicines practice guideline. Publication expected March 2016.
- [Multimorbidities: system integration to meet population needs](#). Publication expected TBC.
- [Multimorbidity: clinical assessment and management.](#) Publication expected September 2016.

3 Methods

This chapter sets out in detail the methods used to review the evidence and to generate the recommendations that are presented in subsequent chapters. This guideline was developed in accordance with the methods outlined in the NICE guidelines manual 2012.

At the start of guideline development, the key issues listed in the scope were translated into review questions. Each review question in this guideline is presented in a separate section that includes:

- An 'evidence review'
    - o Summary of included studies
    - o Analysis of randomised controlled trials (RCTs)
    - o Analysis of observational studies (section 5 only)
    - o Key themes matrix (section 5 only)
- Health economic evidence
- Evidence statements
- Evidence to recommendations
- Recommendations and research recommendations

Additional information is provided in the appendices for each review question, including:

- Evidence tables
- GRADE profiles
- Forest plots
- Full health economic report

3.1 Developing the review questions and outcomes

3.1.1 Review questions

Review questions were developed in a PICO (patient, intervention, comparison and outcome) format and intervention reviews were carried out. For each review question a review protocol was developed. The review protocols then informed the literature search strategy for each review question. The methods used are detailed fully in the NICE guidelines manual 2012 section 4.3.

During the scoping phase 9 review questions were identified. These were all questions to identify the effectiveness and cost-effectiveness of interventions. In line with the NICE guidelines manual 2012 section 4.3, review questions relating to interventions are usually best answered by RCTs, because this is most likely to give an unbiased estimate of the effects of an intervention.

The GDG discussed the draft review questions at GDG meetings and agreed that minor changes were needed to several outlined in the final scope document; see table 2.

Table 2 Summary of changes made to review questions from the final scope

Review question wording in scope	Final review question
What reporting and learning systems are effective and cost-effective in reducing medicines-related patient safety incidents, compared to usual care?	What systems for identifying, reporting and learning from medicines-related patient safety incidents are effective and cost-effective in reducing medicines-related patient safety incidents, compared to usual care?

Review question wording in scope	Final review question
What is the effectiveness and cost-effectiveness of medication reviews to reduce sub-optimal use of medicines and medicines-related patient safety incidents, compared to usual care?	No change from wording in final scope.
What is the effectiveness and cost-effectiveness of medicines reconciliation to reduce sub-optimal use of medicines and medicines-related patient safety incidents, compared to usual care?	No change from wording in final scope.
What is the effectiveness and cost-effectiveness of using decision support to improve patient outcomes from medicines, compared to usual care?	What is the effectiveness and cost-effectiveness of using clinical decision support to reduce sub-optimal use of medicines and improve patient outcomes from medicines, compared to usual care or other intervention?
What is the effectiveness and cost-effectiveness of using patient decision aids in consultations to improve shared decision-making between patients, carers and practitioners, compared to usual care?	What is the effectiveness and cost-effectiveness of using patient decision aids in consultations involving medicines use to improve patient outcomes, compared to usual care or other intervention?
What is the effectiveness and cost-effectiveness of using self-management plans to improve patient outcomes from medicines, compared to usual care?	No change from wording in final scope.
What models of profession-led or multidisciplinary team-led working are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines, compared to usual care?	What models of organisational and cross-sector working are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines, compared to usual care, or other intervention?
What models of cross-organisational collaborative working are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines, compared to usual care?	Question amalgamated – see below.
What communication systems are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines when patients move from one care setting to another, compared to usual care?	What communication systems are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines when patients move from one care setting to another, compared to usual care, or other intervention?

1 The GDG agreed to amalgamate the following 2 review questions:

2 'What models of profession-led or multidisciplinary team-led working are effective and cost-
3 effective in reducing sub-optimal use of medicines and improving patient outcomes from
4 medicines, compared to usual care?'

5 and

6 'What models of cross-organisational collaborative working are effective and cost-effective in
7 reducing sub-optimal use of medicines and improving patient outcomes from medicines,
8 compared to usual care?'

9 Therefore, 8 review questions in total were finalised by the GDG. They are shown in table 3.
10
11 **Table 3 Final review questions**

Section	Theme	Review question
5	Systems for	What systems for identifying, reporting and learning from

Section	Theme	Review question
	identifying, reporting and learning from medicines-related patient safety incidents	medicines-related patient safety incidents are effective and cost-effective in reducing medicines-related patient safety incidents, compared to usual care or other intervention?
6	Medicines-related communication systems	What communication systems are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines when patients move from one care setting to another, compared to usual care, or other intervention?
7	Medicines reconciliation	What is the effectiveness and cost-effectiveness of medicines reconciliation to reduce sub-optimal use of medicines and medicines-related patient safety incidents, compared to usual care?
8	Medication review	What is the effectiveness and cost-effectiveness of medication reviews to reduce sub-optimal use of medicines and medicines-related patient safety incidents, compared to usual care?
9	Self-management plans	What is the effectiveness and cost-effectiveness of using self-management plans to improve patient outcomes from medicines, compared to usual care?
10	Patient decision aids	What is the effectiveness and cost-effectiveness of using patient decision aids in consultations involving medicines use to improve patient outcomes, compared to usual care or other intervention?
11	Clinical decision support	What is the effectiveness and cost-effectiveness of using clinical decision support to reduce sub-optimal use of medicines and improve patient outcomes from medicines, compared to usual care or other intervention?
12	Organisational and cross sector working	What models of organisational and cross sector working are effective and cost-effective in reducing sub-optimal use of medicines and improving patient outcomes from medicines, compared to usual care, or other intervention?

3.1.2 Writing the review protocols

For each review question a review protocol was developed in accordance with the NICE guidelines manual 2012 section 4.4; the final review protocols can be found in appendix C.2.

Review protocols outline the background, the objectives and planned methods to be used to undertake the review of evidence to answer the review question. They explain how each review is to be carried out and help the reviewer plan and think about different stages. They also provide some protection against the introduction of bias and allow for the review to be repeated by others at a later date (see NICE guidelines manual 2012 section 4.4).

Additionally, for each review protocol the GDG considered how any equality issues could be addressed in planning the review work.

Each review protocol was discussed and agreed by the GDG. This included the GDG agreeing the critical and important outcomes for each review question. These are shown in the review protocols.

3.2 Identifying the evidence

3.2.1 Clinical literature searching

Scoping searches were undertaken in July 2013 in order to identify previous clinical guidelines, health technology assessment reports, key systematic reviews and economic evaluations relevant to the topic. A list of sources searched can be found in appendix C.1.

Systematic literature searches were carried out by an information specialist from NICE guidance information services between November 2013 and May 2014 to identify published clinical evidence relevant to the review questions. The clinical evidence search strategies can be found in appendix C1.2. Searches were carried out according to the methods in the NICE guidelines manual 2012 section 5.2. Databases were searched using relevant medical subject headings and free-text terms. Searches were restricted to systematic reviews, RCTs and observational studies (where appropriate). Studies published in languages other than English were not reviewed and searches were restricted to studies published from 2000 onwards. The following databases were searched for all questions: MEDLINE, Embase and the Cochrane Library. CINAHL, Social Care Online, Social Policy and Practice, ASSIA, Social Service Abstracts and Sociological Abstracts were searched where appropriate for the review question. The clinical evidence search strategies can be found in appendix C1.2. No papers published after the date of the search were considered in the evidence review.

3.2.2 Health economic literature searching

Systematic literature searches were carried out by an information specialist in the NICE guidance information services between December 2013 and May 2014 to identify all published health economic evidence relevant to the review questions. Searches were carried out according to the methods in the NICE guidelines manual 2012 section 5.3. Medline and Embase were searched using specific economic evaluation and quality of life search filters. The NHS Economic Evaluation Database (NHS EED) and the Health Economic Evaluations Database (HEED) were searched using topic terms. Studies published in languages other than English were not reviewed. The health economic search strategies can be found in appendix C1.3. No papers published after the date of the search were considered in the health economic evidence review.

3.3 Reviewing the evidence

The evidence retrieved from the search strategy was systematically reviewed for each review protocol. Evidence identified from the literature search was reviewed by title and abstract (first sift). Those studies not meeting the inclusion criteria were excluded. Full papers of the included studies were requested. All full text papers were then reviewed and those studies not meeting the inclusion criteria were excluded (2nd sift). Relevant data on the population, intervention, comparator and outcomes (PICO) for each included study was extracted and included in the 'Summary of included studies' table. These tables can be found in the relevant 'Evidence review' section. An overview of the systematic review process followed is outlined in figure 1 in accordance with the NICE guidelines manual 2012 section 6.

1   **Figure 1 Overview of the systematic review process**

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        │  Analyse results (carry out meta-analysis where         │
        │  necessary)                                             │
        └───────────────────────────────────────────────────────┘
                                    │
                                    ▼
            ┌───────────────────────────────────────────────┐
            │      Assess evidence by quality of outcome      │
            └───────────────────────────────────────────────┘
                                    │
                                    ▼
        ┌───────────────────────────────────────────────────────┐
        │  Guideline Development Group to interpret the evidence  │
        └───────────────────────────────────────────────────────┘
```

2

3   ### 3.3.1   Inclusion and exclusion criteria

4   Selection of relevant studies was carried out by applying the inclusion and exclusion criteria
5   listed in the review protocols (see appendix C.2). All excluded studies including reasons for
6   exclusion can be found in appendix C.5. The GDG was consulted about any uncertainty and
7   made the final decision for inclusion or exclusion of these studies.

1 Guideline development group members

2

Name	Role
Weeliat Chong	Chief Pharmacist, Humber NHS Foundation Trust
Stephen Dean	Consultant In Intensive Care And Anaesthesia, Leeds Teaching Hospital NHS Trust
David Erskine	Director of London & South East Regional Medicines Information Service, Guys Hospital
Leslie Galloway (until end May 2014)	Chairman, Ethical Medicines Industry Group (EMIG)
Brian Hawkins	Chief Pharmacist, Cwm Taf LHB
John Holden	General Practitioner, Garswood Surgery, St Helens
Tessa Lewis	General Practitioner and Medical Advisor in therapeutics
Harriet Lewis	Regional Partnership Manager, Association of the British Pharmaceutical Industry (ABPI)
Margaret Ogden	Lay member
Bunis Packham	Nurse Consultant Thrombosis & Anticoagulation, Royal Free London NHS Foundation Trust
Richard Seal	Chief Pharmacist and Clinical Lead for Medicines Optimisation, NHS Trust Development Authority (Birmingham Office)
David Terry	Director – Pharmacy Practice Unit, Birmingham Children's Hospital
Katrina Vout	Medicines Management Development Manager, Northern, Eastern and Western Devon CCG
Mary Weatherstone	Specialist Pharmacist and Practice Pharmacist, Norfolk and Waveney CCGs and Coastal Partnership Practice
Nigel Westwood	Lay member

3 **Guideline producing team members**

Name	Role
Johanna Hulme	Associate Director, NICE medicines and prescribing centre
Michelle Jenks	Research Consultant, York Health Economics Consortium Ltd
James Mahon	Senior Associate, York Health Economics Consortium Ltd
Shelly Patel	Senior Adviser, NICE medicines and prescribing centre
Louise Picton	Senior Adviser, NICE medicines and prescribing centre
Ian Pye	Assistant Project Manager, NICE medicines and prescribing centre

4

5 3.3.2 Types of studies

6 Only evidence in the English language was considered. For all review questions the following
7 types of studies were considered in the reviews:

8 • Systematic reviews of RCTs

9 • RCTs

10 • Observational studies (where RCTs not available)

11 National guidance from the UK, Europe and other countries with similar developed health
12 systems, for example Australia, Canada and New Zealand was used to provide context for
13 the introductory sections of each evidence review.

Systematic reviews of RCTs were only included in full if all RCTs met the criteria listed in the review protocol. When this was not the case, relevant RCTs included in the systematic review were identified and full papers requested to determine their eligibility. Systematic reviews of observational studies and observational studies were only considered if evidence from RCTs was not identified. Conference abstracts were not considered as part of the review as higher quality evidence was identified for each question.

Characteristics of data from included studies were extracted into a standard template for inclusion in an evidence table, which can be found in appendix D. Evidence tables help to identify the similarities and differences between studies, including the key characteristics of the study population and interventions or outcome measures. This provides a basis for comparison.

All studies were quality assessed using the appropriate NICE methodology checklist (see NICE guidelines manual 2012 appendices B–I.

3.3.3 Methods of combining clinical studies

3.3.3.1 Data analysis for the intervention reviews

All review questions included interventions. Where possible, a meta-analysis was carried out to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. However, as many different interventions were considered, for example different medicines-related communication systems this was only possible for the review questions on medication review (section 8) and patient decision aids (section 10).

Risk ratios (relative risk) and odds ratios were calculated for the dichotomous outcomes, such as number of patients with a medication error. Mean differences were calculated for continuous outcomes.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, further analyses were conducted.

Absolute risk differences were also calculated when possible using software called GRADEpro, developed by the GRADE working group.

Dependent on the outcome measures used, a short narrative was written for data that could not be combined, or where risk ratios or mean differences could not be calculated.

3.3.4 Appraising the quality of evidence by outcomes

For each review, question, the GDG identified up to 8 outcomes which were specified as being critical or important outcomes. It is important that the relative importance is specified in the review protocol before reviewing the evidence to minimise the introduction of bias. Specifying those outcomes that are critical or important helped the GDG to make judgements about the importance of the different outcomes and their impact on decision making - for example, mortality would usually be considered a critical outcome and would be given greater weight when considering the clinical effectiveness of an intervention than an important outcome with less serious consequences.

Evidence for outcomes identified from included RCTs, and where RCTs were not available observational studies were analysed. The results of the analysis were presented to the GDG in the form of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE)'. The NICE guidelines manual 2012 explains that 'GRADE is a system developed by an international working group for rating the quality of evidence across outcomes in systematic reviews and guidelines. The system is designed for reviews and guidelines that

examine alternative management strategies or interventions, and these may include no intervention or current best management. The key difference from other assessment systems is that GRADE rates the quality of evidence for a particular outcome across studies and does not rate the quality of individual studies. The software used to do this was GRADEpro, developed by the GRADE working group.

For each outcome GRADEpro was used to assess the quality of the study, considering the individual study quality factors and any meta-analysis results. Results of the analysis were presented in 'GRADE profiles' (see appendix D.2. for all GRADE profiles).

The evidence for each outcome was examined separately for the quality elements listed and defined in table 4. Each element was graded using the quality levels listed in table 5. The main criteria considered in the rating of these elements are discussed below (see Section 3.3.5 Grading of evidence). Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall quality assessment for each outcome (table 6).

Table 4 Description of the elements in GRADE used to assess the quality of intervention studies

Quality element	Description
Risk of bias (study limitations)	Limitations in the study design and implementation may bias the estimates of the treatment effect. High risk of bias for the majority of the evidence decreases confidence in the estimate of the effect
Inconsistency	Inconsistency refers to an unexplained heterogeneity (as assessed by the I-squared or Chi-squared statistic studies) or variability in estimates of treatment effect across studies
Indirectness	Indirectness refers to differences between the population, intervention, comparator for the intervention and outcome of interest
Imprecision (random error)	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of the effect
Publication bias	Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies

Table 5 Levels of quality elements in GRADE

Level	Description
None	There are no serious issues with the evidence
Serious	The issues are serious enough to downgrade the outcome evidence by 1 level
Very serious	The issues are serious enough to downgrade the outcome evidence by 2 levels

Table 6 Overall quality of outcome evidence in GRADE

Level	Description
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

3.3.5 Grading the quality of clinical evidence

When results from GRADE were pooled, the overall quality of evidence for each outcome was considered. This process was followed when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start as high, observational studies as low.

2. The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed below. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose–response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.

3. The reasons or criteria used for downgrading were specified in the footnotes of the GRADE tables.

The NICE guidelines manual 2012 summarises the GRADE approach to rating the quality of evidence (see NICE guidelines manual 2012 section 6.2).

3.3.6 Risk of bias

Bias can be defined as anything that causes a consistent deviation from the truth. Bias can be perceived as a systematic error, for example, if a study was to be carried out several times and there was a consistently wrong answer, the results would be inaccurate.

The risk of bias for a given study and outcome is associated with the risk of over- or underestimation of the true effect. The risks of bias are listed in table 7. When the risk of bias was judged to be serious or very serious, the quality of evidence was downgraded (see table 6).

Table 7 Risk of bias in randomised controlled trials

Risk of bias	Explanation
Allocation concealment	Those enrolling patients are aware of the group to which the next enrolled patient will be allocated
Lack of blinding	Patient, caregivers, those recording outcomes, those adjudicating outcomes, or data analysts are aware of the arm to which patients are allocated
Incomplete accounting of patients and outcome events	Missing data not accounted for and failure of the trialists to adhere to the intention-to-treat principle when indicated
Selective outcome reporting	Reporting of some outcomes and not others on the basis of the results
Other risks of bias	For example: Stopping early for benefit observed in randomised trials, in particular in the absence of adequate stopping rules Use of unvalidated patient-reported outcomes Recruitment bias in cluster-randomised trials

3.3.7 Inconsistency

Inconsistency refers to an unexplained heterogeneity of results. When estimates of the treatment effect across studies differ widely (that is, there is heterogeneity or variability in

results), this suggests true differences in underlying treatment effect. When heterogeneity was apparent (I-squared inconsistency statistic of >50%, or evidence from examining forest plots), but no plausible explanation can be found, the quality of evidence was downgraded (see table 5).

3.3.8 Indirectness

Directness refers to the extent to which the populations, intervention, comparisons and outcome measures are similar to those defined in the inclusion criteria for the reviews. Indirectness is important when these differences are expected to contribute to a difference in effect size, or may affect the balance of harms and benefits considered for an intervention.

3.3.9 Imprecision

Imprecision in guidelines concerns whether the uncertainty (confidence interval) around the effect estimate means that it is not clear whether there is a clinically important difference between interventions or not. Criteria such as the width of the confidence intervals and the number of events (as defined and reported in the study) are used to make judgements about imprecision and to assess the uncertainty of the results. This uncertainty is reflected in the width of the confidence interval. The 95% confidence interval (95% CI) is defined as the range of values that contain the population value with 95% probability. The larger the trial, the smaller the 95% CI and the more certain the effect estimate. When imprecision was apparent the quality of the evidence was downgraded (see table 5).

3.3.10 Evidence statements (summarising and presenting results for effectiveness)

Evidence statements for outcomes were developed to include a summary of the key features of the evidence. For each question, evidence statements for clinical and cost effectiveness were summaries of the evidence, produced to support the GDG in their review of the evidence and decision-making when linking evidence to recommendations. The wording of the statement reflects the certainty or uncertainty in the estimate of effect.

3.4 Evidence of cost-effectiveness

The GDG needs to make recommendations based on the best available clinical and cost effectiveness evidence. Guideline recommendations should be based on the estimated costs of the interventions or services in relation to their expected health benefits (that is, their 'cost effectiveness'), rather than on the total cost or resource impact of implementing them. Thus, if the evidence suggests that an intervention or service provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature.
- Undertook new cost-effectiveness analysis in a priority area.

3.4.1 Literature review

The Health Economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion / exclusion criteria to identify relevant studies (see below for details).

1 • Critically appraised relevant studies using the economic evaluations checklist as specified
2   in the NICE guidelines manual 2012 appendix G.
3 • Extracted key information about the study's methods and results into evidence tables
4   (evidence tables are included in appendix D.1).

3.4.1.1 Inclusion and exclusion criteria

Full economic evaluations (studies comparing costs and health consequences of alternative
courses of action: cost–utility, cost-effectiveness, cost–benefit and cost–consequence
analyses) and comparative costing studies that addressed the review question in the relevant
population were considered potentially includable as economic evidence.

Studies that reported average cost effectiveness without disaggregated costs and effects
were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles,
unpublished studies and studies not in English were excluded. Studies that only reported
cost per hospital (not per patient) were excluded unless they were the only available
economic evidence on an intervention.

Remaining studies were prioritised for inclusion based on their relative applicability to the
development of this guideline and the study limitations. For example, if a high quality, directly
applicable UK analysis was available, then other less relevant studies may not have been
included. Where selective exclusions occurred on this basis, this is noted in the relevant
section.

For more details about the assessment of applicability and methodological quality see the
economic evaluation checklist (appendix G of the NICE guidelines manual and the health
economics review protocol in appendix C.2).

3.4.1.2 Economic evidence profiles

When relevant economic studies are identified a NICE economic evidence profile is used to
summarise cost and cost-effectiveness estimates. The profile shows an assessment of
applicability and methodological quality for each economic evaluation, with footnotes
indicating the reasons for assessment. These assessments are made by the health
economist using the economic evaluation checklist. The profile also shows:

• incremental costs

• incremental effects (for example, quality-adjusted life years [QALYs])

• incremental cost-effectiveness ratio for the base case analysis in the evaluation

• information about the assessment of uncertainty in the analysis.

See table 8 for more details.

If a non-UK study was included in the profile, the results were converted into pounds sterling
using the appropriate purchasing power parity.

Table 8 Content of NICE economic profile

Item	Description
Study	First author name, reference, date of study publication and country perspective.
Limitations	An assessment of methodological quality of the study*: Minor limitations – the study meets all quality criteria, or the study fails to meet one or more quality criteria, but this is unlikely to change the conclusions about cost effectiveness. Potentially serious limitations – the study fails to meet one or more quality criteria, and this could change the conclusion about cost effectiveness.

Item	Description
	Very serious limitations – the study fails to meet one or more quality criteria and this is very likely to change the conclusions about cost effectiveness. Studies with very serious limitations would usually be excluded from the economic profile table.
Applicability	An assessment of applicability of the study to the clinical guideline, the current NHS situation and NICE decision-making*: Directly applicable – the applicability criteria are met, or one or more criteria are not met but this is not likely to change the conclusions about cost effectiveness. Partially applicable – one or more of the applicability criteria are not met, and this might possibly change the conclusions about cost effectiveness. Not applicable – one or more of the applicability criteria are not met, and this is likely to change the conclusions about cost effectiveness.
Other comments	Particular issues that should be considered when interpreting the study.
Incremental cost	The mean cost associated with one strategy minus the mean cost of a comparator strategy.
Incremental effects	The mean QALYs (or other selected measure of health outcome) associated with one strategy minus the mean QALYs of a comparator strategy.
ICER	Incremental cost-effectiveness ratio: the incremental cost divided by the respective QALYs gained.
Uncertainty	A summary of the extent of uncertainty about the ICER reflecting the results of deterministic or probabilistic sensitivity analyses, or stochastic analyses of trial data, as appropriate.

* Limitations and applicability were assessed using the economic evaluation checklist from the NICE guidelines manual 2012.

3.4.2 Undertaking new health economic analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was undertaken by the Health Economist in a priority area. The priority area for new health economic analysis was agreed by the GDG after formation of the review questions and consideration of the available health economic evidence.

The GDG identified medicine reconciliation as the highest priority area for original economic modelling. This was due to having sufficient data to populate the model in an area where potential costs and health benefits occurring from medication taken in error are large. In 2007, NICE and the National Reporting and Learning System (part of the National Patient Safety Agency [NPSA])[1] issued joint guidance Technical patient safety solutions for medicines reconciliation on admission of adults to hospital (PSG001). A cost-utility model comparing methods of medicine reconciliation at hospital admission had been developed for this guidance (Karnon et al 2009). The GDG felt that the model structure used in Technical patient safety solutions for medicines reconciliation on admission of adults to hospital (PSG001) was appropriate, therefore this model was updated to utilise evidence from the clinical effectiveness review.

The following general principles were adhered to in developing the cost-effectiveness analysis:

- Methods were consistent with the NICE reference case[2].

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[2]National Institute for Health and Clinical Excellence. Guide to the methods of technology
6 appraisal 2013. 2nd Ed edition. London: National Institute for Health and Clinical Excellence;
7 2013. Available from: http://publications.nice.org.uk/pmg9

- The GDG was involved in agreeing to use the published model structure, selection of model inputs and interpretation of results.
- Model inputs were based on the systematic review of the clinical literature supplemented with other published data sources where possible.
- When published data was not available GDG expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- The model was peer-reviewed by another health economist at York Health Economics Consortium.

The full methods for the cost-effectiveness analysis of medicine reconciliation are described in appendix F.

3.4.3 Cost-effectiveness criteria

NICE's document on Social value judgements: Principles for the development of NICE guidance (2nd edition) sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. An intervention was considered to be cost-effective if either of the following criteria applied (given that the estimate was considered plausible):

- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant interventions)
- The intervention cost less than £20,000 per QALY gained compared with next best intervention.

3.5 Developing recommendations

The GDG reviewed the clinical and cost effectiveness evidence in the context of each of the 8 review questions to develop recommendations that would be useful to health and social care practitioners and commissioning and provider organisations. For each review question the GDG were presented with:

- evidence tables for clinical and cost-effectiveness evidence (see appendix D for the evidence tables)
- summaries of the clinical and economic evidence and quality (see appendix D for the summary of included studies and the GRADE tables)
- forest plots (where applicable see appendix D).

The recommendations were drafted based on the GDG's interpretation of the evidence presented, where they considered the relative values of different outcomes, trade-offs between benefits and harms, quality of the evidence, costs of different interventions and other factors they may need to be consider in relation to the intervention. For each review question the clinical effectiveness evidence was presented first, considering the net benefit over harm for the prioritised critical outcomes (as set out in the review protocols [see appendix C.2]). This involved an informal discussion, details of which are captured in the 'Linking Evidence to Recommendations' (LETR) table for each review question.

The GDG then reviewed cost-effectiveness evidence and considered how this impacted on the decisions made after presentation of the clinical cost-effectiveness. The recommendation wording considered the quality of the evidence and the confidence the GDG had in the evidence that was presented, in addition to the importance of the prioritised outcomes (the GDG's values and preferences).

Where clinical or cost-effectiveness evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. Consensus based recommendations considered the balance between potential benefits and harms, economic costs compared with benefits, current practice, other guideline recommendations, patient preferences and equality issues and were agreed through discussion with the GDG.

The wording of the recommendations took into account the strength of the evidence and wording was based on the NICE guidelines manual 2012 principles; 'some recommendations are strong in that the GDG believes that the vast majority of health and other professionals and patients would choose a particular intervention if they considered the evidence in the same way that the GDG has.' This is generally the case if the benefits of an intervention outweigh the harms for most people and the intervention is likely to be cost effective. Where the balance between benefit and harm is less clear cut, then the recommendations are 'weaker'; some patients may not choose an intervention, whereas others would. The NICE guidelines manual 2012 states that 'A general principle of NICE clinical guidelines is that patients should be informed of their choices and be involved in decisions about their care'. This was particularly important in this guideline, where many review questions focused on involving the patient in decisions about their medicines.

See section 9 of the NICE guidelines manual 2012 for more information on developing and wording recommendations.

3.5.1 Research recommendations

When areas were identified for which good evidence was lacking, the GDG considered making recommendations for future research. Decisions about inclusion were based on factors such as:

- the importance to patients or the population

- national priorities

- potential impact on the NHS and future NICE guidance

- ethical and technical feasibility.

3.5.2 Validation process

This short clinical guideline is subject to a 4 week public consultation. This allows stakeholders, members of the public and other NICE teams to peer review the document as part of the quality assurance process. All comments received from registered stakeholders within the specified deadline will be responded to. All comments received and responses given will be posted on the NICE website (see NICE guidelines manual 2012 section 11).

3.5.3 Updating the guideline

The guideline will be updated in accordance with the process outlined in the NICE guidelines manual 2012 section 14.

3.5.4 Disclaimer

Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their family members or carer.

3.5.5 Funding

NICE commissioned the NICE medicines and prescribing centre to produce this guideline.

4 Guideline summary

4.1 Key priorities for implementation

From the full set of recommendations, the GDG selected 4 key priorities for implementation. The criteria used for selecting these recommendations are listed in detail in the NICE guidelines manual 2012. The reasons behind selection of each of these recommendations are shown in the table linking the evidence to the recommendation in the relevant chapter.

Medicines reconciliation

Recommendation 24

Ensure that medicines reconciliation is carried out by a trained and competent health professional – ideally a pharmacist, pharmacy technician, nurse or doctor – with the necessary knowledge, skills and expertise including:

- effective communication skills
- technical knowledge of processes for managing medicines and
- therapeutic knowledge on medicines use.

Identifying, reporting and learning from medicines-related patient safety incidents

Recommendation 8

Consider using several methods to identify medicines related patient safety incidents – for example, health record review, direct observation of medicines administration and patient surveys. Agree the approach locally and review arrangements regularly to reflect local and national learning.

Medicines related communication systems when patients move from one care setting to another

Recommendation 17

Include all of the following in medicines discharge information when a person transfers from one care setting to another:

- details of the person and their GP
- details of other relevant contacts identified by the person and/or their family members or carers (for example, their nominated community pharmacy)
- known drug allergies and reactions to medicines or their ingredients, and the type of reaction experienced
- medicines the person is currently taking, including name, strength, form, dose, timing and frequency, how the medicines are taken (route of administration) and what they are being taken for (indication).
- changes to medicines, including medicines started or stopped, or dosage changes, and reason for the change
- date and time of the last dose, such as for weekly or monthly medicines, including injections
- other information, including when the medicines should be reviewed or monitored, and any support the person needs to carry on taking the medicines
- what information has been given to the person and/or their family members or carers, as appropriate

Recommendation 18

Consider sending a person's medicines discharge information to their nominated community pharmacy, when possible and in agreement with the person.

4.2 Full list of recommendations

Identifying, reporting and learning from medicines-related patient safety incidents

Improving learning from medicines-related patient safety incidents is important to guide practice and minimise patient harm. Medicines-related patient safety incidents are unintended or unexpected incidents that are specifically related to medicines use, which could have or did lead to patient harm. These include potentially avoidable medicines-related hospital admissions and re-admissions, medication errors, near misses and potentially avoidable adverse events.

1. Organisations should ensure that robust and transparent processes are in place for identifying, reporting, prioritising, investigating and learning from medicines-related patient safety incidents, in line with national patient safety reporting systems – for example, the National Reporting and Learning System.

2. Ensure that patients and/or their family members or carers understand how to identify and report any medicines-related patient safety incidents.

3. Report identified medicines-related patient safety incidents consistently and in a timely manner to ensure that the safety of the patient is not compromised, in line with local and national patient safety reporting systems.

4. Organisations should support a 'no-blame culture' that encourages reporting and learning from medicines-related patient safety incidents.

5. Organisations should consider exploring what barriers exist that may reduce reporting and learning from medicines-related patient safety incidents. Any barriers that are identified should be addressed, for example, in a documented action plan.

6. Ensure that action is taken to reduce further risk when medicines-related patient safety incidents have been identified. Apply and share learning – for example, as part of continuing professional development.

7. Ensure that national medicines safety guidance, such as patient safety alerts, is actioned within the specified or locally agreed timeframe.

8. Consider using several methods to identify medicines-related patient safety incidents – for example, health record review, direct observation of medicines administration and patient surveys. Agree the approach locally and review arrangements regularly to reflect local and national learning.

9. Consider applying the principles of the PINCER intervention to reduce the number of medicines-related patient safety incidents, taking account of existing systems and resource implications. These principles include:

   - using information technology support

   - using educational outreach with regular reinforcement of educational messages

   - actively involving a multidisciplinary team, including GPs, nurses and support staff

- having dedicated pharmacist support

- agreeing an action plan with clear objectives

- providing regular feedback on progress

- providing clear, concise, evidence-based information.

10. Consider using a screening tool (for example, the STOPP/START tool in older people) to identify potential medicines-related patient safety incidents in some patient groups. These may include:

- people taking multiple medicines (polypharmacy)

- people with chronic or long-term conditions

- older people.

Medicines-related communication systems when patients move from one care setting to another

Relevant information about medicines should be shared with patients and/or their family members or carers and between health and social care practitioners when a person moves from 1 care setting to another, to support high-quality care. This includes transfers within an organisation (for example, when a person moves from intensive care to a hospital ward) or from 1 organisation to another (for example, when a person is admitted to hospital, or discharged from hospital to their home or other location).

11. Organisations should ensure that robust and transparent processes are in place so that:

- when a person is transferred to another care setting, complete and accurate information about medicines is shared with the appropriate provider(s), **and**

- when a person is transferred from another care setting, complete and accurate information about medicines is received, documented and acted on.

They should clearly define organisational and individual roles and responsibilities and regularly review and monitor the effectiveness of local processes (see also section on medicines reconciliation).

12. Organisations should ensure that information about medicines is shared with the person (and/or their family members or carers as appropriate) and their GP. They should:

- identify when existing local systems are in place for this when a person moves from one care setting to another

- take account of the Health and Social Care Information Centre's A guide to confidentiality in health and social care (2013).

13. Discuss relevant information about medicines (for example medicines that have been changed) with the person and/or their family members or carers at the time of transfer, especially when they are being discharged from hospital. Give the person a complete and accurate list of their medicines, in a patient-friendly format. This should include all current medicines and any changes to medicines made during the hospital admission.

14. Encourage people to tell their GP, community pharmacist and any other relevant people if they have been in hospital, and to inform these people about any changes to their medicines.

15. Proactively share complete and accurate information about medicines in a timely way, ideally within 48 hours of the person being transferred, to ensure that patient safety is not compromised (see also recommendation 12).

16. Securely share relevant information about medicines in the most effective way, such as by secure electronic communication. Recognise that more than one approach may be needed.

17. Include all of the following in medicines discharge information when a person transfers from one care setting to another:

    • details of the person and their GP

    • details of other relevant contacts identified by the person and/or their family members or carers (for example, their nominated community pharmacy)

    • known drug allergies and reactions to medicines or their ingredients, and the type of reaction experienced

    • medicines the person is currently taking, including name, strength, form, dose, timing and frequency, how the medicines are taken (route of administration) and what they are being taken for (indication).

    • changes to medicines, including medicines started or stopped, or dosage changes, and reason for the change

    • date and time of the last dose, such as for weekly or monthly medicines, including injections

    • other information, including when the medicines should be reviewed or monitored, and any support the person needs to carry on taking the medicines

    • what information has been given to the person and/or their family members or carers, as appropriate.

18. Consider sending a person's medicines discharge information to their nominated community pharmacy, when possible and in agreement with the person.

19. Organisations should consider additional support for some patient groups when they have been discharged from hospital, such as pharmacist counselling, telephone follow-up, GP and/or nurse follow-up home visits. These may include:

    • people taking multiple medicines (polypharmacy)

    • people with chronic or long-term conditions

    • older people.

Medicines reconciliation

Medicines reconciliation is the process of identifying the most accurate list of a person's current medicines and comparing them to the current list in use, recognising any discrepancies, and documenting any changes, thereby resulting in a complete list of medications, accurately communicated. The medicines reconciliation process will vary depending on the care setting that the person has just moved into (for example, from primary care into hospital, or from hospital back to a care home). Algorithms have been produced to show the different processes.

20. In an acute setting, accurately list all of the person's medicines (medicines reconciliation) within 24 hours, when they move from one care setting to another – for example, when they are admitted to hospital.

21. Recognise that medicines reconciliation may need to be carried out on more than one occasion during a hospital stay – for example, when a person is admitted, transferred between wards or discharged.

22. In primary care, carry out medicines reconciliation for all people who have been discharged from hospital. This should happen as soon as is practically possible, before a prescription or new supply of medicines is issued and no more than 1 week after the GP practice receives the information.

23. Organisations should consider identifying a senior, responsible pharmacist to oversee the medicines reconciliation process. The process should be determined locally and include:

    • organisational responsibilities

    • responsibilities of people involved in the process (including who they are accountable to)

    • individual training and competency needs.

24. Ensure that medicines reconciliation is carried out by a trained and competent health professional – ideally a pharmacist, pharmacy technician, nurse or doctor – with the necessary knowledge, skills and expertise including:

    • effective communication skills

    • technical knowledge of processes for managing medicines and

    • therapeutic knowledge on medicines use.

25. Involve patients whenever possible in the medicines reconciliation process. If the person agrees, or is unable to be involved, include their family members or carers.

26. When carrying out medicines reconciliation, record relevant information (see section medicines-related communication systems) on an electronic or paper-based form.

Medication review

Medication review can have many different interpretations and there are also different types which vary in their quality and effectiveness. In this guideline medication review is defined as 'a structured, critical examination of a person's medicines with the objective of reaching an agreement with the person about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste'.

27. Consider carrying out a medication review for some patient groups when a clear purpose for the review has been identified. These groups may include:

    • people taking multiple medicines (polypharmacy)

    • people with chronic or long-term conditions

    • older people.

28. Determine locally the most appropriate health professional to carry out a medication review, based on their knowledge and skills, including all of the following:

- technical knowledge of processes for managing medicines

- therapeutic knowledge on medicines use

- effective communication skills.

The medication review may be led, for example, by a pharmacist (professional-led) or by an appropriate health professional who is part of a multidisciplinary team.

29. During a medication review, take into account:

- the person's (and/or the family members or carers, as appropriate) views and understanding about their medicines

- the person's (and/or their family members' or carers') concerns, questions or problems with the medicines

- all prescribed, over-the-counter and complementary medicines that the person is taking or using, and what these are for

- how safe the medicines are, how well they work, how appropriate they are, and whether their use is in line with national guidance

- any monitoring tests that are needed.

Self-management plans

Self-management plans can be patient-led or profession-led and they aim to support people to be empowered and involved in managing their condition. Different types of self-management plan exist and they vary in their content depending on the needs of the individual person. In this guideline self-management plans are structured, documented plans that are developed to support an individual person's self-management of their condition using medicines.

30. When discussing medicines with people who have chronic or long-term conditions, consider using an individualised self-management plan to support people who want to be involved in managing their medicines. Discuss all of the following:

- the person's knowledge and skills needed to use the plan, using a risk assessment if needed

- the benefits and risks of using the plan

- the person's values and preferences

- how to use the plan

- any support the person needs

Record the discussion in the person's medical notes.

31. When developing an individualised self-management plan for a patient, consider including:

- the plan's start and review dates (review the plan on a regular basis to ensure the person does not have problems using or following it)

- the condition(s) being managed

- a description of medicines being taken under the plan

- any strength or dose restrictions or limitations of a medicine that may be taken under the plan, how long a medicine may be taken for, or what medicines that may be self-administered under the plan are being used

- the person's allergies and intolerances to medicines

- the arrangements for the person to report suspected or known adverse reactions to any medicines

- the circumstances in which the person should refer to, or seek the advice from, a health professional

- the individual responsibilities of the health professional and the person

- any other instructions the person needs to safely and effectively self-manage their medicines.

Patient decision aids used in consultations involving medicines

Many people wish to be active participants in their own healthcare, and to be involved in making decisions about their medicines. Patient decision aids can support health professionals to adopt a shared decision-making approach in a consultation, to ensure that patients are able to make well-informed choices that are consistent with their values and preferences.

32. Offer all people the opportunity to be involved in making decisions about their medicines. Find out what level of involvement in decision-making the person would like and avoid making assumptions about this.

33. Find out about a patient's values and preferences by discussing what is important to them about managing their condition(s) and their medicines. Recognise that the patient's values and preferences may be different from those of the health professional and avoid making assumptions about them.

34. Apply the principles of evidence-based medicine when discussing the available treatment options with a person in a consultation about medicines. Use the best available evidence carefully when making decisions with or for individual patients, together with clinical expertise and the patients' values and preferences.

35. In a consultation about medicines, offer the person the opportunity to use a patient decision aid (when one is available), to help them make a preference-sensitive decision (a decision based on the patient's preferences and personal values of each treatment option presented) that involves trade-offs between benefits and risks. Ensure the patient decision aid is appropriate in the context of the consultation as a whole.

36. Do not use a patient decision aid to replace discussions with a person in a consultation about medicines.

37. Recognise that it may be appropriate to have more than 1 consultation to ensure that a person can make an informed decision about their medicines. Give people the opportunity to review their decision, as appropriate, because this may change over time (for example, a person's baseline risk may change).

38. Ensure that patient decision aids used in consultations about medicines have followed a robust and transparent development process, in line with the IPDAS criteria.

39. Before using a patient decision aid with a person in a consultation about medicines, read and understand its content, paying particular attention to its limitations and the need to adjust discussions according to the patient's baseline risk.

40. Have the necessary knowledge, skills and expertise, when using a patient decision aid, including:

- relevant clinical knowledge

- effective communication and consultation skills, especially when finding out patients' values and preferences

- effective numeracy skills, especially when explaining the risks and benefits in natural frequencies, and relative and absolute risk

- explaining the trade-offs between particular benefits and risks.

41. Consider training and education needs to support health professionals and patients in developing the appropriate skills and expertise to use patient decision aids effectively in consultations about medicines.

42. Organisations should consider identifying and prioritising which patient decision aids are needed for their patient population through, for example, a local medicines decision-making group. Agree a consistent, targeted approach in line with local pathways and review the use of the patient decision aids regularly.

43. Organisations should ensure that patient decision aids prioritised for use locally are disseminated to all relevant health professionals and stakeholders.

Clinical decision support

Clinical decision support software is a component of an integrated clinical IT system providing support to clinical services, such as in a GP practice or secondary care setting. These integrated clinical IT systems are used to support health professionals to manage a person's condition. In this guideline the clinical decision support software relates to computerised clinical decision support, which may be active or interactive, at the point of prescribing medicines.

44. Consider computerised clinical decision support systems (taking account of existing systems and resource implications) to support clinical decision-making and prescribing, but ensure they do not replace clinical judgement.

45. When using a computerised clinical decision support system to support clinical decision-making and prescribing, ensure that it:

- identifies important safety issues

- includes a system for health professionals to acknowledge the alert (for mandatory alerts) which is not customisable for alerts relating to medicines-related 'never events'

- reflects the best available evidence

- contains useful clinical information that is relevant to the health professional to reduce 'alert fatigue', where a prescriber's responsiveness to a particular type of alert declines as they are repeatedly exposed to that alert over time.

- is up-to-date.

46. Ensure that robust and transparent processes are in place for developing, using, reviewing and updating computerised clinical decision support systems.

47. Ensure that health professionals using computerised clinical decision support systems at the point of prescribing have the necessary knowledge and skills to use the system, including an understanding of its limitations.

Medicines-related models of organisational and cross-sector working

The introduction of skill mixing of various health and social care practitioners to meet the needs of different patient groups has led to different types of models of care emerging across health and social care settings. Cross-organisational working further provides seamless care during the patient care pathway when using health and social care services. The type of model of care used will be determined locally based on the resources and health and social care needs of the population in relation to medicines.

48. Consider a multidisciplinary team approach to improve outcomes for people who have long-term conditions and take multiple medicines (polypharmacy).

49. When medicines are being discussed at any point in the care pathway, involve a pharmacist with relevant clinical knowledge and skills.

4.2.1 Research recommendations

1. What is the clinical and cost effectiveness of using clinical decision support systems to reduce the suboptimal use of medicines and improve patient outcomes from medicines, compared with usual care, in the UK setting?

2. What models of cross-organisational working, for example between NHS and social care, or primary and secondary care, improve clinical and cost effectiveness in relation to the suboptimal prescribing of medicines?

5 Identifying, reporting and learning from medicines-related patient safety incidents

5.1 Introduction

The Francis Report (2013) emphasised the need to put patients first at all times, and that they must be protected from avoidable harm. The Berwick report (2013) recommends 4 guiding principles for improving patient safety, 2 of which are:

- 'place the quality and safety of patient care above all other aims for the NHS

- engage, empower, and hear patients and carers throughout the entire system, and at all times'.

Furthermore, the NHS outcomes framework for 2013 to 2014 requires commissioners and providers of NHS services to reduce the incidence of medication errors causing serious harm. The Medication Safety Thermometer (part of the NHS Safety Thermometer) is a tool to improve medicines safety locally that focuses on medicines reconciliation (see section 7), allergy status, medication omission and identifying harm from high-risk medicines, in line with Domain 5 of the NHS Outcomes Framework.

Definitions

EU Directive 2010/84/EU1 defines the term 'adverse drug reaction' (ADR) as 'a response to a medicinal product which is noxious and unintended'. This includes effects resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse, off-label use and abuse of the medicinal product.

The National Reporting and Learning System (NRLS) defines a 'patient safety incident' as 'any unintended or unexpected incident, which could have or did lead to harm for one or more patients receiving NHS care.'

For the purpose of this review question, medicines-related patient safety incidents are unintended or unexpected incidents that were specifically related to medicines use, which could have or did lead to patient harm. These include:

- potentially avoidable medicines-related hospital admissions and re-admissions

- medication errors – any patient safety incidents where there has been an error in the process of prescribing, preparing, dispensing, administering, monitoring or providing advice on medicines

- potentially avoidable adverse events

- near misses (a prevented medicines-related patient safety incident which could have led to patient harm)

- never events (serious, largely preventable patient safety incidents that should not occur if the available preventative measures have been implemented by healthcare providers).

National reporting systems

The key responsibilities for patient safety developed by the National Patient Safety Agency (NPSA) transferred to NHS England in 2012. NHS England is working with the MHRA to simplify reporting, improve learning and guide practice to minimise harm from medicines-related incidents. The system for reporting medicines-related incidents in England is the National Reporting and Learning System (NRLS).

The current pattern for reporting medicines-related patient safety incidents is shown below:

1

2

Type of medicines-related patient safety incident	Preventable medication errors reported to NRLS, including never events and near misses		Adverse drug reactions[1] reported to MHRA yellow card scheme
	Where no harm occurred to the patient but there was potential for harm, or where harm resulted from omission or delay in using a medicine	Where harm occurred to the patient when a medicine was used	
Who takes action	NHS England review	NHS England review and NHS England share report with MHRA	MHRA review
[1] Suspected adverse drug reactions that are not the result of a medication error continue to be reported to the MHRA through the Yellow Card Scheme. This is outside the scope of this guidance. Adapted from 'Supporting information for patient safety alert on improving medication error incident reporting and learning', NHS England 2014.			

3 Patient safety alerts are issued by NHS England via the Central Alerting System (CAS), a
4 web-based cascading system for issuing alerts, important public health messages and other
5 safety critical information and guidance to the NHS and other organisations, including
6 independent providers of health and social care. NHS England and the MHRA jointly issued
7 a stage 3 patient safety alert (directive), Improving medication error incident reporting and
8 learning in March 2014. New NHS governance structures are now in place to support the
9 safe reporting of medicines-related patient safety incidents through the NRLS and MHRA,
10 including a national medication safety network of medication safety officers. This network
11 discusses potential and recognised safety issues and identifies trends and actions to improve
12 the safe use of medicines.

13 The Medicines optimisation prototype dashboard (NHS England, 2014) includes several
14 metrics relevant to this review question:
15 • Safe prescribing in the community setting:
16   o GP practices accessing PINCER (pharmacist-led information technology intervention
17   for medication errors) audit software
18 • Medication safety in the hospital setting:
19   o number of medication-related never events reported to NRLS
20   o total reporting of medication incidents to NRLS
21   o percentage medication incidents reported to NRLS that are harmful.

22 **How common are medicines-related patient safety incidents?**

23 Medicines-related patient safety incidents are common and are more likely to occur in people
24 taking multiple medicines (polypharmacy) for long-term conditions. The EQUIP study (2009)
25 investigated prescribing errors made by foundation trainees in secondary care and found that
26 almost 1 in 10 prescriptions were incorrect, with almost 1 in 50 errors considered to be
27 potentially lethal. The Practice study (2012) analysed the prevalence and causes of
28 prescribing errors in general practice and found that 1 in 20 prescription items contained
29 either a prescribing or monitoring error, which affected 1 in 8 patients. The CHUMS study
30 (2009) found that on any 1 day, 7 out of 10 elderly residents in care homes experienced
31 errors with their medicines. In the National Diabetes Inpatient Audit (2012) of hospitals in
32 England and Wales, almost 1 in 3 patients with diabetes experienced at least 1 medication
33 error in the previous 7 days of their hospital stay.

34 Given the potential risks to patient safety when medicines-related patient safety incidents
35 occur, this review question aimed to assess the clinical effectiveness and cost effectiveness
36 of systems for identifying, reporting and learning from medicines-related patient safety

incidents are effective and cost effective in reducing medicines-related patient safety incidents, compared with usual care or other intervention.

5.2 Review question

What systems for identifying, reporting and learning from medicines-related patient safety incidents are effective and cost effective in reducing medicines-related patient safety incidents, compared with usual care or other intervention?

5.3 Evidence review

Medicines-related patient safety incidents include medication errors (such as prescribing errors, dispensing errors, administration errors and monitoring errors) and preventable adverse events. Non-preventable adverse events, such as well-recognised adverse drug reactions, were not included.

This review question did not aim to compare the effectiveness of other systems that may help to reduce the incidence of medicines-related patient safety incidents, such as bar coding administration systems, electronic prescribing systems and computerised physician order entry systems (CPOE). Any studies relating to pharmacovigilance were also excluded.

A systematic literature search was conducted (see appendix C1.2), which identified 4036 references. After removing duplicates the references were screened on their titles and abstracts and 737 references were obtained and reviewed against the inclusion and exclusion criteria, as described in the review protocol (appendix C2.1).

Overall, 727 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C5.1.

Ten studies met the eligibility criteria and were included. In addition, 7 relevant systematic reviews of observational studies were identified. The references included in these systematic reviews were also screened on their titles and abstracts, to identify any further studies that met the eligibility criteria. Eight additional studies were included.

Of the 18 included studies, 2 were RCTs and the remaining 16 were observational studies. One RCT investigated PINCER (Avery 2012). The other RCT investigated the use of the STOPP/START tool (Screening Tool of Older Person's Prescription/Screening Tool to Alert to Right Treatment) (Gallagher 2011). Observational studies that reported data on the STOPP/START tool were not considered, because a RCT was identified (see appendix C2.1).

The 16 observational studies investigated a wide range of systems for identifying, reporting and learning from medicines-related patient safety incidents, including:

- incident reporting systems
- health record review, for example, hospital medication charts, clinical case notes, hospital discharge summaries
- direct observation
- pharmacist surveillance
- patient reports and surveys
- tools to identify potentially inappropriate medicines.

No studies were identified that met the eligibility criteria on:

- the National Reporting and Learning System
- significant event audits
- medication safety thermometer

1   • root cause analysis.

2   Available data were extracted into detailed evidence tables (see appendix D.1.1) and are
3   summarised in the table below.

Table 9 Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Avery (2012) *UK*	Primary care patients: • with history of peptic ulcer prescribed a non-selective NSAID without a PPI • with asthma prescribed a beta-blocker • aged 75 years or older prescribed an ACE inhibitor/loop diuretic long-term who have not had a computer-recorded check of renal function and electrolytes in the previous 15 months	PINCER	Computerised feedback for at-risk patients	Clinical outcomes
Chang (2010) *Taiwan*	Hospitalised adults aged 65 years or older who had either: • been prescribed 8 or more chronic medications or • visited 3 or more different physicians during 3-month screening	6 different methods to identify PIMs: • Beers criteria (2003) • Rancourt • Laroche • STOPP • Winit-Watjana • NORGEP	Comparison of 6 methods	Medicines-related problems
Field (2004) *USA*	Patients aged 65 years or older receiving medical care in the ambulatory setting	6 methods to identify ADEs: • Healthcare provider reports • Manual review of hospital discharge summaries • Manual review of notes from emergency department visits • Computer-generated signals • Automated review of electronic clinic notes • Manual review of incident reports	Comparison of 6 methods	Medicines-related problems
Flynn (2002)	Patients in hospital or skilled-	3 methods for identifying medication	Comparison of 3 methods	Medicines-related problems

Study	Population	Intervention	Comparison	Outcomes
USA	nursing facility	administration errors: • Incident report review • Chart review • Direct observation		
Franklin (2007) *UK*	Hospitalised patients	Data collection by the ward pharmacist	Prescribing errors reported to the hospital medication incident database	Medicines-related problems
Franklin (2009) *UK*	Hospitalised patients	4 methods for identifying prescribing errors: • Prospective data collection by ward pharmacist • Retrospective health record review • Retrospective use of trigger tool • Incident reporting	Comparison of 4 methods	Medicines-related problems
Franklin (2010) *UK*	Hospitalised patients	Trigger tool (adapted for UK use)	Retrospective health record review	Medicines-related problems
Gallagher (2011) *Ireland*	Hospitalised patients aged 65 years or older admitted via emergency department under care of a general physician	STOPP/START screening tool	Usual hospital care	Clinical outcomes
Haw (2007) *UK*	Elderly hospitalised patients (psychiatric hospital)	Direct observation	• Medication chart review • Incident reports	Medicines-related problems
Hope (2003) *USA*	Aged 18 years or older with outpatient appointments at ambulatory care clinics during a 4-month period	Tiered review to identify ADEs and medication errors	Pharmacist-based chart review	Medicines-related problems
Kaboli (2010) *USA*	Hospitalised patients admitted to an inpatient ward, and who remained there for their hospital stay	4 methods of identifying 'medication misadventures': • Physicians report • Nursing report • Patient report	Reporting system – historical	Medicines-related problems

Study	Population	Intervention	Comparison	Outcomes
		• Medical record review		
Kennedy (2004) *USA*	Community-based patients who had prescriptions dispensed in the participating community pharmacies	Reporting system – dictation system for reporting prescribing errors in community pharmacies	Reporting system – paper-based system for reporting prescribing errors in community pharmacies	Medicines-related problems
Kunac (2008) *New Zealand*	Hospitalised children and young people (under 17 years)	A multi-faceted approach using 4 methods to identify medication-related events: • Chart review • Attendance at multidisciplinary ward meetings • Interview of parents/carers (and children) • Voluntary and verbally solicited reports from staff	Hospital incident reporting system	Medicines-related problems
Olsen (2007) *UK*	Patients discharged from hospital	3 methods of identifying adverse events and potential adverse events: • Incident reports • Surveillance of prescription charts by pharmacists • Record review at discharge	Comparison of 3 methods	Medicines-related problems
Peshek (2004) *USA*	Hospitalised patients	Reporting system – nonpunitive, voicemail-based	Reporting system – paper based	Medicines-related problems
Stump (2000) *USA*	Hospitalised patients	Reporting system – standardised, nonpunitive medication error reporting system	Reporting system – historical medication error reporting system	Medicines-related problems
Tam (2008) *Hong Kong*	Primary care patients	3 methods for identifying medication misadventures: • Voluntary incident report • Chart review • Patient survey	Comparison of the 3 methods	Medicines-related problems
Weissman (2008)	Patients discharged from hospital	Post-discharge patient interviews	Medical record review	Medicines-related problems

Study	Population	Intervention	Comparison	Outcomes
USA				
Abbreviations: ADE, adverse drug event; NORGEP, Norwegian General Practice criteria; NSAID, non-steroidal anti-inflammatory drug; PIM, potentially inappropriate medicine; PINCER, pharmacist-led information technology intervention; PPI, proton pump inhibitor; START, Screening Tool to Alert to Right Treatment; STOPP, Screening Tool of Older Person's Prescription				

5.3.1 Analysis of the randomised controlled trials

The RCTs were quality assessed using the NICE methodology checklist for RCTs (see NICE guidelines manual 2012). The PINCER study (Avery 2012) was found to be of high quality. The STOPP/START study (Gallagher 2011) was found to be of low quality. The evidence across outcomes was appraised using the GRADE framework (see appendix D2.1).

Pharmacist-led information technology intervention for medication errors (PINCER)

In 1 RCT (Avery 2012), at 6-months follow-up, patients in the PINCER group were less likely to have been prescribed a non-selective non-steroidal anti-inflammatory drug (NSAID) without a proton pump inhibitor (PPI) if they had a history of peptic ulcer; a beta-blocker if they had asthma; or an ACE inhibitor or loop diuretic without appropriate monitoring, compared with the control group (see GRADE profile 1 in appendix D2.1).

At 12-months follow-up, patients in the PINCER group were significantly less likely to have been prescribed a beta-blocker if they had asthma; or an ACE inhibitor or loop diuretic without appropriate monitoring, compared with the control group. There was no significant difference between the PINCER and control group in the number of patients prescribed a non-selective NSAID if they had a history of peptic ulcer without a PPI (see GRADE profile 1 in appendix D2.1).

The results for the secondary outcomes (critical outcomes only) are shown in GRADE profile 1 in appendix D2.1.

STOPP/START tool

One RCT (Gallagher 2011) investigated use of the STOPP/START tool. There was no difference in mortality between the STOPP/START and control groups, but the study was not powered to detect a statistically significant difference. The primary outcomes measured the prevention of potentially inappropriate prescribing in elderly patients (such as inappropriate polypharmacy, use of medicines at incorrect doses and potential drug interactions) using the medication appropriateness index (MAI) and assessment of underutilisation (AOU) index.

Medication appropriateness index (MAI)

MAI evaluates each regular medicine using 10 criteria, including indication, effectiveness, correct dosage, correct directions and drug interactions. Each criterion is rated as 'appropriate', 'marginally appropriate' or 'inappropriate'. Each rating in the 'inappropriate' category receives a weighted score. A summary score of the measure of inappropriateness for each medicine is produced, ranging from 0 to 18. A total score for each patient is obtained by combining the score for each individual medicine. An improvement in MAI score means a lower score, which indicates less inappropriate prescribing.

From hospital admission to discharge, the number of patients with an improvement in MAI scores was significantly higher in the STOPP/START group (rate ratio 2.01, 95% CI 1.62 to 2.48), compared with the control group (usual pharmaceutical care). The number of patients in whom MAI scores stayed the same (rate ratio 0.56, 95% CI 0.38 to 0.81) or got worse (rate ratio 0.35, 95% CI 0.22 to 0.54) was significantly lower in the STOPP/START group, compared with the control group (see GRADE profile 2 in appendix D2.1).

Assessment of underutilisation (AOU) index

AOU identifies medicines that have been missed, despite being indicated and potentially beneficial. The outcome measure was the proportion of patients with at least 1 medication

omission detected by the AOU. An improvement in AOU means a lower score, which indicates fewer medication omissions.

From hospital admission to discharge, the number of patients with an improvement in MAI AOU scores was significantly higher in the STOPP/START group (rate ratio 3.03, 95% CI 1.90 to 4.82), compared with the control group. The number of patients in whom AOU scores stayed the same (rate ratio 0.82, 95% CI 0.73 to 0.92) or got worse (rate ratio 0.04, 95% CI 0.00 to 0.68) was significantly lower in the STOPP/START group, compared with the control group (see GRADE profile 2 in appendix D2.1).

5.3.2   Analysis of the observational studies

The observational studies were quality assessed using the relevant NICE methodology checklists for cohort studies and qualitative studies (see NICE guidelines manual 2012); 14 studies were of low quality and 2 studies were of very low quality. The studies had serious limitations, which limited the analysis, for example:

- The definitions used for medicines-related patient safety incidents varied widely across studies.
- It was not always clear if the medicines-related patient safety incident was preventable.
- Many different systems were investigated across the studies. The most frequently investigated were incident reporting systems and health records review.
- There was a lack of clarity on the terminology used to describe the interventions.
- There was variation in how the interventions were implemented. Therefore, comparison of the same intervention across different studies was not possible.
- Incident reporting systems were locally developed, for example within a hospital, and may not be reproducible in other settings. There was also variation in the methods used to report medicines-related patient safety incidents across studies.
- Other interventions, for example trigger tools, were adapted for local use and may not be reproducible in other settings.
- Quantitative data was often not presented, or not clear.
- The number of events and number of patients was very low in some studies.
- 11/16 observational studies were conducted outside the UK and may lack transferability.
- Studies were conducted in different settings; most studies were conducted in hospital settings.
- Studies were conducted in different populations and many children, young people and adults using medicines were not represented in the studies.

Because of the limitations of the available data, the GRADE framework was not considered appropriate for quality assessment of the observational studies. Therefore, a key themes matrix was used to present the key themes from the included observational studies (see table 10).

Table 10 Key themes matrix

Study	Underreporting	Multifaceted approach	Health record (chart) review	Direct observation of administration errors	Organisational culture
Chang (2010) *Taiwan*	—	Variation in PIMs identified when 6 different criteria were used	—	—	—
Field (2004) *USA*	Incident reporting was the least effective method of identifying preventative ADEs (2%), compared with 5 other methods	96% of preventable ADEs, were identified by a single method only	—	—	—
Flynn (2002) *USA*	Incident reporting was the least effective method of identifying administration errors (<1%), compared with 2 other methods	—	—	Direct observation was most effective at identifying administration errors (66%), compared with chart review (4%) and incident reports (<1%)	—
Franklin (2007) *UK*	Pharmacists indicated that they would report 4% of the prescribing errors identified by the ward pharmacist to the hospital medication incident database	—	—	—	—
Franklin (2009) *UK*	Incident reporting was the least effective method of identifying prescribing errors (1%), compared with 3 other methods	95% of prescribing errors were identified by a single method only	Health record review was most effective at identifying prescribing errors (69%), compared with ward pharmacist data collection (36%), trigger tool (0%) and incident reporting (1%)	—	—
Haw (2007) *UK*	Incident reporting was the least effective	—	—	Direct observation was most effective at	—

Study	Underreporting	Multifaceted approach	Health record (chart) review	Direct observation of administration errors	Organisational culture
	method of identifying administration errors (0%), compared with 2 other methods			identifying administration errors (26%), compared with chart review (10%) and incident reports (0%)	
Kaboli (2010) *USA*	—	Nearly 80% of all medication misadventures were identified by a single method only	Health record review was most effective at identifying medication misadventures (51%), compared with physician reports (9%), nursing reports (8%) and patient reports (11%)	—	—
Kunac (2008) *NZ*	Incident reporting was the least effective method of identifying medication-related events (<1%), compared with 3 other methods	Authors suggest a multifaceted approach is needed	Health record review was most effective at identifying medication-related events (83%), compared with voluntary staff quality improvement reporting (14.6%), parent interview (2%) and incident reports (<1%)	—	—
Olsen (2007) *UK*	Incident reporting was the least effective method of identifying unintended adverse events and potential adverse events, compared with 2 other methods	96% of unintended adverse events and potential adverse events were identified by a single method only	Health record review was most effective at identifying unintended adverse events and potential adverse events (62%), compared with pharmacist surveillance (28%) and incident reporting (10%)	—	—
Peshek (2004) *USA*	—	—	—	—	Redesign of medication error reporting system significantly increased reporting of medication errors, near misses and

Study	Underreporting	Multifaceted approach	Health record (chart) review	Direct observation of administration errors	Organisational culture
					potential errors. Characteristics of new system: • nonpunitive • voicemail-based system • written policy • clear definitions • medication safety coordinator pharmacist • summary reports used as educational tool • solutions discussed weekly and system changes implemented • confidential reports
Stump (2000) *USA*	—	—	—	—	Redesign of medication error reporting system increased reporting of medication errors more than 5-fold over 6 months. Characteristics of new system: • nonpunitive • centralised reporting to pharmacy department • unified database, managed by clinical coordinator • near misses captured and analysed • structured, 'check-box' reports, with minimal free text

Study	Underreporting	Multifaceted approach	Health record (chart) review	Direct observation of administration errors	Organisational culture
					• staff involvement Choice of reporting format best determined on individual basis
Weissman (2008) *USA*	—	Authors suggest a multifaceted approach is needed	—	—	—

Abbreviations: ADE, adverse drug event; PIM, potentially inappropriate medicine

Definitions: Medication misadventure, ADE or medication error

5.4 Health economic evidence

Summary of evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies comparing systems used for identifying, reporting and learning from medicines-related patient safety incidents with an active comparator. This identified 2789 records, of which 2767 were excluded based on their title and abstract. The full papers of 21 records were assessed and 18 studies excluded at this stage. The excluded studies and reason for their exclusion are shown in appendix C6.1.

The 3 included studies are summarised in the economic evidence profile in table 11. The included studies were cost-effectiveness analyses with health outcomes expressed in terms of medication errors, dispensing errors avoided or adverse drug events.

Avery et al. (2012) compared a pharmacist-led information technology intervention for medication errors (PINCER) with simple feedback. This study was judged to be partially applicable to the guidelines and had minor limitations.

Flynn *et al.* (2002) (a cost-effectiveness analysis study) compared interventions aimed at identifying dispensing errors: incident reporting, chart review and direct observation. This study was partially applicable to the guidance and had very serious limitations. Ordinarily, such studies would be excluded from further consideration; however, given the lack of evidence relating to this review question, the results of the study are included.

Hope *et al.* (2000) compared a tiered review system, aimed at identifying adverse drug events and medication errors, with traditional pharmacist review. This study was judged to be partially applicable to the guidelines and had potentially serious limitations. Study evidence tables for each of the included studies are shown in appendix E1.1.

Given the large variation in settings and patient population combined with a lack of data to populate a potential model, it was judged that a *de novo* economic model in this area would be unlikely to offer insight to aid decision-making.

Table 11 Economic evidence profile: identifying, reporting and learning systems

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost effectiveness	
Avery et al. (2012) (UK, CCA)	Minor limitations[1]	Partially applicable[2,3]	Study employed a simple calculation with 6-month time horizon. Intervention: PINCER; Comparator: simple feedback	£871.88	–2.90	£65.60 per error avoided	£66.53 per error avoided 12 months after intervention[4]
Flynn et al. (2002) (US, CCA)	Very serious limitations[5,6]	Partially applicable[3,7]	Observational study employing a comparative labour cost analysis. Interventions: Incident reporting and direct observation. Comparators: Chart review	Cost per dose checked: More expensive[8] £2.65[9,15]	Number of true errors[10]: -16 (less effective)[11] 283[11]	Dominated £0.01 per true error identified[12,15]	No uncertainty analysis
Hope et al. (2003) (US, CCA)	Potentially serious limitations[5,13]	Partially applicable[3,7]	Observational study employing a comparative cost analysis Intervention: Tired review system Comparator: pharmacist review	–£14,056[15]	293 adverse drug events; 458 medication errors[14]	Dominant[14]	No uncertainty analysis

[1] Modelling was undertaken over a 12-month time horizon; however it is likely that all relevant costs were captured because the intervention would need to be delivered annually

[2] The cost-effectiveness model was based on specific patients with high risk of potentially serious medical errors; this may not be generalisable to the whole population

[3] Disease-specific outcomes were used rather than QALYs

[4] No other sensitivity analyses were carried out

[5] Only labour costs included

[6] Time horizon and sources of unit costs not reported

[7] Study undertaken in USA, so costs not measured from NHS perspective

[8] Magnitude of cost difference depends upon healthcare professional carrying out incident report review. Incremental cost for incident report review by licenced practice nurse versus chart review = £3.53; Incremental cost for incident report review by registered nurse versus chart review = £2.32; Incremental cost for incident report review by pharmacy technician versus chart review = £1.24

[9] Chart review average cost=£0.43; Direct observation average cost=£3.08

[10] True errors were deviations between prescriber's orders and what was observed that were not justified

[11] Chart review true errors=17; Direct observation true errors=300; incident report review = 1.

[12] ICER can be calculated for direct observation compared with chart review: (cost of direct observation – cost of chart review)/(true errors identified with chart review – true errors identified with direct observation)

[13] Modelling was undertaken over a short time horizon and no sensitivity analysis was conducted

[14] Intervention is cheaper and identified more adverse drug events and medication errors

[15] Costs were converted into pounds sterling using the appropriate purchasing power parity

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; CCA, Cost-consequence analysis

5.5 Evidence statements

Clinical evidence

High-quality evidence from 1 RCT showed that the PINCER intervention was effective in reducing potential medicines-related patient safety incidents, compared with simple feedback.

Low-quality evidence from 1 RCT showed that the STOPP/START tool was effective in reducing potential medicines-related patient safety incidents (such as inappropriate polypharmacy, use of medicines at incorrect doses and potential drug interactions) in elderly patients discharged from hospital, compared with usual care.

Low-quality evidence from 7 studies showed that only a small number of medicines-related patient safety incidents are identified by incident reporting systems. Other interventions, such as health record review, direct observation of administration errors and pharmacist surveillance appear to be more effective in identifying medicines-related patient safety incidents.

Low-quality evidence from 7 studies showed that there is little overlap between different interventions for identifying medicines-related patient safety incidents. A multifaceted approach appears to be most effective.

Low-quality evidence from 4 studies suggests health record review was more effective in identifying medicines-related patient safety incidents, compared with other interventions.

Low-quality evidence from 2 studies that focused specifically on medication administration errors showed that direct observation was more effective than health record review or incident reporting at identifying medication administration errors in hospital (or skilled nursing facility).

Very low-quality evidence from 2 studies showed that redesigning a medication error reporting system was effective in increasing the reporting of medication errors, near misses and potential errors. Characteristics of more effective reporting systems included: nonpunitive and confidential; documented policy and clear definitions; medication safety coordinator role; regular discussion of solutions and system changes; structured reporting with minimal free text; and staff involvement.

Economic evidence

Partially applicable evidence with minor limitations from one study suggests that the incremental cost per error avoided of the PINCER system compared with simple feedback is £66.53 over 12 months.

Partially applicable evidence with very serious limitations from one study suggests that direct observation of medicines administration compared with chart review has an incremental cost of £0.01 per medication error identified, and that chart review is dominant over incident reporting.

Partially applicable evidence with potentially serious limitations from one study suggests that a tiered review system has a lower cost per adverse drug event identified (£27.12) than pharmacist review £44.58).

5.6 Evidence to recommendations

Table 12 Linking evidence to recommendations

Relative values of different outcomes	The GDG discussed the relative importance of the outcomes and agreed that mortality, medicines-related problems and patient-reported outcomes were critical for decision-making. Clinical outcomes, health and social care utilisation, planned and unplanned contacts and health and social care related quality of life were considered important for decision-making, but not critical.
	No data were available on mortality or patient-reported outcomes.
	The GDG also recognised that there is a lack of standardised definitions for outcome measures relating to medicines-related problems, such as potentially avoidable hospital admissions and re-admissions, medication errors and potentially avoidable adverse effects. Therefore, outcome measures varied widely across the studies and it was not always clear if medicines-related problems could have been prevented.
Trade-off between benefits and harms	The GDG acknowledged that reducing the number of medicines-related patient safety incidents is a high priority for organisations, health and social care practitioners and patients and the public.
	The GDG was concerned that the incidence of identifying and reporting of medicines-related patient safety incidents using local incident reporting systems was very low. The GDG was aware that many different systems for identifying, reporting and learning from medicines-related patient safety incidents were investigated in the studies. There was also local variation in how these different systems were implemented – for example, whether an electronic or paper-based system was used and what information was documented. The GDG agreed that a system that works effectively in one organisation may not be reproducible in another setting.
	The GDG agreed that patients and/or their family members or carers have an important role in identifying and reporting of medicines-related patient safety incidents. The consensus of the GDG was that health and social care practitioners should ensure that patients and/or their carers understand how to identify and report medicines-related patient safety incidents and are encouraged and supported to do so.
	The GDG recognised that not all medicines-related patient safety incidents cause the same level of harm, or potential harm, to patients. Many incidents do not cause harm, but some may have very serious consequences for the patient, including long-term disability or death. The GDG noted that the available evidence did not identify systems to promote learning from medicines-related patient safety incidents. Learning may be facilitated by local significant event audits or root cause analysis, as appropriate. The GDG agreed by consensus that learning from incidents is an essential component of an effective incident reporting system to reduce the risk of future harm to patients. The GDG agreed that all organisations should have robust and transparent processes in place for identifying, reporting, prioritising, investigating and learning from medicines-related patient safety incidents and that this should be in line with national patient safety reporting systems – for example, the National Reporting and Learning System.
	The GDG agreed that the organisational culture is important in

determining the effectiveness of a local system. The available evidence (very low quality) suggests that a blame-free culture that encourages nonpunitive reporting appears to be the most successful in promoting reporting and learning, whereas a disciplinary based system appears to be a barrier to reporting and learning. The GDG also recognised that health and social care practitioners consider reporting to be time-consuming. In addition, health and social care commissioners, providers and practitioners should ensure that identified medicines-related patient safety incidents are reported consistently and in a timely manner, in line with local and national patient safety reporting systems. The GDG agreed that organisations should explore and address barriers that may reduce reporting and learning from medicines-related patient safety incidents. Any identified barriers should be addressed – for example, in a documented action plan. Organisations should also consider applying and sharing learning from incidents that have been identified – for example, as part of continual professional development.

The available evidence (low quality) suggests that there is little overlap between different methods for identifying medicines-related patient safety incidents. Although no single method is effective, health record review appears to be more effective than other methods (low-quality evidence). Direct observation of people administering medicines appears to be more effective than health record review or local incident reporting systems at identifying medication administration errors in hospital (low-quality evidence). As the evidence was based on low-quality observational studies, the GDG could not recommend any particular methods for identifying medicines-related patient safety incidents. However, it agreed that the approach should be considered and determined locally and arrangements reviewed regularly to reflect local and national learning. The GDG agreed that a clear theme from the evidence was that organisations should not rely on a single method and that a multifaceted approach was needed.

The GDG considered the PINCER intervention. It agreed that this was a more specific way of identifying medicines-related patient safety incidents in primary care that focused on some well-recognised potential medication errors in key therapeutic areas. The GDG considered whether the PINCER intervention would apply to other healthcare settings because there is no evidence of its use outside GP practices.

The GDG agreed that there was strong evidence PINCER is effective and cost effective in reducing some well-recognised clinically important prescription and medication monitoring errors in GP practices computerised with electronic prescribing, compared with simple pharmacist feedback. The GDG agreed that simple pharmacist feedback of a known medication error did not appear to be effective in changing practice.

The GDG discussed the feasibility of implementing the PINCER intervention. It recognised that PINCER was a complex multifaceted intervention, and not just an information technology intervention. Although the evidence was strong in the primary care setting, the GDG was not able to make a strong recommendation to implement PINCER in all GP practices computerised with electronic prescribing. The considerable workload and resource implications would need to be considered, while taking account of existing systems.

The GDG agreed that the principles of a multifaceted intervention, such as PINCER may also apply to other well-recognised situations

and may help to support changes in practice. The principles of PINCER include:

- information technology support
- educational outreach with regular reinforcement of educational messages
- actively involving a multidisciplinary team, including GPs, nurses and support staff
- dedicated pharmacist support
- agreeing an action plan with clear objectives
- providing regular feedback on progress
- providing clear, concise, evidence-based information.

The available evidence (low quality) suggests that the STOPP/START tool is effective in improving the appropriateness of prescribing in elderly hospitalised patients. The effectiveness of the STOPP/START tool in other populations is not clear. The GDG was also aware that this tool was often adapted for local use and has been used during medication reviews with the aim of improving consistency. The GDG was not able to make a strong recommendation to implement the STOPP/START tool specifically, but agreed that a screening tool to identify potential medicines-related patient safety incidents may be considered locally for some patient groups. These patients may include:

- people taking multiple medicines (polypharmacy)
- people with chronic or long-term conditions
- older people.

Consideration of health benefits and resource use	The GDG considered the cost-effectiveness evidence. As the included cost-effectiveness studies reported outcomes such as cost per medication error averted, it was difficult for the GDG to make judgements around the relative cost effectiveness of the interventions, or between the different interventions. The GDG agreed that despite this limitation, the cost per error averted with the PINCER intervention appeared to be a good use of NHS resources. This was because the cost per error averted was judged low enough to justify spending to avoid errors given the cost and detrimental effects which can occur as a result of medication errors. The GDG felt that spending around £60 to avert a medical error was worth the potential health benefits and cost savings of averting errors. The GDG recognised that the remaining cost-effectiveness evidence identified for this review question had methodological limitations and was of limited applicability to this guideline.
Quality of evidence	Overall, the quality of the evidence was low or very low. The studies contributing to the evidence did not always provide adequate information. Quantitative data were often not presented, or not clear. The number of events and number of patients was very low in some studies. Therefore, the GDG developed recommendations by supplementing the evidence using their knowledge and experience.
Other considerations	The GDG recognised that the studies were conducted in different populations. Most were conducted in elderly or at-risk populations. There were very few data in children, young people and other adult users of medicines. Furthermore, studies were conducted in different settings with most studies being conducted in hospital settings. The GDG considered whether the available evidence could be extrapolated to all settings, including social care settings and include all users of medicines. The GDG agreed by consensus that in relation to identifying, reporting and learning from medicines-related patient safety incidents, the principles would apply to all people using

medicines in all settings.

The GDG recognised the importance of the National Reporting and Learning System (NRLS) although no published evidence was identified that met our inclusion criteria. The GDG was aware that 6-monthly NRLS data (1 April to 30 September 2013) showed an increase of 8.9% in the number of incidents reported compared with the same period in the previous year.

The GDG agreed that NHS England has an important role in providing advice to prevent potential incidents identified through the NRLS that may lead to harm or death. The GDG concluded by consensus that organisations should ensure that local governance arrangements for identifying, reporting, prioritising and learning from medicines-related patient safety incidents support and coordinate with national patient safety reporting systems.

The GDG was also aware that patient safety alerts relating to medicines are issued by NHS England and MHRA. The directive 'Improving medication error incident reporting and learning' required organisations to take specific actions within an agreed timeframe. These included:

- Large healthcare providers:
  o identifying a board-level director or superintendent pharmacist to oversee medication error incident reporting and learning
  o identifying a medication safety officer to support local medication error reporting and learning
  o identifying an existing or new multi-professional group to regularly review medication error incident reports, improving reporting and learning and taking action to improve medication safety locally.
- Small healthcare providers including GP practices, dental practices, community pharmacies and those in the independent sector:
  o continuing to report medication error incidents to the NRLS and taking action to improve reporting and medication safety locally, supported by medication safety champions in local professional committees, networks, multi-professional groups and commissioners.

The evidence (very low quality) suggests that local systems were more effective when there was a dedicated medicines safety coordinator pharmacist role in place, to manage the process at an operational level. To ensure that medicines safety is prioritised locally, the GDG concluded that all health and social care commissioners, providers and practitioners should ensure that national medicines safety guidance, such as patient safety alerts issued by NHS England or MHRA, are actioned within the specified or locally agreed timeframe.

5.7 Recommendations and research recommendations

Improving learning from medicines-related patient safety incidents is important to guide practice and minimise patient harm. Medicines-related patient safety incidents are unintended or unexpected incidents that are specifically related to medicines use, which could have or did lead to patient harm. These include potentially avoidable medicines-related

hospital admissions and re-admissions, medication errors, near misses and potentially avoidable adverse events.

1. **Organisations should ensure that robust and transparent processes are in place for identifying, reporting, prioritising, investigating and learning from medicines-related patient safety incidents, in line with national patient safety reporting systems – for example, the National Reporting and Learning System.**

2. **Ensure that patients and/or their family members or carers understand how to identify and report any medicines-related patient safety incidents.**

3. **Report identified medicines-related patient safety incidents consistently and in a timely manner to ensure that the safety of the patient is not compromised, in line with local and national patient safety reporting systems.**

4. **Organisations should support a 'no-blame culture' that encourages reporting and learning from medicines-related patient safety incidents.**

5. **Organisations should consider exploring what barriers exist that may reduce reporting and learning from medicines-related patient safety incidents. Any barriers that are identified should be addressed, for example, in a documented action plan.**

6. **Ensure that action is taken to reduce further risk when medicines-related patient safety incidents have been identified. Apply and share learning – for example, as part of continuing professional development.**

7. **Ensure that national medicines safety guidance, such as patient safety alerts, is actioned within the specified or locally agreed timeframe.**

8. **Consider using several methods to identify medicines-related patient safety incidents – for example, health record review, direct observation of medicines administration and patient surveys. Agree the approach locally and review arrangements regularly to reflect local and national learning.**

9. **Consider applying the principles of the PINCER intervention to reduce the number of medicines-related patient safety incidents, taking account of existing systems and resource implications. These principles include:**
   - using information technology support
   - using educational outreach with regular reinforcement of educational messages
   - actively involving a multidisciplinary team, including GPs, nurses and support staff
   - having dedicated pharmacist support
   - agreeing an action plan with clear objectives
   - providing regular feedback on progress
   - providing clear, concise, evidence-based information.

10. Consider using a screening tool (for example, the STOPP/START[3] tool in older people) to identify potential medicines-related patient safety incidents in some patient groups. These may include:

- people taking multiple medicines (polypharmacy)
- people with chronic or long-term conditions
- older people.

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[3] STOPP, Screening Tool of Older Persons' potentially inappropriate Prescriptions; START, Screening Tool to Alert to Right Treatment

6 Medicines-related communication systems when patients move from one care setting to another

6.1 Introduction

The implications of poor communication across health and social care have been well known for several years. In 2003, the Department of Health published Discharge from hospital: pathway, process and practice, which provided guidance to 'assist commissioners, practitioners and managers in their efforts to improve discharge planning'. The guidance highlights the importance of organisations and practitioners working together to meet the needs of individuals and carers and that effective communication between primary, secondary and social care is needed to ensure each individual receives the care and treatment they need. Poor communication can have a negative effect on the quality of care a patient receives, particularly when the information is about medicines.

In 2007, NICE and the National Reporting and Learning Service (part of the National Patient Safety Agency [NPSA])[4] published joint guidance Technical patient safety solutions for medicines reconciliation on admission of adults to hospital (PSG001), which is aimed at pharmacists in the hospital setting (see section 7). The aim of this guidance is to ensure that hospitals put systems and processes in place to ensure that medicines prescribed on admission to adult inpatients correspond with those that the patient was taking before admission. The details that need to be recorded include the name of the medicine(s), dosage, frequency and route of administration, and establishing those details might involve discussion with the patient and/or their carer, and the use of records in primary care. At that time there was insufficient evidence to recommend the use of particular packages or IT-based information transfer initiatives to facilitate the delivery of reconciliation of medicines at the point of admission. To support the implementation of the guidance, the National Prescribing Centre published Medicines reconciliation: A guide to implementation (2008). Hospital trusts were encouraged to apply the principles of medicines reconciliation at every point when a patient is transferred from one care setting to another; every time a transfer of care takes place it is essential that accurate and reliable information about a patient's medicines is transferred at the same time.

In 2009, Medicines adherence (NICE clinical guideline 76) reiterated the importance of good communication between health professionals when supporting patients to be involved in decisions about their medicines and medicines adherence. The guideline also provides recommendations for health professionals of different disciplines who may be managing a patient's care at any one time, including making a written report available to patients and subsequent healthcare providers that includes details of all medicines being taken and any changes to the patient's regimen each time a patient is transferred between services. Also, in this year, Safety in doses was published by the NPSA. This paper provided an overview of the analysis of 72,482 medication incidents reported to the National Reporting and Learning System (see section 5) by frontline NHS staff in acute, mental health and primary care sectors between January and December 2007. This paper further highlighted the risks of poor communication in terms of medication incidents that can occur when patients move between care settings.

In 2012, the Royal Pharmaceutical Society published Keeping patients safe when they transfer between care providers – getting the medicines right. The report includes details of core information that should be recorded when patients move from one care setting to

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[4] On 1 June 2012 the key functions and expertise of the NPSA were transferred to NHS England.

another, for example allergies, information about medicines (including name, reason for use where known, form, dose, strength, frequency or time and route), changes to medicines and any additional relevant information, such as monitoring requirements and adherence support.

The Royal Pharmaceutical Society report identifies 4 core principles for health professionals:

- 'Health care professionals transferring a patient should ensure that all necessary information about the patient's medicines is accurately recorded and transferred with the patient, and that responsibility for ongoing prescribing is clear.
- When taking over the care of a patient, the healthcare professional responsible should check that information about the patient's medicines has been accurately received, recorded and acted upon.
- Patients (or their parents, carers, or advocates) should be encouraged to be active partners in managing their medicines when they move, and know in plain terms why, when and what medicines they are taking.
- Information about patients' medicines should be communicated in a way which is timely, clear, unambiguous and legible; ideally generated and/or transferred electronically.'

The report also identified 3 key responsibilities for organisations as follows:

- 'Provider organisations must ensure that they have safe systems that define roles and responsibilities within the organisation, and ensure that healthcare professionals are supported to transfer information about medicines accurately
- Systems should focus on improving patient safety and patient outcomes. Organisations should consistently monitor and audit how effectively they transfer information about medicines.
- Good and poor practice in the transfer of medicines should be shared to improve systems and encourage a safety culture.'

In 2013, the General Medical Council published updated guidance Good practice in prescribing and managing medicines and devices. The guidance includes specific information for doctors about sharing information with colleagues, particularly when a patient's care is transferred, including 'all relevant information about their current and recent use of other medicines, other conditions, allergies and previous adverse reactions to medicines', highlighting the important of doing this for 'essential safe care'.

Poor communication about medicines when a person moves between care settings can lead to sub-optimal use of medicines and may affect the outcomes a person gets from their medicines. This review question aimed to assess the clinical and cost effectiveness of different interventions to improve these.

6.2 Review question

What communication systems are effective and cost effective in reducing suboptimal use of medicines and improving patient outcomes from medicines when patients move from one care setting to another, compared with usual care, or other intervention?

6.3 Evidence review

The aim of this review question was to review the effectiveness and cost effectiveness of communication systems specifically relating to medicines that are used when patients move from one care setting to another. This includes transfers within an organisation or from 1 organisation to another. For example, when patients:

- are admitted to hospital, or discharged from hospital to their home or other location, such as intermediate care

- are moving between levels of care in the same hospital, for example, from intensive care to a hospital ward
- are moving to or from respite care
- are changing their GP.

Because the scope of this guideline is 'medicines optimisation', communication systems that were not specifically related to medicines use when patients move from one care setting to another were not included in this review question. For example, studies that investigated the broader process of discharge planning (which has many aspects, including medicines) were excluded. However, studies that focused on medicines aspects of discharge planning were included, such as the use of a medication discharge plan.

A systematic literature search was conducted (see appendix C.1) that identified 1764 references. After removing duplicates, the references were screened on their titles and abstracts, after which 73 references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol (appendix C2.2).

Overall, 66 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C5.2.

Seven RCTs met the eligibility criteria and were included. Observational studies were not considered for this analysis (see appendix C2.2). In addition, systematic reviews identified in the literature search were also screened on their titles and abstracts, to identify any further RCTs that met the eligibility criteria. Four additional RCTs were included.

All 11 included RCTs investigated a range of medicines-related communication systems when patients move from one care setting to another, compared with usual care or another intervention. These interventions included:

- Electronic discharge summary communication.
- Medication or pharmacy discharge plan and/or follow-up support.
- Post-discharge home visit by GP and district nurse, with 2 follow-up contacts.
- Pharmacist discharge counselling and/or follow-up support.
- Medicines-related discharge planning interventions.

Available data were extracted into detailed evidence tables (see appendix D1.2) and are summarised in the table below.

Table 13 Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Balaban (2008) *USA*	Discharged from hospital	A 4-step intervention consisting of: • a comprehensive, 'user-friendly' patient discharge form provided to patients, in 1 of 3 languages • the electronic transfer of the patient discharge form to the RNs at the patient's primary care site • telephone contact by a primary care RN to the patient • PCP review and modification of the discharge-transfer plan	Usual care	• Readmission within 31 days • ED visit within 31 days • No outpatient follow-up within 21 days • Incomplete outpatient work-up recommended by doctor • Patients with 1 or more undesirable outcomes (any of the above outcomes)
Chen (2010) *Australia*	Older people, discharged from hospital	Electronic discharge summary sent by: • email • fax • post • patient hand delivery	Comparison of 4 methods	• Receipt of discharge summary by GP practice
Kunz (2007) *Germany*	Discharged from hospital	1 sentence evidence summaries appended to consultants' letters to PCP	Usual care (consultant letter)	• Discontinuation of discharge medication
Lalonde (2008) *Canada*	Discharged from hospital	MDP sent to community pharmacies and treating physicians	Usual care (MDP not sent)	• Medication discrepancies
Maslove (2009) *Canada*	Discharged from hospital	Electronic discharge summary	Dictated discharge summary	• Overall discharge summary quality (assessed using a 100-point VAS, ranging from 0 (worst) to 100 (best) • Housestaff satisfaction (VAS) • Adverse outcomes after discharge (combined end point of ED visit, readmission or death)

Study	Population	Intervention	Comparison	Outcomes
				• Attendance at outpatient follow-up tests and appointments
Nazareth (2001) *UK*	Discharged from hospital, aged 75 years and older, on 4 or more medicines	Pharmacy discharge plan (included details of medication and support required by the patient). Copy given to patient and all relevant professionals and carers. Follow-up domiciliary assessment by a community pharmacist	Usual care (standard procedures that included a discharge letter to the GP listing current medications)	• Mortality (at 3 months and 6 months) • Readmission (at 3 months and 6 months) • Outpatient department attendance (at 3 months and 6 months) • GP attendance (at 3 months and 6 months) • Number of days in hospital as % of days of follow-up • Patient satisfaction questionnaire score • Medicines adherence • Patient knowledge of prescribed medicines
Rytter (2010) *Denmark*	Discharged from hospital (aged ≥78 years)	Structured home visit by the GP and the district nurse 1 week after discharge, followed by 2 contacts after 3 and 8 weeks	Usual care	• Mortality • Readmission • Patients using prescribed medicines that GP was unaware of • Patients not taking medication as prescribed by the GP • Patient-reported outcomes – functional ability, self-rated health, patient satisfaction, patient perception that GP better informed about their hospitalisation

Study	Population	Intervention	Comparison	Outcomes
Schnipper (2006) *USA*	Discharged from hospital	Pharmacist counselling at discharge and a follow-up telephone call 3 to 5 days later	Usual care	• Preventable ADE • All ADE • ED visit or readmission • ED visit or readmission – medicines-related • ED visit or readmission – preventable medicines-related • Any medication discrepancy • Patient satisfaction • Median adherence score on previous day (IQR)
Shah (2013) *USA*	Diabetes, discharged patients	Pharmacist counselling before usual care and discharge	Usual care (diabetes education pamphlet, routine diabetes education from nurse)	Diabetes medicines adherence: • Overall adherence • 30 days after discharge • 60 days after discharge • 90 days after discharge • 120 days after discharge Other outcomes: • Mean actual follow-up visits made • Change in HbA_{1c} • HbA_{1c} at follow-up • Patients achieving HbA_{1c} target
Shaw (2000) *UK*	Discharged from hospital, from acute admission to psychiatric ward	A pharmacy discharge planning intervention consisting of: • baseline pharmaceutical needs assessment • medicines information • pharmacy discharge plan sent to their	Usual care (no additional pharmaceutical care)	• Patient knowledge about medication • Readmissions • Mean number of medication problems per patient

Study	Population	Intervention	Comparison	Outcomes
		community pharmacy		
Vuong (2008) *Australia*	Discharged from hospital, >55 years, returning to independent living	Standard care plus a home visit from a community liaison pharmacist within 5 days of discharge	Usual care (discharge counselling, provision of compliance aid, communication with primary care providers, if necessary)	• Medicines adherence • Patient self-perceived medication understanding • Patient knowledge about medication

Abbreviations: ADE, adverse drug event; ED, emergency department; IQR, interquartile range; MDP, medication discharge plan; PCP, primary care physician; RN, registered nurse; VAS, visual analogue scale

The RCTs were quality assessed using the NICE methodology checklist for RCTs (see NICE guidelines manual 2012) and the evidence across the outcomes was appraised using the GRADE framework (see appendix D2.2).

Ten RCTs were found to be of low quality and 1 RCT (Schnipper 2010) was found to be of moderate quality. All studies investigated medicines-related communication systems at the time of hospital discharge. No eligible studies were identified in other settings where patients move from one care setting to another. The number of participants and number of events was very low in many of the studies. Only 2 of the 11 RCTs were conducted in the UK and may lack transferability.

6.4 Health economic evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies comparing communication systems aimed at reducing sub-optimal use of medicines with usual care in patients moving between care settings. This search identified 1217 studies, of which 1184 were excluded based on their title and abstract. The full papers of 33 studies were assessed and all 33 were excluded at this stage. The excluded studies and a list of reasons for their exclusion are given in appendix C6.2. Two additional studies were identified and included 1 from the search for the medicines reconciliation review question (section 7) and another from the initial scoping searches.

The studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. Both included studies are summarised in table 14. The study by Chinthammit et al. (2012) included a cost-effectiveness analysis comparing pharmacist discharge counselling with usual care. This study was judged to be partially applicable to the guidance with potentially serious limitations.

The study by Karnon et al. (2009) included a cost–utility analysis comparing an intervention of current medication lists faxed from the GP practice on patient admission to hospital with no intervention. Other interventions were also considered; however, these are outside of the scope of this review question. This study was judged to be partially applicable to the guidelines and had potentially serious limitations.

The study evidence tables for the included studies are shown in appendix E1.2.

This area was not identified as an area for health economic modelling by the GDG, given the variation in practice of communication systems during patient transfer between care settings.

Table 14 Economic evidence profile – Communication systems at transfer of care

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost effectiveness	
Chinthammit et al. (2012) (US, CCA)	Potentially serious limitations[1,2,3]	Partially applicable[4,5]	Study employed a cost-effectiveness analysis over a 1-month time horizon Intervention: pharmacist discharge counselling for patients leaving hospital Comparator: no intervention	£0[6,15] −£17[7,15]	0.01 patients discharged without suffering an ADE 0.02 high risk elderly discharged without suffering an ADE	Dominant[8] Dominant[9]	48% dominant[8]; 100% dominant[9]
Karnon et al. (2009) (CUA, UK)	Potentially serious limitations[3,11]	Partially applicable[12,13]	Study employed a cost-utility analysis[14] Intervention: current medication list faxed from the GP practice on patient admission to hospital[10] Comparator: no intervention	−£1147 per 1000 prescription orders	−2.0 QALYs lost per 1000 prescription orders	Dominant (95% CI: Dominant – £623 per QALY gained)	Deterministic sensitivity analysis does not change direction of results

[1] Short time horizon may mean that not all ADEs were captured
[2] Hospital costs only following ADE included, other healthcare costs assumed to be equal
[3] The model was populated with clinical evidence that did not meet the inclusion criteria for the clinical evidence review
[4] QALYs are not used to represent health outcomes
[5] US healthcare system perspective
[6] Intervention cost minus comparator cost in all patients being discharged from hospital

[7] Intervention cost minus comparator cost in high-risk elderly patients being discharged from hospital

[8] For all patients being discharged from hospital

[9] For high-risk elderly patients being discharged from hospital

[10] Other interventions are also considered; however, these are outside the scope of this review question

[11] Where possible the best available data were used to populate the model. QALYs were calculated in a non-standard way, using NHS litigation costs, which may have overestimated the effectiveness of interventions

[12] QALYs were derived from NHS litigation claims rather than being directly reported from patients and/or carers

[13] Patients being admitted to hospital are a subgroup of the whole guideline population (all patients taking medicines)

[14] The model time horizon is not reported, but the analysis suggests that this is the time taken for 1000 prescriptions to be ordered and any adverse effects of these to be realised

[15] Costs were converted into pounds sterling using the appropriate purchasing power parity

Abbreviations: ADE, adverse drug event; QALYs, quality-adjusted life years; CCA, Cost-consequence analysis; CUA, Cost-utility analysis

6.5 Evidence statements

Clinical evidence

Low-quality evidence from 2 RCTs showed that a medicines-related communication intervention was not effective in reducing mortality, compared with usual care.

Low-quality evidence from 3 RCTs showed that a medicines-related communication intervention was not effective in reducing hospital readmission, compared with usual care. Low-quality evidence from 1 RCT showed that a post-discharge home visit by a GP and district nurse, with 2 follow-up contacts, was effective in reducing hospital readmission, compared with usual care.

Low-quality evidence from 1 RCT showed that pharmacist discharge counselling and telephone follow-up was effective in reducing medicines-related emergency department visits or hospital readmission, compared with usual care.

Low-quality evidence from 3 RCTs showed that a medicines-related communication intervention was effective in reducing outpatient follow-up attendance. Low-quality evidence from 1 RCT showed that an electronic discharge summary was not effective in reducing outpatient follow-up attendance, compared with a dictated discharge summary.

Low- to moderate-quality evidence from 4 RCTs showed that a medicines-related communication intervention was not effective in improving medicines adherence, compared with usual care.

Low- to moderate-quality evidence from 3 RCTs showed that a medicines-related communication intervention was not effective in improving patient satisfaction, compared with usual care.

Low-quality evidence from 2 RCTs showed that a medicines-related communication intervention was not effective in improving patient knowledge about medicines, compared with usual care. Low-quality evidence from 1 RCT showed that a home visit from a community liaison pharmacist was effective in improving patient knowledge about medicines, compared with usual care.

Low-quality evidence from 1 RCT showed that pharmacist discharge counselling was effective in reducing patient HbA_{1c} levels, compared with usual care, but not the number of patients achieving their HbA_{1c} target.

Economic evidence

Partially applicable evidence from one study with potentially serious limitations populated with the most relevant evidence identified following a literature review suggests that GPs faxing medication lists to hospitals on patient admission is dominant over no intervention.

Partially applicable evidence from one study with potentially serious limitations populated with the most relevant evidence identified following a literature review suggests that pharmacist discharge counselling is dominant compared with no intervention. This finding is particularly robust in high-risk older patients.

6.6 Evidence to recommendations

Table 15 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG discussed the relative importance of the outcomes and agreed that mortality, patient-reported outcomes, clinical outcomes as reported in the study, and health and social care use were critical for decision-making. A wide range of critical outcomes were measured in the studies, including patient-reported outcomes such as medicines adherence, patient knowledge, patient satisfaction and general health status. Limited data on medicines adherence showed that it may or may not be improved by additional communication systems. Practitioner-reported outcomes such as reduced workload, professional satisfaction, medicines-related problems, health and social care-related quality of life and suboptimal medicines use were considered important for decision-making, but not critical.
Trade-off between benefits and harms	The GDG was aware that the evidence identified focused on communication systems at the time of patient discharge from hospital, but recognised that there are many other situations when a patient's care transfers from 1 setting to another, including in social care settings. The GDG agreed that the principles of effective communication are the same for transfers of care in organisations, such as from 1 hospital department to another. It also acknowledged that hospital discharge is a whole systems process that covers more than medicines, but for the purpose of this guideline, only the medicine aspects will be considered.
	The GDG discussed whether the evidence could be extrapolated to other transfer of care settings and agreed that the principles of effective communication in relation to medicines would apply in all settings, but will be particularly relevant at the time of hospital discharge. The GDG was aware of existing guidance from professional bodies, including the Royal Pharmaceutical Society's Keeping patients safe when they transfer between care providers – getting the medicines right (2012) and the General Medical Council's Good practice in prescribing and managing medicines and devices (2013). The GDG agreed that relevant health professionals should be mindful of this guidance and their practice should be consistent with these principles.
	The GDG was concerned that communication about patients' medicines when they transfer from one care setting to another appears to be ad-hoc and unreliable. Even when information about medicines is communicated, it is not always dealt with in a timely way. It recognised that there is a wider communications issue that is not only related to medicines; however, this guideline focuses on medicines optimisation. The GDG agreed by consensus that patient safety must be the utmost priority and there is a risk to patient care when complete and accurate information about medicines is not transferred effectively between care providers. The GDG recognised that organisations need to make sure that systems are consistent with all medicines prescribed, especially when medicines are only prescribed from a specific setting, for example, hospital-only medicines.
	The GDG agreed that effective communication is a 2-way process, in which both parties, for example, primary and secondary care, actively share information, The GDG concluded that robust processes should be in place to ensure that complete and accurate information about medicines is transferred appropriately. This includes the sharing of information when a patient's care is transferred to another care setting, but also ensuring that information received is documented and acted upon when a patient is transferred from another care setting. The roles and responsibilities of organisations and individual people involved in this process should be clearly defined. The process should be monitored and reviewed regularly to ensure that information about medicines is shared effectively, and dealt with, when a

patient's care is transferred.

The GDG discussed who information about medicines needs to be shared with at the time of transfer of care. It agreed that the approach should be patient-centred. Information about medicines needs to be shared with patients and they should be actively involved in discussions when their care is transferred to an alternative care provider. The GDG was aware that some electronic discharge summaries can automatically produce a patient-friendly version. It concluded that care providers should discuss the medicines patients are taking when their care transfers from 1 provider to another. Patients should be provided with a complete and accurate list of medicines at the time of transfer, in a patient-friendly format that is suitable for them, for example, a patient hand-held device or 'medication passport'. This should include all current medicines and any changes to medicines, such as medicines started, stopped or dosage changed. Patients should also be encouraged to inform their GP, community pharmacist and any other relevant people that they have been in hospital, and communicate relevant information about changes to their medicines, as appropriate.

The GDG agreed that there is an inherent risk to patient safety if a GP is not aware that a patient was admitted or discharged from hospital. The GDG agreed that the GP often finds out through other communication channels. For example, if a patient is admitted through the accident and emergency department, a pharmacist may contact the GP so they can undertake medicines reconciliation. The GDG agreed that GPs also need to proactively supply relevant information when a patient has been admitted to hospital, as well as receiving relevant information about changes made to medicines at discharge.

The GDG also discussed whether information should additionally be communicated to the community pharmacist. It agreed that not all patients have a designated community pharmacy and this may not be feasible in all circumstances. However, the GDG concluded by consensus that health professionals should consider sending medicines discharge information to the patient's nominated community pharmacy for safety purposes, when possible, and in agreement with the patient. When sharing information, health and social care practitioners should take into account the 5 rules set out in the Health and Social Care Information Centre's 'A guide to confidentiality in health and social care' (2013).

The GDG concluded that there is a significant risk to patient safety if there is no, or ineffective, communication about medicines when a patient transfers from 1 care provider to another. Information should be shared routinely with patients (and/or their family members or carers, as appropriate) and their GP. Locally, care providers should consider sharing this information with other individuals, particularly the community pharmacist.

The GDG discussed how soon important information about medicines needs to be communicated when a patient's care is transferred. The GDG was aware that NICE guidance on 'Technical patient safety solutions for medicines reconciliation on admission of adults to hospital' states that medicines reconciliation within 24 hours of admission was a reasonable target to include in local policies. From the evidence identified, the GDG could not determine an optimal time in which information should be sent or received by. However, they agreed that 48 hours represented usual practice in many settings, particularly in hospital settings, but may not be appropriate or achievable in all settings. The GDG was aware of the possible resource implications, particularly in primary care. The GDG concluded that the timeframe should be considered and determined locally, depending on the needs of the particular service. However, this should be as soon as possible

after the patients move, and ideally no longer than 48 hours, to ensure that patient safety is not compromised.

The GDG was aware that the hospital discharge summary was usually the primary source of information about medicines when a patient is discharged from hospital. It was concerned that this information is often not received by the relevant care provider, usually the GP. This information is usually given to the patient to hand-deliver to their GP. The GDG agreed this was appropriate if the information was available to the patient in a patient-friendly format (see above). However, this should not be the primary, or only, means of communicating this information to the GP. The limited evidence showed that no single method was reliable in ensuring medication discharge information was received. The GDG concluded that the discharge summary should be communicated securely in the most reliable way, preferably by secure electronic communication. It was likely that multiple approaches would be needed and care providers should take steps to ensure information is received by the intended recipient(s).

The GDG reviewed the available evidence, which considered a range of communication systems compared with usual care. These were usually in addition to the usual communication of medication discharge information. The GDG discussed the interventions and recognised the complexity of some of the studies. It agreed that these additional interventions may be safer than, for example, communicating only by a single discharge letter. The limited evidence showed that some interventions in addition to communication of medication discharge information (for example, pharmacist discharge counselling, GP post-discharge visits and telephone counselling) may provide positive benefits with no evidence of harms (such as increased hospital admissions), for some patient groups (for example, patients taking multiple medicines [polypharmacy], older patients and people with long-term or chronic conditions). However, the GDG recognised that there are also considerable resource and workload implications to consider locally with additional communication systems. The GDG could not recommend specific interventions that should be implemented based on the limitations of the evidence. However, they concluded that commissioners and care providers may want to consider additional support that may optimise communication with patients at hospital discharge, such as pharmacist discharge counselling for some patient groups.

The GDG discussed what information about the patient and their medicines needs to be transferred. From the evidence identified, the GDG could not determine exactly what information should be included. However, it was aware of other publications from the Royal Pharmaceutical Society and the National Prescribing Centre (now the NICE Medicines and Prescribing Centre) that have outlined what information about medicines is needed. This helped the GDG to inform their consensus understanding in the absence of evidence The GDG discussed the use of an initial discharge letter, followed by full discharge information. The GDG agreed that the information needs to be full, accurate and complete, including all medicines taken by the patient, not just those that have been dispensed at the time of the patient's transfer of care. The GDG concluded by consensus that the following patient information about medicines is available when a patient transfers:

- details of the patient and their GP
- details of other relevant contacts identified by the patient and/or their carers (for example, their nominated community pharmacy)
- known drug allergies and reactions to medicines or ingredients, and the type of reaction experienced
- medicines the patient is currently taking, including name, strength, form, dose, timing and frequency, how the medicine is taken (route of

	administration) and what for (indication).
	• changes to medicines, including medicines started, stopped or dosage changed, and reason for the change
	• date and time of the last dose, such as for weekly or monthly medicines, including injections
	• other information, including when the medicines should be reviewed or monitored, and any support the patient needs to carry on taking the medicines
	• what information has been given to the patient and/or their family members or carers, as appropriate.
Consideration of health benefits and resource use	The GDG recognised that very limited cost-effectiveness evidence was available in this area. Many of the interventions were multi-faceted and potentially needed significant resources to implement. The 2 studies identified in the literature suggested that both pharmacist discharge counselling and GP faxing medication lists to hospitals were cost-effective uses of resources, both being cheaper and more effective than no intervention. The GDG were mindful, however, of the limitations around both studies. The GDG discussed the evidence and their experiences and felt both supported the need for robust processes for transfer of information during patient transfer of care. The resources required to implement and maintain processes for information transfer during transfer of care were judged to potentially offer significant health benefits resulting from optimal medication usage.
Quality of evidence	Only RCTs were considered for this review question, although the GDG recognised that most studies were low quality. All studies investigated medicines-related communication systems at the time of hospital discharge. No eligible studies were identified in other settings in which patients move from one care setting to another. The number of participants and number of events was very low in many of the studies. Most studies were conducted outside the UK so may lack transferability.
Other considerations	Evidence identified was focused on a single healthcare setting (hospital). The literature search aimed to identify relevant studies in social care settings but no information was found. The GDG agreed by consensus that the principles would also apply to other transfers of care across different settings.

The GDG requested that the developer contact the Health and Social Care Information Centre (HSCIC) for any information that they may hold in relation to communication systems when a patient moves from one care setting to another, which would support the decision making process when developing recommendations. The HSCIC advised that Hospital Episode Statistics (HES) data contains admissions data and reasons for admission, based on ICD10 codes. The ICD10 codes include different categories of medicines and one refers to 'non-administration of surgical or medical care'. The GDG agreed that it was not worth pursuing this data further as it would not add anything more to the decision making process. |

6.7 Recommendations and research recommendations

Relevant information about medicines should be shared with patients and/or their family members or carers and between health and social care practitioners when a person moves from 1 care setting to another, to support high-quality care. This includes transfers within an organisation (for example, when a person moves from intensive care to a hospital ward) or from 1 organisation to another (for example, when a person is admitted to hospital, or discharged from hospital to their home or other location).

11. Organisations should ensure that robust and transparent processes are in place so that:

- when a person is transferred to another care setting, complete and accurate information about medicines is shared with the appropriate provider(s), **and**

- when a person is transferred from another care setting, complete and accurate information about medicines is received, documented and acted on.

They should clearly define organisational and individual roles and responsibilities and regularly review and monitor the effectiveness of local processes (see also section on medicines reconciliation).

12. **Organisations should ensure that information about medicines is shared with the person (and/or their family members or carers as appropriate) and their GP. They should:**

   - identify when existing local systems are in place for this when a person moves from one care setting to another

   - take account of the Health and Social Care Information Centre's A guide to confidentiality in health and social care (2013).

13. **Discuss relevant information about medicines (for example medicines that have been changed) with the person and/or their family members or carers at the time of transfer, especially when they are being discharged from hospital. Give the person a complete and accurate list of their medicines, in a patient-friendly format. This should include all current medicines and any changes to medicines made during the hospital admission.**

14. **Encourage people to tell their GP, community pharmacist and any other relevant people if they have been in hospital, and to inform these people about any changes to their medicines.**

15. **Proactively share complete and accurate information about medicines in a timely way, ideally within 48 hours of the person being transferred, to ensure that patient safety is not compromised (see also recommendation 12).**

16. **Securely share relevant information about medicines in the most effective way, such as by secure electronic communication. Recognise that more than one approach may be needed.**

17. **Include all of the following in medicines discharge information when a person transfers from one care setting to another:**

   - details of the person and their GP

   - details of other relevant contacts identified by the person and/or their family members or carers (for example, their nominated community pharmacy)

   - known drug allergies and reactions to medicines or their ingredients, and the type of reaction experienced

   - medicines the person is currently taking, including name, strength, form, dose, timing and frequency, how the medicines are taken (route of administration) and what they are being taken for (indication).

   - changes to medicines, including medicines started or stopped, or dosage changes, and reason for the change

- date and time of the last dose, such as for weekly or monthly medicines, including injections
- other information, including when the medicines should be reviewed or monitored, and any support the person needs to carry on taking the medicines
- what information has been given to the person and/or their family members or carers, as appropriate.

18. **Consider sending a person's medicines discharge information to their nominated community pharmacy, when possible and in agreement with the person.**

19. **Organisations should consider additional support for some patient groups when they have been discharged from hospital, such as pharmacist counselling, telephone follow-up, GP and/or nurse follow-up home visits. These may include:**

- people taking multiple medicines (polypharmacy)
- people with chronic or long-term conditions
- older people.

7 Medicines reconciliation

7.1 Introduction

Medicines reconciliation is not a new process in relation to medicines optimisation. In 2005, the Institute for Healthcare Improvement defined medicines reconciliation as: 'the process of identifying the most accurate list of a patient's current medicines – including the name, dosage, frequency and route – and comparing them to the current list in use, recognising any discrepancies, and documenting any changes, thus resulting in a complete list of medications, accurately communicated'. This definition has been used for the purpose of this guideline. Medicines reconciliation is a different process to a medication review (see section 8).

Background

In 2007, NICE and the National Reporting and Learning Service (part of the National Patient Safety Agency [NPSA])[5] issued joint guidance Technical patient safety solutions for medicines reconciliation on admission of adults to hospital (PSG001) aimed at pharmacists in the hospital setting that included a review of the cost effectiveness of medicines reconciliation. The guidance focused on a review of patients admitted to hospital and considered the effectiveness and cost effectiveness of medicines reconciliation undertaken by both pharmacists and nurses using both standardised forms and IT-based programmes.

To support the implementation of the guidance, the National Prescribing Centre issued Medicines reconciliation: a guide to implementation (2008). The NICE and NPSA guidance aimed to reduce medication errors, which occur most commonly on transfer between care settings and on admission to hospital. The deadline for action of this guidance was December 2010. While practice in hospitals should have changed as a result of this guidance, the guidance focused on medicines reconciliation as a single process that happened only once when a patient was admitted.

When optimising a patient's medicines it is important to identify what medicines they are currently taking; this is particularly important when they move from one care setting to another. Examples of when medicines reconciliation should take place include:

- when a patient is admitted to hospital
- when a patient is discharged from a hospital admission back into primary care
- when a patient moves into a care home
- when a patient moves from one hospital ward to another.

The purpose of medicines reconciliation is to:

- make sure the right patient gets the right medicine, in the right dose and at the right time
- reduce the risk of medication errors occurring when the care of the patient moves from one care setting to another
- provide ongoing, individualised care for each patient for their medicines
- minimise confusion about a patient's medicines regime
- improve the efficiency of a service, making the best use of staff skills and time.

Historically the process of medicines reconciliation has focused on admission to hospital. However, it is widely acknowledged that the medicines reconciliation process should also happen when the patient is discharged from hospital or moves into another care setting. In a hospital setting, medicines reconciliation may involve a process to ensure that the medicines

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[5] On 1 June 2012 the key functions and expertise of the NPSA were transferred to NHS England.

prescribed in hospital reflect what the patient was taking before admission or it may be used identify what the patient was taking on another ward. In a primary care setting, medicines reconciliation involves a process to ensure that the medicines prescribed by the GP (or other prescriber) reflect what the patient was taking after discharge from hospital.

Challenge

The NICE and NRLS guidance was issued several years ago, focused on the hospital setting and was aimed at pharmacists. Within medicines optimisation, medicines reconciliation is a wider safety issue than just at admission and therefore this review question aims to consider medicines reconciliation as a continuous process, in hospital and in primary care. Medicines reconciliation is as important for patients returning back to primary care as it is for patients going into hospital, particularly when the patient may be taking many medicines (polypharmacy).

In 2009, the Care Quality Commission published a report of a national study carried out on 'Managing patients' medicines after discharge from hospital'. The study looked at what organisations were doing to ensure the safety of patients who had been discharged from hospital with a change of medication. The study showed that information shared between GP practices and hospitals when a patient moves between settings is often patchy, incomplete and not shared quick enough. Additionally, reconciliation of the patient's GP records with discharge communication is often not carried out by clinical staff, but by administrative staff. Current practice suggests that how and when medicines reconciliation is carried out varies. As care records are generally not integrated across different health settings nor across health and social care settings, seamless sharing of information continues to be a challenge.

The process of medicines reconciliation can involve many different people, including the patient, doctors (GP and hospital), non-medical prescribers, pharmacists and pharmacy technicians (community and hospital), nurses and other allied health professionals and social care staff involved in the care of the patient.

It is important that, at any point in the care pathway, a patient receives the correct medicines. This review question aimed to assess the clinical effectiveness and cost effectiveness of medicines reconciliation as an intervention to reduce sub-optimal medicines use and medicines-related patient safety incidents. The question builds further on the joint guidance issued by NICE and the NPSA in 2007 by considering medicines reconciliation at several points of the patient pathway, not just on admission to hospital.

This review question is closely linked to other review questions on:
- the effective systems for identifying, reporting and learning from medicines-related patient safety incidents in reducing medicines-related patient safety incidents
- the effective communication systems effective and cost effective in reducing suboptimal use of medicines and improving patient outcomes from medicines when patients move from one care setting to another.

7.2 Review question

What is the effectiveness and cost-effectiveness of medicines reconciliation to reduce sub-optimal use of medicines and medicines-related patient safety incidents, compared to usual care?

7.3 Evidence review

A systematic literature search was conducted (see appendix C.1) that identified 1565 references. The review protocols identified the same parameters for the review question on medication review and medicines reconciliation. Therefore a single search was carried out.

After removing duplicates the references were screened on their titles and abstracts and each included study was identified as being relevant for inclusion for review. Twenty references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol for medicines reconciliation (appendix C2.3).

Overall, 17 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C5.3.

Three studies met the eligibility criteria and were included. In addition, 5 relevant systematic reviews of RCTs and observational studies were identified. The references included in these systematic reviews were also screened on their titles and abstracts, to identify any further studies that met the eligibility criteria. One additional RCT was identified and included.

All the included 4 studies were RCTs investigating the effect of medicines reconciliation compared with usual care (see appendix D1.3 evidence tables for details). The studies were quality assessed using the NICE methodology checklists for RCTs (see NICE guidelines manual 2012).

Appraisal of the quality of the study outcomes was carried out using GRADE. When applicable, the reported outcomes from the RCTs were analysed using GRADE (see appendix D2.3 for grade profiles). The included studies were not pooled because the outcomes measures used in each study differed and the follow-up periods reported varied among the studies. All the included studies reported dichotomous data and risk ratios were used as reported in the studies or calculated to show outcome effect.

Table 16 Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Bolas (2004) *Northern Ireland*	Aged 55 years or over receiving more than 3 drugs taken regularly (not on a 'when required' basis)	Enhanced service involving community pharmacy liaison pharmacist including full medication history as one of the components	Standard clinical pharmacy service	• Mean error rates between discharge prescription and home medication
Kripalani (2012) *USA*	Adults hospitalised for acute coronary syndrome or acute decompensated heart failure	Pharmacist-assisted medication reconciliation at hospital admission and discharge	Usual care	• Number of clinically important medication errors per patient during the first 30 days after hospital discharge • Preventable or ameliorable adverse drug events • Potential adverse drug events
Nickerson (2005) *Canada*	All patients discharged on at least one medicine	Clinical pharmacist carried out medication reconciliation process by reviewing discharge prescriptions	Usual care	• Drug therapy inconsistencies and omissions • Drug therapy problems for seamless monitoring
Schnipper (2009) *USA*	All patients	Computerised medication reconciliation (admission and discharge) tool and process redesign involving physicians, nurses and pharmacists	Usual care	• Unintentional discrepancies with potential adverse drug events per patient

7.4 Health economic evidence

Summary of evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies comparing the effect of medicines reconciliation on reducing the suboptimal use of medicines and medicine-related patient safety incidents with usual care. This search (combined with the search for review question on medication review) identified 1507 records, of which 1474 were excluded based on their title and abstract. The full papers of 33 records were assessed and 31 studies were excluded at this stage. The excluded studies and reason for their exclusion are shown in appendix C6.3.

The studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. One study, a cost comparison study, was considered to be not applicable to the guidance because the results were not relevant to a current NHS context (Kilcup et al. 2013). Also, a better quality study had been included (considering health-related quality of life) that was more relevant to a UK NHS setting and considered medicines reconciliation in hospital (Karnon et al. 2009).

The included study is summarised in the economic evidence profile in table 17. In this study, a cost–utility analysis was undertaken comparing several medicines reconciliation interventions at admission with no intervention. The interventions considered were pharmacist-led reconciliation, reconciliation by a pharmacist and a pharmacy technician using a standardised form, nurse-led reconciliation using a standardised form, and pharmacist reconciliation using a computer system. Faxing a list of a patient's medicines from a patient's GP surgery was also considered, but this was judged to be outside the scope of this review question. This study was believed to be partially applicable to the guideline and had potentially serious limitations.

A study evidence table for the included study is shown in appendix E1.3.

This topic area was identified by the GDG as a priority for *de novo* economic modelling. The GDG were aware that evidence existed on the cost-effectiveness of medicine reconciliation, but that this was based on fairly outdated clinical evidence from observational studies. As medicine reconciliation was something the GDG had found useful to optimise medication use in their previous experience, the Group were interested in having an up-to-date cost-effectiveness analysis based on the best available data on which to base their recommendations. The GDG also identified this topic area as one where the data required to populate an economic model may not be too scarce. A summary of the economic modelling undertaken is provided following table 18.

Table 17 Economic evidence profile – Medicines reconciliation

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	**Effects**	**Cost effectiveness**	
Karnon et al. (2009) (UK, CUA)	Potentially serious limitations[1]	Partially applicable[2,3]	Study used a cost–utility analysis[4] Interventions (at admission to hospital): Pharmacist-led medicine reconciliation; reconciliation by a pharmacist and pharmacy technician using a standardised form; nurse-led medicine reconciliation using a standardised form; pharmacist-led medicine reconciliation using a computerised system. Comparator: No intervention	Per 1000 prescription orders: −£1105[5]; −£549[6]; £341[7]; £233[8]	QALYs lost per 1000 prescription orders: −2.2[5]; −1.5[6]; −1.9[7]; −1.7[8]	Dominant[5]; Dominant[6]; £184 per QALY[7]; £138 per QALY[8]	60% cost effective at £10,000 threshold (or above) Deterministic sensitivity analysis does not change direction of results

[1] When possible the best available data were used to populate the model. QALYs were calculated in a non-standard way using NHS litigation costs, which may have overestimated the effectiveness of interventions

[2] QALYs were derived from NHS litigation claims rather than being directly reported from patients and/or carers

[3] Patients being admitted to hospital are a subgroup of the whole guideline population (all patients taking medicines)

[4] The model time horizon is not reported. However, the analysis suggests that this is the time taken for 1000 prescriptions to be ordered and any adverse effects of these to be realised

[5] Pharmacist-led medicines reconciliation at hospital admission

[6] Reconciliation by a pharmacist and a pharmacy technician using a standardised form

[7] Nurse-led medicines reconciliation using a standardised form

[8] Pharmacist-led medicines reconciliation using a computerised system

Abbreviation: QALYs, quality-adjusted life years; CUA, cost-utility analysis

Summary of economic modelling

A summary of the modelling carried out for this area of the guidance is provided. The GDG identified medicine reconciliation as the highest priority area for original economic modelling. This was due to having sufficient data to populate the model in an area where potential costs and health benefits occurring from medication taken in error are large (see section 3.4.2).

See appendix F for a full report of the modelling carried out for this clinical guideline topic.

Methods

The decision-analytic model assessed the costs and effectiveness of medicine reconciliation based on the RCT evidence identified during the clinical evidence review using a decision tree approach. The model compared medicine reconciliation throughout a hospital stay (as described by Schnipper et al. (2009)) with usual care. The purpose of the analysis was to update the cost-effectiveness study by Karnon et al. (2009) that was identified in the cost-effectiveness review as agreed by the GDG.

Time horizon, perspective, discount rates

Costs within the analysis were considered from a UK NHS and personal social services perspective, and health outcomes were expressed as QALYs in accordance with the NICE guidelines manual. Because of the short time horizon of the model (time for prescription to be issued and any errors to materialise), discounting was not carried out, with the exception of QALY losses relating to severe harm from preventable adverse drug events (pADEs) which were discounted at 3.5% per year, consistent with the NICE guidelines manual.
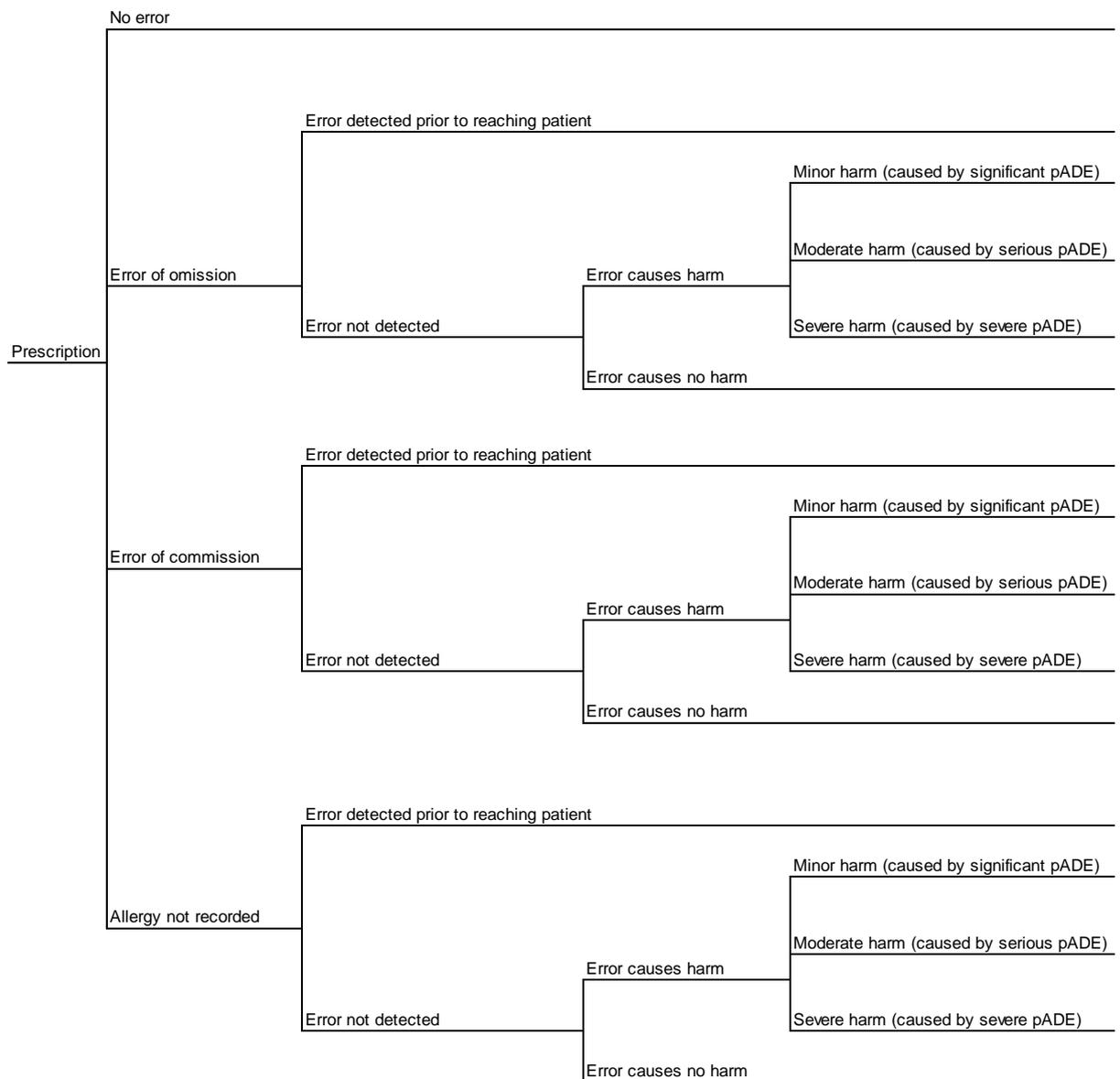
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Model structure

The structure of the model is show in figure 2 and copies the structure of the model by Karnon et al. The decision-analytic model models errors in medication following a prescription order. Each prescription order may result in either a medication error or no error. Three types of medication errors are included within the model:

- An error of omission – a required drug is not supplied;
- An error of commission – the wrong drug or dose is supplied;
- An error because of a known allergy – a drug is prescribed when it is known that the patient has an allergy to that drug.

For each error type there is a probability that the error will be detected before it reaches the patients. When errors are not detected they may cause or not cause harm. For errors causing harm, this harm is split into minor (caused by significant pADE), moderate (caused by serious pADE) or severe harm (caused by severe pADE). Costs and QALY loss were applied to pADEs that occurred.

Figure 2 Model structure (Karnon et al. 2009)

Model inputs

Full details around all of the data used within the health economic model are presented in appendix F. All model inputs and the ranges used for sensitivity analysis are provided in table 18.

Baseline error rates for errors of omission, errors of commission and errors because of known allergies were taken from McFadzean et al. (2003). Relative risk as reported by Schnipper et al. (2009) was applied to these baseline error rates in order to derive the error rate following the implementation of medicine reconciliation.

The probability of error detection before the error reached the patient for each type of error and the probability of an error causing harm to a patient was taken from Karnon et al., who

provided estimated ranges of detection rates derived from the literature. The mid-point of each range was utilised in the base case. No additional studies suitable for use within the model published since the analysis by Karnon et al. were identified.

Within the model, pADEs were split into severe (fatal or life threatening), serious or significant. The base case used proportions reported by Hug et al. (2010) in their analysis of pADE by severity in a US inpatient population. No UK-based studies were identified.

The medicine reconciliation intervention utilised in the RCT undertaken by Schnipper et al. involved reconciliation at both admission and discharge with the assistance of a computer programme. Four components of the intervention were identified: creation of a pre-admission medication list (GP-led); use of computer programme; medicine reconciliation at admission (pharmacist-led); and medicine reconciliation at discharge (nurse-led). Resource use was not reported by Schnipper et al., but was determined as accurately as possible from other sources. This was combined with unit costs of healthcare professionals (PSSRU 2013). All other costs associated with patients undergoing medicine reconciliation were assumed to be equal to usual care and were therefore not included within the model. The cost of pADE were taken from Karnon et al. and inflated to 2012/13 prices using the PSSRU pay and price index.

A literature review was undertaken in order to identify any studies reporting the utility loss associated with pADEs. The review is described in detail in the full economic modelling report (appendix F). A pragmatic search strategy was designed that incorporated three concepts: hospitalisation, adverse drug events and utilities. A range of databases and information sources were searched and 3513 unique records identified. Following a review of study titles and abstracts and application of the eligibility criteria, 3477 records were excluded. The full papers of the remaining 36 studies were considered and three studies were identified as meeting the inclusion criteria.

Rattanvipapong et al. (2013) undertook an economic evaluation of screening for carbamazepine-induced severe adverse drug reactions with utility measures reported directly from patients. The adverse drug events considered within this study were specific to a particular drug and only applicable to patients with newly diagnosed epilepsy or neuropathic pain; as such, the paper was judged not generalisable to this economic model considering all hospitalised patients taking medicines.

The two remaining papers were both by Karnon and included Karnon et al. (2009), on which this model is based. The utilities provided in each of these two papers related to adverse drug events in hospitalised patients, as required for this economic model (given the model was based on that constructed by Karnon et al.). In both studies utility estimates were derived from assumptions rather than being elicited from patients themselves. In Karnon et al. (2008), utility values were estimated through an analysis of NHS litigation payments. In the 2009 paper, both this method and estimations of QALY loss based on expert opinion were utilised. Both papers have limited validity; however, given that the 2009 paper elicited utilities via two methods, this study was considered to be slightly more robust.

Table 18 Summary of model inputs

Parameter	Point estimate	Probability distribution and Alpha where applicable	Distribution range[1]	Source
Relative risk with intervention	0.72	Lognormal	0.52–0.99	Schnipper (2009)
Baseline risk of error of omission	0.26	Uniform	0.22–0.34	Karnon (2009) and McFadzean (2003)
Baseline risk of error of commission	0.11	Uniform	0.09–0.14	Karnon (2009) and McFadzean (2003)
Baseline risk of error because of known allergy	0.05	Uniform	0.04–0.06	Karnon (2009) and McFadzean (2003)
Probability of error detection – error of omission	0.55	Uniform	0.4–0.7	Karnon (2009)
Probability of error detection – error of commission	0.35	Uniform	0.2–0.5	Karnon (2009)
Probability of error detection – error because of known allergy	0.55	Uniform	0.4–0.7	Karnon (2009)
Probability of harm from error of omission	0.006	Uniform	0.001–0.01	Karnon (2009)
Probability of harm from error of commission	0.03	Uniform	0.01–0.05	Karnon (2009)
Probability of harm from error because of known allergy	0.006	Uniform	0.001–0.01	Karnon (2009)
Proportion of severe pADE	0.2[1,2]	Dirichlet (Alpha = 22)	0–0.4	Hug (2010). Range assumed
Proportion of serious pADE	0.41[1,2]	Dirichlet (Alpha = 79)	0–0.82	Hug (2010). Range assumed
Proportion of significant pADE	0.39[1,2]	Dirichlet (Alpha = 35)	0–0.39	Hug (2010). Range assumed
Cost of medicine reconciliation per patient	£54.36	Gamma	£36 – £124	See section 2.3.2.1
Cost of detected medication error	£3.60	Uniform	£0–£7.20	See section 2.3.2.2
Cost of significant pADE	£129	Uniform	£78.01–£180.01	See section 2.3.2.2
Cost of serious pADE	£1316	Uniform	£855.66–£1780.92	See section 2.3.2.2
Cost of severe pADE	£1923	Uniform	£1302.09–£2544.18	See section 2.3.2.2

QALY loss from significant pADE	0.0045	Uniform	0.001–0.008	Karnon (2009)
QALY loss from serious pADE	0.0755	Uniform	0.061–0.09	Karnon (2009)
QALY loss from severe pADE	2.705	Uniform	1–4.41	Karnon (2009)

[1] The distribution range was used in both deterministic and probabilistic sensitivity analysis, with the exception of the proportion of type of pADE where the range provided was used for deterministic analysis only. Probabilistic sensitivity analysis for this variable used Dirichlet distribution (Briggs et al. 2006)

[2] During deterministic sensitivity analysis it was assumed that an increase in any type of pADE was complemented by a decrease in the number of patients experiencing no harm from medication errors

Abbreviations: pADE, preventable adverse drug events; QALY, quality-adjusted life year
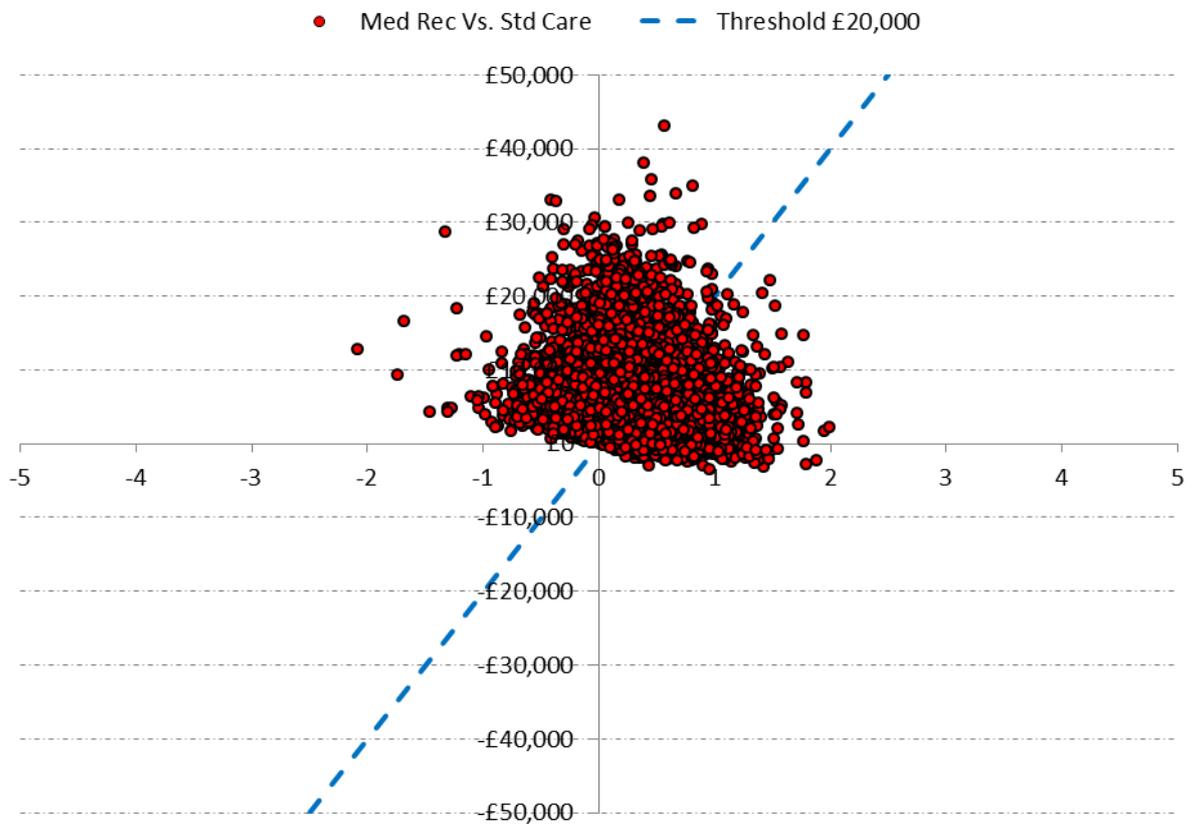
Results and discussion

The base case results show that compared with usual care, medicine reconciliation throughout a hospital stay has an incremental cost per QALY of £12,726 and a probabilistic incremental cost per QALY of £18.085. The base case results are shown in Table 19.

Table 19 Base case results

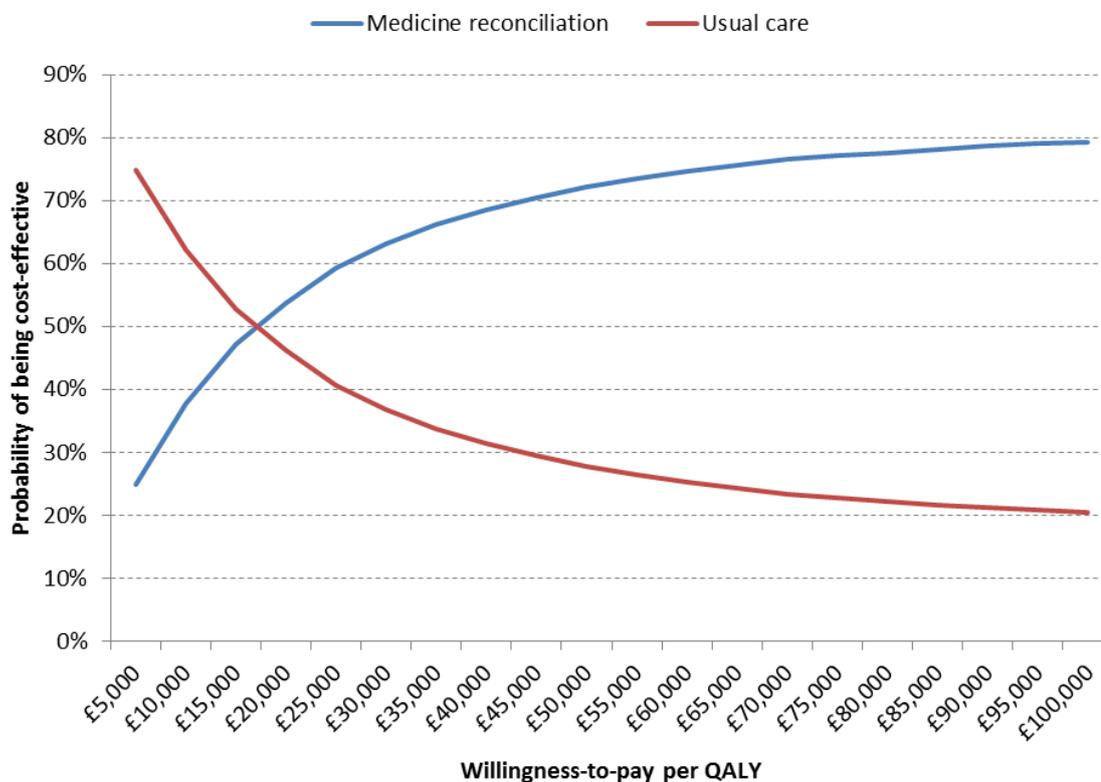|	Medicine reconciliation	Usual care
Intervention cost	£6,040	£0
pADE cost	£2,834	£3,936
Total cost (per 1000 prescription orders)	**£8,874**	**£3,936**
QALY loss (per 1000 prescription orders)	**-1.00**	**-1.39**
Incremental cost (per 1000 prescription orders)		£4,938
Incremental QALY gain (per 1000 prescription orders)		0.39
Deterministic Incremental cost per QALY		**£12,726**
Deterministic Net benefit (with threshold of £20,000)		**£2,822**
Deterministic Net benefit (with threshold of £30,000)		**£6,702**
Probabilistic Incremental cost per QALY		**£18,085**

Probabilistic sensitivity analysis found that with a threshold of £20,000 per QALY, medicine reconciliation was cost effective compared with usual care in 53.74% of iterations. This is displayed in figure 3, where the blue dotted line represents the threshold for cost effectiveness and points to the right of this line are considered cost effective. At a WTP threshold of £30,000 medicine reconciliation is cost effective compared with usual care in 63.15% of iterations. The lack of information available to inform distribution around point estimates for many parameter inputs and the fact that many of the inputs were reported in the literature as ranges meant that uniform distribution was assumed across the range. This limited the usefulness of the probabilistic sensitivity analysis.

Figure 3 Probabilistic sensitivity analysis (£20,000 threshold)

A cost-effectiveness acceptability curve (CEAC) was generated and is displayed in figure 4. The CEAC shows the likelihood that medicine reconciliation is cost effective compared with usual care as the WTP per QALY is varied. As the WTP increases, the likelihood that medicine reconciliation is cost effective also increases. Figure 4 shows that medicine reconciliation is more likely to be cost effective than not compared with usual care at a WTP threshold of around £17,000.

Figure 4 Cost-effectiveness acceptability curve

Extensive one-way and two-way deterministic sensitivity analyses were also undertaken, the results of which are reported in detail in appendix F. This identified the relative risk of medicine reconciliation to be the key driver of the model. Schnipper et al. (2009) reported a wide 95% confidence interval (0.52–0.99) around the relative risk of medication errors, and when sensitivity analysis was carried out in the model using this range, relative risk was to be a key driver of the model. Future research could provide more certainty around the effectiveness of medicine reconciliation, particularly in a UK NHS setting or in settings other than an acute setting. A number of other limitations existed around the analysis, notably a lack of UK-specific data available to populate the model. The effectiveness of medicine reconciliation and many of the baseline risks were drawn from US studies because no UK studies were identified. This limits the applicability of the results to a UK NHS setting. Further, no quality-of-life data reported directly from patients and/or their carers was identified and as such the model was populated by QALY losses determined through the use of NHS litigation payments and expert opinion.

The extensive sensitivity analysis undertaken to assess the impact of the lack of UK applicable good-quality data highlights a number of areas where further research is important. This includes collection of EQ-5D data from patients experiencing adverse drug events and UK-based RCTs comparing medicine reconciliation with usual care in various settings by various healthcare professionals.

7.5   Evidence statements

Clinical evidence

One study investigated the effect of pharmacist-led medicines reconciliation at admission and discharge in adults hospitalised with acute coronary syndrome or acute decompensated heart failure. It showed no significant difference in reducing clinically important medication errors, preventable or ameliorable adverse drug events and potential adverse drug events after the first 30 days after discharge when compared with usual care (moderate-quality evidence). Another study also investigated the effect of medicines reconciliation at admission and discharge using a hospital-based community pharmacy liaison service. It found a significant improvement (in the accuracy of medicines names and frequency of dosing) in the error rates between discharge prescriptions and medicines being taken at home 10–14 days after discharge in the intervention group compared with the control group (very low-quality evidence).

One study investigating the effect of pharmacist-led medicines reconciliation at discharge showed a significant reduction in drug therapy inconsistencies and omissions compared with usual care. However, this study used retrospective chart analysis to compare the effects of the intervention with the control group, and 28 out of the 134 charts in the intervention group were analysed compared with 119 in the control group (very low-quality evidence). This study also reported on the number of drug therapy problems for seamless monitoring (DTPsm) in the intervention group and found that 129 out of 134 patients had a DTPsm identified. Drug therapy problems were not investigated in the control group that received usual care.

One study showed that medicines reconciliation (using a computerised medicines reconciliation tool and process redesign involving physicians, nurses and pharmacists) overall significantly reduced the number of unintentional discrepancies with potential adverse drug events (PADEs) per patient compared with usual care, when carried out at discharge but not at admission. This study reported 43 PADEs in the intervention arm (0.27 per patient) and 55 PADEs in those assigned to usual care (0.34 per patient) that were considered to be serious (for example, to have the potential to cause serious harm such as rehospitalisation or persistent alteration in health function). This study also reported no significant difference in healthcare utilisation between medication reconciliation and usual care. However, the study was not powered to detect this outcome. Subgroup analysis in this study showed that the intervention was more successful in patients at high risk for medication discrepancies, based on a risk score derived from the control group (low-quality evidence).

Economic evidence

Partially applicable evidence from 1 study with potentially serious limitations built on the best available data from a systematic review suggests that pharmacist-led medicines reconciliation and pharmacy technician/pharmacist-led reconciliation using a standardised form are dominant over no intervention.

Partially applicable evidence from 1 study with potentially serious limitations built on the best available data from a systematic review suggested that nurse-led medicines reconciliation using a standardised form and pharmacist-led medicines reconciliation using a computer system are likely to be cost effective, with ICERs below £200 per QALY gained.

De novo economic modelling suggests that medicine reconciliation throughout a hospital stay appears to be a cost effective use of NHS resources; however, considerable uncertainty exists around this finding. There is no evidence to confirm whether medicines reconciliation in settings outside of the acute sector is cost effective.

No evidence was identified informing cost effectiveness of medicines reconciliation in any settings other than hospitals.

7.6 Evidence to recommendations

Table 20 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG was presented with 1 outcome for this review question, which was 'medicines-related problems'. Different outcome measures were used for this outcome – for example, mean error or potential adverse drug events. One study reported health care utilisation as an outcome, but the study was not powered to detect this outcome.
Trade-off between benefits and harms	Medicines reconciliation shows improved medicines-related outcomes (as reported in the study) over usual care in two studies that involved pharmacist-led medicines reconciliation at discharge (very low quality evidence) or multidisciplinary team (MDT) led medicines reconciliation at discharge (low quality evidence). The GDG discussed the study by Kripalani (2012) (moderate quality evidence), which showed no significant difference in medicines-related outcomes between medicines reconciliation (at admission and discharge) and usual care. They noted that although there was no statistical difference shown between the 2 groups, medicines reconciliation resulted in fewer clinically important medicines errors and potential adverse drug reactions compared to usual care. The GDG discussed the findings by Schnipper (2009) that medicines reconciliation was more effective at discharge than at admission. The GDG was aware that in practice medicines reconciliation is carried out more frequently on admission in hospitals as it would be carried out by junior (foundation) doctors who take a medication history as part of the patient's full medical history. The GDG was also aware that, there is often a dedicated pharmacy team (in most hospitals) consisting of pharmacists and pharmacy technicians to carry out medicines reconciliation at admission and also at discharge when preparing medicines for the patient to take home. The GDG went on to discuss the timeframe in which medicines reconciliation is carried out and referred to the Technical patient safety solutions for medicines reconciliation on admission of adults to hospital (NICE patient safety guidance 1). The GDG found that the guidance mentions medicines reconciliation to be carried out within 24 hours of admission and that this timeframe would be a reasonable target to include in policies. The GDG acknowledged that resources required carrying out medicines reconciliation may vary in different care settings and agreed that this may need to be determined locally. The GDG therefore agreed that in an acute setting, medicines reconciliation should be carried out within 24 hours, when a patient moves from one care setting to another such as when a patient is admitted to hospital. The GDG discussed that medicines reconciliation is a process that continues from admission to discharge and highlighted that in the hospital setting it may need to be considered differently at admission and at discharge. At admission medicines reconciliation would require information from several sources to provide the most accurate list of what the patient was taking before admission. By contrast, at discharge the sources commonly used to reconcile medicines would be the medicines chart, medical notes and final discharge prescription. Some or all of these may not involve the patient and it would be the responsibility of the hospital to provide accurate information to the patient's GP.

	The GDG discussed and agreed by consensus that medicines reconciliation may need to be carried out on more than one occasion during a hospital stay. For example, when a patient is admitted, transferred between wards or discharged. The GDG also discussed and agreed by consensus that health professionals should involve the patient and/or their family members or carers in the medicines reconciliation process, when possible, to enable any medicines they are taking to be identified, thereby helping to avoid any medicines-related harm. The GDG was aware that pharmacists and trained pharmacy technicians carry out medicines reconciliation in hospital settings. However, during out-of-hours this may not be possible. Other health professionals such as nurses may therefore need to carry it out instead, although they would need to be trained, having the knowledge and skills (competence) to do it. The GDG then went onto discuss that overall, medicines reconciliation is carried out using a collaborative approach that involves more than 1 health professional. The health professionals involved in undertaking medicines reconciliation at admission and discharge would need to be identified in the care setting. The GDG agreed that medicines reconciliation should be carried out by a trained and competent health professional, ideally a pharmacist, pharmacy technician, nurse or doctor based on their knowledge and skills (competence). Competencies include effective communication skills, and technical knowledge of processes for managing medicines and therapeutic knowledge for medicines use. The GDG discussed the evidence and agreed that medicines reconciliation should be carried out at admission and at discharge to avoid medicines-related errors occurring during transitions of care (for example, when someone is admitted to hospital from a care home). The health professionals to be involved in the process should be identified, trained and competent to carry out medicines reconciliation. The GDG discussed and agreed by consensus that organisations should consider identifying a senior, responsible pharmacist to oversee the medicines reconciliation process. The process should be determined locally and include: • organisational responsibilities • responsibilities of people involved in the process (including who they are accountable to) • individual training and competency requirements. The GDG was aware of the National Prescribing Centre 'Medicines reconciliation: A guide to implementation (2008), which includes a flowchart of 'medicines reconciliation', showing a patient admission from primary care to secondary care and also a patient discharge from secondary care to primary care (see appendix D.3 for medicines reconciliation algorithm). From this guide, the GDG was aware of the barriers that may exist to implementing medicines reconciliation effectively, for example, poor quality documentation, transfer of information when a patient moves from one care setting to another, availability of trained and competent staff, organisational and professional responsibilities and the value of involving patients in the process.
Consideration of health benefits and resource use	The GDG discussed the published cost-effectiveness evidence; this consisted of one study which suggested that medicine reconciliation at hospital admission when undertaken by a pharmacist, pharmacy technician or nurse is a cost-effective use of NHS resources. The GDG was aware that this cost-effectiveness evidence was built upon observational studies that did not meet the inclusion criteria for the clinical evidence review. The GDG considered the economic analysis undertaken for this guideline

	which estimated the cost-effectiveness of medicine reconciliation throughout a hospital stay versus usual care. The results of this model suggest that medicine reconciliation is a cost-effective use of NHS resources (deterministic ICER of around £13,000 per QALY); however, it is evident from the sensitivity analysis conducted that considerable uncertainty underpins this result. The GDG discussed the model inputs and had concerns around the quality of data used to populate the model due to a paucity of available evidence.
	The RCT data on which the economic model was built was a US study. The GDG discussed the applicability of US data to a current NHS context given that the definition of medicine reconciliation differs between the UK and the US. The GDG judged that the economic model could only be used in conjunction with evidence from the clinical and cost-effectiveness reviews and their own experiences to guide their making of recommendations. This was due to concerns around the use of US data, the paucity of other data to populate the model (notably quality of life data) and the uncertainty around the model results.
	The GDG felt that relatively low levels of resources may be required to undertake medicine reconciliation and that the health benefits of carrying out medicine reconciliation are likely to outweigh use of these resources. Health benefits include both reduction in medication errors and subsequent problems as well as optimising medication for patients and therefore providing better treatment. The GDG were aware that the medicine reconciliation intervention reported in the RCT used in the de novo economic modelling was a robust process taking place at many stages of a hospital stay. They discussed that a less thorough intervention, for example medicine reconciliation at hospital discharge only is likely to have lower costs than that included in the economic modelling. The effectiveness and therefore health benefits of a less thorough intervention are likely to be reduced, also, but perhaps to a lower magnitude.
	The combined evidence from the clinical and cost-effectiveness reviews, modelling and GDG experiences allowed the GDG to recommend the use of medicine reconciliation during a visit to secondary care, notably when the patient moves between care settings. The GDG was unable to use the economic evidence to make judgements around which health professionals should undertake medicine reconciliation, but deemed this should be determined locally.
Quality of evidence	The included studies looking at the effectiveness of medicines reconciliation were carried out in adults and in a hospital setting. There were no RCTs identified in children or in primary care. The GDG discussed that there are several observational studies that looked at the effectiveness of medicines reconciliation in children where medicines-related discrepancies are mainly identified by medicines reconciliation than usual care.
	One study was carried out in Northern Ireland, 2 studies were carried out in the USA and 1 study was carried out in Canada. All but 1 study had a small study size. Interpretation of the findings of all of the studies was complicated because of different definitions of medication error, lack of a gold standard for correct medicines, and other methodological flaws in study design. The GDG was aware of the limitations relating to the applicability of some of these studies to the UK setting given the differences in healthcare systems and processes and populations.
	The GDG discussed that medicines reconciliation helps to identify unintentional discrepancies that may otherwise be unresolved. Also, RCTs are difficult to conduct solely for medicines reconciliation. This is because it would be difficult to identify any discrepancies in the control group without

	themselves undergoing medicines reconciliation to compare with the intervention group.
Other considerations	NICE has published guidance on medicines reconciliation: [Technical patient safety solutions for medicines reconciliation on admission of adults to hospital](#) (NICE patient safety guidance 1). The GDG discussed that medicines reconciliation would be beneficial in primary care – for example, when a patient has been discharged from the hospital and their GP receives the discharge summary and reconciles medicines before the next prescription is requested. The GDG discussed the importance of this in great detail and the following points were considered: • Medicines reconciliation may be part of a wider process within primary care. • Medicines reconciliation in primary care may trigger the need for a medicines review. • The GP may not be aware that their patient has had their medicines reconciled during the transition of care and it may be useful for the GP to know if medicines reconciliation has been undertaken at the point of discharge and what it involved. • The content of discharge summaries varies and may limit medicines reconciliation in primary care. The GDG discussed that a minimum data set would need to be considered when compiling discharge summaries and explaining any changes to medicines. The General Medical Council provides doctors with guidance on what should be included in care records. The GDG agreed that discharge information of medicines needs to reflect what medicines the patient is taking and not just those supplied by the pharmacy. • The time taken for the discharge summary to reach the GP varies, and this may limit medicines reconciliation being carried out in a timely manner. The GDG discussed and agreed by consensus that medicines reconciliation in primary care should be carried out as soon as is practically possible. It should be before a prescription or new supply of medicines is issued and no more than 1 week after the GP practice receives the information so that any medicines-related errors can be identified and to ensure patient safety. • The Care Quality Commission published a report based on a study 'Managing patients' medicines after discharge from hospital' (2009), based on how well patients' medicines are managed after leaving hospital. In addition, the GDG discussed undertaking medicines reconciliation for patients who attend day care or respite care – for example, when patients attend for the first time and to consider making suitable arrangements for patients who attend frequently. The GDG considered the use of a medicines reconciliation form to record all the relevant medicines-related information required at admission that would form part of the patient's medical record. The content of these forms may be determined locally. The GDG discussed and agreed by consensus that health professionals carrying out medicines reconciliation should consider recording relevant information on a locally determined electronic or paper-based form (see section medicines-related communication systems). The GDG discussed the recommendations from [Managing medicines in care homes](#) (NICE social care guideline 1) (recommendations 1.7.1-1.7.3), which sets out a list of information required to reconcile medicines that could be used. The GDG was aware that this may be covered in the review question that looks at communication between transitions of care within the guidance. The GDG discussed medicines use reviews (MURs). They agreed that these may support the medicines reconciliation process for patients who have

recently been discharged from hospital.

Some organisations have started an 'in-reach' programme to undertake medicines reconciliation before discharge, such as a community pharmacy liaison service.

The GDG discussed that hospitals request information from the GP when a patient is admitted to hospital, and hospitals also send out information to GPs at discharge. They should have systems and processes in place to ensure that accurate information is communicated and recorded. This also applies to GP practices providing information relating to medicines when their patients are undergoing elective admission to hospital. The GDG mentioned that access to and the use of summary care records would facilitate medicines reconciliation.

The GDG requested that the developer contact the Health and Social Care Information Centre (HSCIC) for information that they may hold for medicines reconciliation to identify if this information would support the decision making process when developing recommendations. The HSCIC provided a response that stated that they do not currently hold data that would directly answer this question. They also stated 'The key data set based on care provided by hospitals is the Hospital Episode Statistics (HES). This is a very detailed data set, but does not include information about prescribing or medicines administered in hospital. We understand that some hospital collect this data locally, though often for a limited number of wards and settings.'
The GDG also agreed that requesting further general information from the HSCIC would not support the decision making process when developing recommendations for this review question as information would not be specifically related to medicines use.

7.7 Recommendations and research recommendations

Medicines reconciliation is the process of identifying the most accurate list of a person's current medicines and comparing them to the current list in use, recognising any discrepancies, and documenting any changes, thereby resulting in a complete list of medications, accurately communicated. The medicines reconciliation process will vary depending on the care setting that the person has just moved into (for example, from primary care into hospital, or from hospital back to a care home). Algorithms have been produced to show the different processes.

20. **In an acute setting, accurately list all of the person's medicines (medicines reconciliation) within 24 hours, when they move from one care setting to another – for example, when they are admitted to hospital.**

21. **Recognise that medicines reconciliation may need to be carried out on more than one occasion during a hospital stay – for example, when a person is admitted, transferred between wards or discharged.**

22. **In primary care, carry out medicines reconciliation for all people who have been discharged from hospital. This should happen as soon as is practically possible, before a prescription or new supply of medicines is issued and no more than 1 week after the GP practice receives the information.**

23. **Organisations should consider identifying a senior, responsible pharmacist to oversee the medicines reconciliation process. The process should be determined locally and include:**
    - organisational responsibilities
    - responsibilities of people involved in the process (including who they are accountable to)
    - individual training and competency needs.

24. **Ensure that medicines reconciliation is carried out by a trained and competent health professional – ideally a pharmacist, pharmacy technician, nurse or doctor – with the necessary knowledge, skills and expertise including:**
    - effective communication skills
    - technical knowledge of processes for managing medicines and
    - therapeutic knowledge on medicines use.

25. **Involve patients whenever possible in the medicines reconciliation process. If the person agrees, or is unable to be involved, include their family members or carers.**

26. **When carrying out medicines reconciliation, record relevant information (see section medicines-related communication systems) on an electronic or paper-based form.**

8 Medication review

8.1 Introduction

Medication review, as an overarching term, has been considered to be an important intervention for many years. Medication review can have many different meanings. It could be a review of medicines carried out every day when a prescriber sees a patient and there is a decision to prescribe or stop a medicine, or a multidisciplinary medication review, with the patient (and their family members or carers) present, using a comprehensive and structured approach supported by the patient's full medical records.

As early as 2001, the National Service Framework for older people included a milestone stating that 'all people over 75 years should normally have their medicines reviewed at least annually and those taking four or more medicines should have a review 6 monthly'. The National Service Framework (NSF) did not provide information as to what this medication review should entail and how it should be carried out. To support the implementation of this milestone, it was incorporated into the General Medical Services Quality and Outcomes Framework (QOF) from 2006 until 2013.

Room for review – a guide to medication review: the agenda for patients, practitioners and managers was published by the Taskforce on Medicines Partnership, The National Collaborative Medicines Management Services programme in 2002. This document suggested key principles for the process of medication review:

- All patients should have a chance to raise questions and highlight problems about their medicines.
- Medication review seeks to improve or optimise impact of treatment for an individual patient.
- The review is undertaken in a systematic way, by a competent person.
- Any changes resulting from the review are agreed with the patient.
- The review is documented in the patient's notes.
- The impact of any change is monitored.

This document, along with a subsequent National Prescribing Centre document A guide to medication review (2008), aimed to clarify the different types of medication review. Box 1 summarises the different types of medication review, adapted from Room for Review (2002) and A guide to medication review (2008).

Box 1 Different types of medication review

Level 0
- Unplanned, opportunistic, unstructured review
- Patient may or may not be present
- May or may not involve a health professional
- Example: may be a single question about a medicine

Level 1 – Prescription review
- Review of medicines without the patient's full medical notes, may not include a review of the full repeat prescription
- Patient may or may not be present
- Usually involves a single health professional
- Example: a medicines use review

Level 2 – Concordance and compliance review
- Review of medicines with the patient's full medical notes

- Patient often not present
- Usually involves a single health professional
- Example: review of medicines for a particular condition such as asthma

Level 3 – Clinical medication review
- Full structured, medication review with the patient's full medical notes
- Patient present
- Can be a single health professional or multidisciplinary
- Example: review of all medicines prescribed

In 2005, the National Service Framework for long-term conditions recommended in its quality requirement 1 that 'people have timely, regular medication review'. Again there were no specific details about what this medication review entailed.

The National Prescribing Centre issued A guide to medication review (2008), which gave further guidance for medication reviews to commissioners and providers of services. This document further emphasised the need to involve patients in discussions about their medicines and stated that patients 'had a varied experience of the review and varied perceptions of its benefits'.

In 2013, the GMC issued updated guidance for Good practice in prescribing and managing medicines and devices. The updated guidance provides more detailed advice on how to comply with the principles outlined in the GMC document Good medical practice (2013). The guidance considers the process of reviewing medicines, and suggests that reviewing medicines is particularly important for patients who may be at risk, who are frail or who have multiple illnesses (which may increase polypharmacy). It is also important for those patients who are taking medicines with potentially serious or common side effects or those taking controlled drugs or other medicines that may be abused or misused. Reviewing medicines that require regular monitoring or blood tests is also important. The guidance also considers the role that pharmacists can play in medication review to 'help improve safety, efficacy and adherence in medicines use, for example by advising patients about their medicines and carrying out medicines reviews'.

Over the years the process of medication review has evolved, but it is not a new approach. It can be carried out in a wide range of settings and the type and depth of medication review carried out varies. The type of health professionals who carry out medication reviews has also changed, with the changing medical model of prescribing, supplying and administering medicines (see section on medicines-related models of care). Regardless of which health professional is carrying out the medication review, there appears to be variation in how and when reviews are carried out.

Furthermore it is important to consider the cost of medication reviews to the NHS. Cost-effectiveness analyses of medication review have been carried out over a number of years, often alongside RCTs or other clinical studies. Costing studies for medication reviews have been carried out in several different countries. Such analyses calculate the costs of performing medication reviews and some aim to determine the subsequent costs and health benefits of the intervention.

Medicines use reviews are different from medication reviews because the pharmacist carrying out the review does not have access to the patient's medical records. A medicines use review can complement a medication review. Information about medicines use reviews is available on the Royal Pharmaceutical Society website. In addition to medicines use reviews, community pharmacists also provide a new medicines service to support people with long-term conditions who are newly prescribed a medicine to improve adherence. Several other NICE guidelines recommend carrying out a medication review. Again in many of the

guidelines details about how the medication review should be carried out, who should be involved and the overall process are not specified.

For the purpose of this guideline when the term medication review is used, this is 'a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste' (National Prescribing Centre 2008).

Medication reviews can be offered at different levels, by different health professionals working in different settings. Therefore the aim of this review question was to review whether the evidence for a full, structured medication review led to a reduction in suboptimal use of medicines and medicines-related safety incidents.

8.2 Review question

What is the effectiveness and cost-effectiveness of medication reviews to reduce sub-optimal use of medicines and medicines-related patient safety incidents, compared to usual care?

8.3 Evidence review

A systematic literature search was conducted (see appendix C.1), which identified 1565 references. The review protocols identified the same parameters for the review question on medication review and medicines reconciliation. Therefore a single search was carried out. After removing duplicates, the references were screened on their titles and abstracts and each included study was identified as being relevant for inclusion for review question on medicines reconciliation or medication review. Sixty-five references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol for medication review (appendix C2.4).

Overall, 52 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C5.4.

Thirteen studies met the eligibility criteria and were included. In addition, 7 systematic reviews of studies (RCTs and observational) were identified. The references included in these systematic reviews were also screened on their titles and abstracts, to identify any further studies that met the eligibility criteria. Fifteen additional studies were included.

All the included 28 studies were RCTs investigating the effect of medication reviews compared with usual care (see appendix D1.4 evidence tables for details). The studies were carried out in an adult population; there were no studies identified that looked at medication reviews in children. Twelve of the studies targeted medication reviews for patients with long-term conditions such as hypertension, angina, asthma, hyperlipidaemia, diabetes, coronary heart disease, arthritis and osteoporosis. Twenty-one RCTs looked at pharmacist-led medication review, six RCTs looked at multidisciplinary team-led medication review and one RCT looked at physician-led medication review.

The studies were quality assessed using the NICE methodology checklists for RCTs (see NICE guidelines manual 2012). Appraisal of the quality of the study outcomes was carried out using GRADE.

See appendix D1.4 for evidence tables summarising included studies.

See appendix D2.4 for GRADE profiles.

There was some pooling of studies, although this was limited because the outcomes measures used differed and the follow-up periods reported varied between the studies.

Mean differences were calculated for continuous outcomes and odds ratios for binary outcomes, as well as the risk ratios for dichotomous data. When a meta-analysis was possible, a forest plot was presented (see appendix D2.4).

Table 21 Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Allard (2001) *Canada*	Age 75 years and over, living in the community, taking 3 or more medicines per day	Medication review by physicians, pharmacist and nurse	Usual care	• Number of PIPs • Number of patients with at least one PIP • Global assessment of any change in the medicines pre- and post-intervention
Armour (2007) *Australia*	Aged 18–75 years with asthma	Intervention pharmacies providing Pharmacy Asthma Care Program involving an ongoing cycle of assessment, goal setting, monitoring and review	Usual care	• Change in overall asthma severity/control • Spirometric parameters over the course of the study • Adherence to preventer medications • Use of a combination of reliever and preventer medicines with or without a long-acting beta-2-agonist as opposed to a reliever only
Barker (2012) *Australia*	Mean age of 72 years with congestive heart failure	Pharmacist-directed post-discharge home medication review	Usual care	• Number of days of all-cause and CHF hospitalisations in 6-month follow-up
Bond (2007) *Scotland*	Aged 65 years and under with angina and hypertension	Pharmacists conducted a single review of the patient medical records, and recommended changes to GP	Usual care	• Prescribing appropriateness of cardiovascular medicines
Bouvy (2003) *Netherlands*	Mean age 69 years	Pharmacist-led structured interview of the patient	Usual care	• Compliance • Mortality
Bryant (2011) *New Zealand*	Aged 65 years or older and on 5 or more prescribed medicines	Comprehensive pharmaceutical care plan medication review	Usual care	• Medication Appropriateness Index • Number of inappropriate medicines
Furniss (2000)	Residents in nursing care homes	Medication review by pharmacist	Usual care	• Mortality

Study	Population	Intervention	Comparison	Outcomes
England	with a mean age of 78.9 years in intervention group and 83.5 years in control group	in the nursing home, GP surgery or under exceptional circumstances over the telephone		
Hay (2006) *England*	Aged 55 years and over with knee pain, stiffness, or both	Enhanced pharmacy review	Usual care	• Change in Western Ontario and McMaster Universities osteoarthritis index • Participants' global assessment of change compared with baseline • Severity of pain over the previous 7 days • Severity rating of patient nominated main functional problem over the previous 3 days • Participants' self-efficacy (arthritis self-efficacy scale) • Psychological distress (hospital anxiety and depression scale) • Treatment usefulness and satisfaction
Holland (2005) *England*	Aged 80 years or over admitted as an emergency	Home-based medication reviews carried out by pharmacists	Usual care	• Mortality
Holland (2007) *England*	Adults with mean age of 85 years with heart failure	Pharmacists reviewed medicines and gave symptom self-management and lifestyle advice	Usual care	• Mortality • Medicines adherence and behaviour change
Jamieson (2010) *England*	Mean age of 59 years with a diagnosis of hypertension (and other comorbidities) and receiving antihypertensive medicines	Practice-based pharmacist providing level 3 medication review to hypertensive patients	Usual care	• Change in blood pressure
Krska J et al. 2001 (Scotland)	Mean age of 65 years with at least 2 chronic diseases	Pharmacist-led medication review	Usual care	• Pharmaceutical care issues
Lenaghan (2007) *England*	Aged 80 years living in their own homes	Home-based medication review by a pharmacist	Usual care	• Mortality • Number of medicines prescribed
Mannheimer (2006)	Mean age of 71 years in hospital for less than 24 hours	Nurse and clinical pharmacologist review of	Usual care	• Mortality • Frequency of medicines-related problems

Study	Population	Intervention	Comparison	Outcomes
Sweden		medicines (hospital-based medication review)		
Mehuys (2008) *Belgium*	Aged 18–50 years with asthma	Pharmacist-led medication and asthma review	Usual care	• Level of asthma control • Patient's peak expiratory flow • Rescue medication use • Night-time awakenings due to asthma • Inhalation technique • Severe exacerbations • Adherence to controller medication
Planas (2009) *USA*	Aged 18 years or over with hypertension or on antihypertensive therapy	Pharmacist-led medication therapy management programme	Usual care	• Blood pressure control • Antihypertensive medication adherence
Schmader (2004) *USA*	Aged 65 years or over, hospitalised on a surgical or medical ward	Geriatrician, nurse, social worker and a pharmacist reviewed the medicines	Usual care	• Adverse drug reactions • Suboptimal prescribing
Sellors (2003) *USA*	Aged 65 years or over	Structured medication assessment by the pharmacist	Usual care	• Reduction in the daily units of medication taken (as a surrogate for optimised medicines therapy)
Sjoberg (2013) *Sweden*	Aged 65 or over at the time of the fracture	Medication reviews, performed by a physician	Usual care	• Changes in treatment with fracture-preventing and fall-risk-increasing medicines 12 months after discharge • Falls • Fractures • Mortality
Spinewine (2007) *Belgium*	Aged 70 or over	Pharmaceutical care provided from admission to discharge by a specialist clinical pharmacist	Usual care	• Appropriateness of prescribing • Unnecessary use of medicines • Death rate • Emergency visits • Patient satisfaction with information received

Study	Population	Intervention	Comparison	Outcomes
Sturgess (2003) *Northern Ireland*	Community-dwelling elderly patients aged 65 years or over	Pharmacy intervention involved education on medical condition, compliance strategies, medicines rationalisation, and appropriate monitoring	Normal pharmacy services	• Sign and symptom control • Patient knowledge of medicines • Compliance • Patient satisfaction • Types of patient problems identified during the study • Number of changes in medicines • Problems with medicines
Sorensen (2004) *Australia*	Adults mean age 45 years with comorbidities, polypharmacy and at risk of medicines-related problems	The multidisciplinary service model	Usual care	• Satisfaction • Reporting of medications-related problems • Severity of illness
Taylor (2003) *USA*	Aged 18 years or over	Usual medical care plus pharmaceutical care that included medication review	Usual care	• Diabetes, blood pressure, dyslipidaemia, and anticoagulation control • Patient satisfaction • Compliance • Prescribing appropriateness and medication misadventures
Community pharmacy medicines management project evaluation team (2007) *England*	Adults with CHD	Pharmacist consultations	Usual care	• Proportion of patients receiving secondary prevention treatment for CHD in accordance with the NSF (2000) • 5-year risk of cardiovascular death • Patient satisfaction • Compliance
Villeneuve (2010) *Canada*	Aged 18 years or over and a candidate for statin monotherapy or already receiving statin monotherapy with inadequate control	Physician and pharmacist-led medication review	Usual care	• Change in LDL cholesterol level • Proportion of patients achieving their target lipid levels • Changes in other risk factors for cardiovascular disease after 12 months of follow-up

Study	Population	Intervention	Comparison	Outcomes
				• Use of lipid therapy
Vinks (2009) *Netherlands*	Aged 65 years or over and using 6 or more medicines	Medication review by the pharmacist	Usual care	• Change in the number of potential medicines-related problems • Change in the number of medicines
Zermansky (2001) *England*	Aged 65 years or over and receiving at least one repeat prescription	Pharmacist-led medication review	Usual care	• Number of changes to repeat prescriptions over 1 year
Zermansky (2006) *England*	Residents in care homes aged 65 years or over taking one or more repeat medicines	Clinical medication review conducted by a pharmacist	Usual care	• Number of changes in medicines per resident • Number of repeat medicines per resident • Medication review rate • Mortality • Falls
Abbreviations: CHD, coronary heart disease; CHF, congestive heart failure; NSF, National Service Framework; PIPs, potentially inappropriate prescriptions				

8.4 Health economic evidence

Summary of evidence

A systematic literature search was undertaken (appendix C.1) to identify cost-effectiveness studies comparing medication reviews to reduce the suboptimal use of medicines. This search identified 1507 results, of which 1480 records were excluded following screening of their titles and abstracts. The full papers of 27 studies were assessed for relevance against the inclusion and exclusion criteria. Sixteen studies did not meet the inclusion criteria, the reasons for which are listed in appendix C.6.4. A further 3 studies were identified as relevant from the clinical evidence review, resulting in a total of 14 studies meeting the inclusion criteria.

The studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. Following this, four studies were judged not applicable to the guidance because better quality studies (considering health-related quality of life), more relevant to a UK NHS setting, had been identified. An additional study (Burns et al. 2000) was judged by the GDG to be not relevant to the current UK NHS because of the age of the study. This study was a cost comparison study with a short time horizon and therefore evidence more relevant to the decision problem had already been included. These five studies judged not applicable to the guidance were excluded from further analysis. Three further studies were considered to have very serious limitations and were excluded on that basis.

Table 22 shows the economic evidence profile based on the 6 included studies. These studies were judged to be partially relevant to the guidance. The evidence was of variable quality: 4 of the 6 included studies were of low quality and 2 were of high quality. The economic evidence on medication review was limited to review by pharmacists in different settings with no analysis beyond a 12-month time horizon (appendix E1.4).

A health economic model was not pursued in this area because of the lack of data on medication reviews carried out by health professionals other than pharmacists. There is already an evidence base of published cost–utility studies relating to pharmacist review, so the GDG judged that a *de novo* model in this area would not help their recommendations. The limited data availability relating to other types of medication review meant that a robust economic model could not be constructed. To aid the GDG discussions a simple costing analysis was undertaken to compare the costs of medication reviews undertaken by a variety of healthcare professionals. A summary of this is provided after Table 23.

Table 22 Economic evidence profile – medication reviews

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	**Effects**	**ICER**	
Bond et al. (2007) (UK, CCA)	Potentially serious limitations[1,2]	Partially applicable[3,4]	Study employed cost consequence calculations based on a clinical study with a 12-month time horizon Intervention: pharmacist medical review Comparator: no review	£43.36	Equal[5]	Cost incurring[6]	No analyses carried out
Desborough et al. (2012) (UK, CCA)	Potentially serious limitations[10,11]	Partially applicable[3]	Before and after study employing cost consequence calculations over a 6-month time horizon Intervention: pharmacist medical review in the home Comparator: no review	−£307	0.015[12]	Dominant[12]	Sensitivity analyses around cost inputs resulted in intervention always being dominant[12]
Pacini et al. (2007) (UK, CUA)	Minor limitations[13,14]	Partially applicable[3,15]	Cost-utility analysis with a 6-month time horizon Intervention: pharmacist medical review in the home Comparator: no review	£407	0.0075	£54,454	25% probability of being cost-effective at £30,000 per QALY threshold. Scenario analysis resulted in ICER generally above £30,000

Sellors et al. (2003) (Canada, CCA)	Potentially serious limitations[1,7,16]	Partially applicable[3,4]	An RCT including cost consequence over a 5-month time horizon Intervention: pharmacist medical review Comparator: no review	£155[22]	Equal[17]	Cost incurring[11]	Scenario analysis of costs with only drug-related hospital stays included results in intervention being cost saving
The Community Pharmacy Medicines Management Project Evaluation Team 2007 (UK, CUA)	Potentially serious limitations[12,19]	Partially applicable[3,18]	An RCT with cost-utility analysis over a 12-month time horizon Intervention: medical management including pharmacist medical review Comparator: no review	£90	Equal	Cost-incurring[11]	No analyses carried out
Wallerstedt et al. (2012) (Sweden, CUA)	Minor limitations	Partially applicable[3,20]	Study employed cost-utility analysis. Intervention: pharmacist medical review Comparator: no review	£1378[22]	0.0051	£261,587[21,22]	20% probability cost effective at £42,465 threshold. No sensitivity analysis changed direction of results

[1] The study was primarily a clinical study with some health economic considerations included. No sensitivity analyses were included

[2] Some of the intervention costs were omitted

[3] The study population was a subgroup of the overall guidance population

[4] QALYs were not considered within the evaluation

[5] Intervention and control groups had no difference in EQ-5D results

[6] This was not reported, but can be calculated from higher cost and equal efficacy

[7] Sensitivity analysis was limited

[8] Some costs were not from an NHS/PSS perspective

[9] Study was a costing study only with no outcomes considered

[10] Primary care costs are omitted

[11] The model was populated with clinical evidence that did not meet the inclusion criteria for the clinical evidence review

[12] Calculated from the information provided in the study

[13] Sometimes unclear where all unit costs were sourced from

[14] Assumptions made without justification and some costs excluded without justification

[15] Perspective is not provided

[16] An Ontarian (Canadian) healthcare system perspective is taken

[17] Intervention and control group had no significant difference in SF-36 scores

[18] The intervention included reviews of patient's medicine compliance and lifestyle as well as medications

[19] No uncertainty analysis was carried out

[20] Swedish healthcare system perspective

[21] This cannot be replicated exactly from incremental cost and effectiveness because of rounding

[22] Costs were converted into pounds sterling using the appropriate purchasing power parity

[19] No uncertainty analysis was carried out

[20] Swedish healthcare system perspective

[21] This cannot be replicated exactly from incremental cost and effectiveness because of rounding

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; RCT, randomised controlled trial; CUA, Cost-utility analysis; CCA, cost-consequence analysis.

Summary of economic modelling

A summary of the simple cost analysis carried out for this area of the guidance is provided. See appendix F for a full report of the cost analysis carried out for this clinical guideline topic.

Summary

Simple costing calculations were carried out to provide the GDG with information around the cost per medication review undertaken dependent upon the healthcare professional delivering the review. These are displayed in Table 23. The length of time utilised for each medicine review was estimated by the GDG and various scenarios are displayed. Healthcare professional costs were sourced from the Personal Social Services Research Unit (PSSRU) (PSSRU, 2013).

A variety of cost options are displayed, which include salary costs only, PSSRU unit cost per healthcare professional and PSSRU unit cost per hour of healthcare professional contact with patients, for consideration by the GDG. It is important to note that an NHS and PSS perspective should be taken for all NICE guidance (NICE, 2012). The costs provided in Table 23 are limited in that they provide no information on the quality and impact of the review, nor the long term cost savings resulting from the review.

Table 23: Estimate of cost per medication review delivered

Health care provider:	Cost per medication review – salary cost only				Cost per medication review – unit cost (without qualification costs)				Cost per medication review – patient contact cost (without qualification costs)			
	10 minutes	12 minutes	15 minutes	20 minutes	10 minutes	12 minutes	15 minutes	20 minutes	10 minutes	12 minutes	15 minutes	20 minutes
Nurse (GP practice)	£2.72	£3.27	£4.09	£5.45	£6.67 (£5.67)	£8.00 (£6.80)	£10.00 (£8.50)	£13.33 (£11.33)	£8.67 (£7.33)	£10.40 (£8.80)	£13.00 (£11.00)	£17.33 (£14.67)
General practitioner	£9.82	£11.78	£14.73	£19.64	£24.50 (£20.33)	£29.40 (£24.40)	£36.75 (£30.50)	£49.00 (£40.67)	£38.33 (£32.00)	£46.00 (£38.40)	£57.50 (£48.00)	£76.67 (£64.00)
Hospital-based nurse (day ward)	£2.73	£3.28	£4.10	£5.47	£6.83 (£5.67)	£8.20 (£6.80)	£10.25 (£8.50)	£13.67 (£11.33)	£16.67 (£14.00)	£20.00 (£16.80)	£25.00 (£21.00)	£33.33 (£28.00)
Community pharmacist	£4.03	£4.84	£6.04	£8.06	£9.33 (£8.50)	£11.20 (£10.20)	£14.00 (£12.75)	£18.67 (£17.00)	£11.67 (£10.67)	£14.00 (£12.80)	£17.50 (£16.00)	£23.33 (£21.33)
Hospital pharmacist	£3.18	£3.82	£4.77	£6.36	£7.83 (£6.83)	£9.40 (£8.20)	£11.75 (£10.25)	£15.67 (£13.67)	£11.17 (£9.83)	£13.40 (£11.80)	£16.75 (£14.75)	£22.33 (£19.67)
Hospital based doctor: Consultant medical	£7.82	£9.38	£11.72	£15.63	£23.17 (£16.50)	£27.80 (£19.80)	£34.75 (£20.75)	£46.33 (£33.00)	NR*	NR*	NR*	NR*

*Direct patient contact time costs are not reported on PSSRU (2012/13) for hospital based doctor: consultant medical.

8.5 Evidence statements

Clinical evidence

Meta-analysis of 10 RCTs showed no significant difference in mortality between patients receiving medication review or usual care (low-quality evidence). The patient populations in the 10 RCTs were people with a mean age of 65 years or over, and who had medication reviews carried out by pharmacists (8 studies), a physician (1 study) and a clinical pharmacologist (1 study).

Ten out of the 29 RCTs that were included reported on different clinical outcomes. Two RCTs were pooled together to show the effect of pharmacist-led medication review on targeted hypertensive patients where there was a significant change in mean blood systolic pressure in the intervention group compared with control group to meet the target blood pressure (low-quality evidence). One of the 2 studies did not provide demographic detail to assess the study population. However, the other study included patients with a mean age of 60 years. One study showed that pharmacist-led medication reviews in a population with a mean age of 65 years significantly increased the percentage of intervention patients to target blood pressure compared with control (low-quality evidence). The same study showed a significant improvement in low-density lipoprotein (LDL) levels, reaching target INR with anticoagulation and improving diabetes control by meeting HbA_{1c} targets with medication reviews (low-quality evidence).

Medication reviews compared with usual care in a population with a mean age of 60 years in 2 studies showed no significant differences in the following clinical outcomes (as reported in the studies): proportion of patients prescribed cardiovascular medicines for secondary prevention, 5-year risk of cardiovascular death score, target lipid levels or reduction in LDL levels and changes in cardiovascular risk factors (moderate- and low-quality evidence).

Two studies reported on asthma clinical outcomes (average age of population included was about 35 years). One study showed that medication review in patients with asthma significantly improved the optimisation of asthma medicines, asthma severity and inhaler technique, but there was no improvement in spirometry results (low-quality evidence). Medication review significantly reduced the need for rescue medicine and night-time awakenings in 1 study that targeted patients with asthma. However, it did not improve the peak expiratory flow, asthma control test (ACT) scores or occurrence of severe exacerbations of asthma (moderate-quality evidence).

Meta-analysis of 2 RCTs showed that medication reviews in a population with a mean age of 84 years significantly reduced the number of falls (moderate-quality evidence). One of the studies also reported that medication reviews did not significantly reduce the number of fractures in the elderly (low-quality evidence). One study carried out in a population with a mean age of 68 years showed that medication reviews when compared with usual care significantly improved pain scores, pain severity score, arthritis self-efficacy pain scale scores and clinical response within the first 3 months of the intervention (moderate-quality evidence).

Nineteen RCTs reported medicines-related problems as outcomes. Outcome measures used across the studies varied. One study showed that medication reviews did not significantly improve the reporting of adverse drug events compared with usual care (low-quality evidence). One study found no significant differences in the number of adverse drug events per 1000 days between the groups that received medication review or usual care (moderate-quality evidence).

Two studies found that medication reviews identified more medicines-related problems compared with usual care, but there was no significant difference between the 2 groups

(moderate-quality evidence). In 1 study, medication reviews significantly reduced the mean number of potential medicines-related problems from baseline to endpoint compared with usual care (moderate-quality evidence). One study identified medicines-related problems in 71% of patients (mean age 71 years) who received usual care before having a medication review (moderate-quality evidence). Another study identified at least 1 medicines-related problem in 79.8% of patients who had a medication review, but there was no comparison with usual care (moderate-quality evidence).

One study reported that medication reviews significantly reduced the prescribing of inappropriate medicines in an elderly population (moderate-quality evidence). One study reported that medication reviews in patients with a mean age of 65 years reduced the Medication Appropriateness Index (MAI) scores in all 10 domains compared with usual care (moderate-quality evidence). However, the statistical significance of the results was not reported. The results of 2 studies pooled together showed that medication reviews significantly reduced the MAI scores compared with usual care (low-quality evidence). One study showed that medication reviews reduced the number of potentially inappropriate medicines per patient compared with usual care, but this was not significant (moderate-quality evidence). One study showed that medication reviews identified more inappropriate medicines (as per Beers criteria) prescribed (although not significant) and also identified significantly more underused medicines (as per ACOVE criteria) compared with usual care (moderate-quality evidence).

Three studies showed that medication reviews resulted in more changes to patients' medicines compared with usual care. A study in patients with dyslipidaemia showed that medication reviews reduced the number of patients being prescribed high-intensity statins compared with usual care (moderate-quality evidence). Six studies all reported on the mean number of medicines per patient for the study and found that there was no significant difference between the control and the intervention group after the follow-up period (2 studies moderate-quality evidence, 4 studies low-quality evidence). Two studies showed that medication reviews significantly reduced the mean number of medicines prescribed compared with usual care (low/moderate-quality evidence). One study reported a significantly smaller increase in the number of medicines prescribed to elderly patients who had medication reviews compared with usual care (moderate-quality evidence).

Patient-reported outcomes were reported differently across 9 studies. Three studies (2 studies of low-quality evidence and 1 study of moderate-quality evidence) showed that medication reviews significantly increased compliance compared with usual care. Three studies showed no significant difference in patient compliance between the groups that received medication reviews or those that received usual care (moderate-quality evidence).

Patient satisfaction was reported in 5 studies, 3 of which showed no significant difference in patient satisfaction between medication review and usual care (2 studies with moderate-quality evidence and 1 study with low-quality evidence). Two studies showed that medication reviews received significantly high patient satisfaction rates compared with usual care (moderate-quality evidence).

One study showed no significant difference in the change in depression and anxiety scores for patients who received medication reviews or usual care (moderate-quality evidence). The same study showed that medication reviews significantly improved patients' clinical response to knee pain management (using the OMERACT-OARSI responder criteria) at 3 months compared with usual care. There was no significant difference at the end of the 12-month study (moderate-quality evidence).

Economic evidence

Partially applicable evidence from 2 studies with minor limitations, built on RCT data, suggests that pharmacist review is not cost effective, with ICERs above £50,000/QALY, compared with no intervention.

Partially applicable evidence from 4 studies with potentially serious limitations provided conflicting evidence, with 3 studies finding pharmacist review to be cost incurring and 1 finding it to be cost saving compared with no intervention.

No evidence was identified informing cost effectiveness of medication reviews by health professionals other than pharmacists.

8.6 Evidence to recommendations

Table 24 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG discussed the relative importance of the outcomes for medication reviews and took into consideration:
	• the health professional(s) carrying out the medication review
	• the process involved for the medication review
	• the level at which medication reviews are carried out.
	All of these will affect the outcomes of medication review.
	The GDG noted the mixed findings of the effect of medication review compared with usual care for all the outcomes except for mortality. The GDG discussed the clinical outcomes for the studies that looked at targeted medications review and noted that for some long-term conditions such as hypertension, arthritis, osteoporosis and asthma, medication reviews optimised therapy and improved clinical outcomes.
	The GDG discussed that some of the critical outcomes (such as mortality) and the important outcomes (such as planned or unplanned contacts and hospital and social care utilisation) may not be related to medicines because most of the studies did not specifically look into those outcomes in relation to medicines.
	The GDG discussed and agreed that the change in the number of medicines prescribed as a medicines-related outcome measure is not an indicator of the quality of the medication review. Medicines can be added or stopped to optimise therapy when managing or treating a condition.
	The GDG discussed and agreed that the purpose of doing a medication review is important in practice as it may be driven by a clinical need or by national/local incentives, which may lead to different clinical or patient-reported outcomes.
	The GDG was aware of Room for Review – A guide to medication review: the agenda for patients, practitioners and managers (2002) guidance and they agreed by consensus which target patient groups outlined in the guidance could be prioritised for review. These include patients who could be at particular risk of medicines related problems, those who have more broadly defined special needs and patients in disease areas where new evidence on treatments or new guidelines have become available. The GDG was aware of the following triggers for medication review:
	• Patients who are at particular risk of medicines-related problems – for example:
	- who are taking 4 or more medicines every day
	- who are recently discharged from hospital with complex medicines

	- who are receiving medicines from more than 1 source – for example, hospital specialist and GP - who have had significant changes to their medicines regimen in the past 3 months - who are taking medicines requiring special monitoring (for example lithium) with a wide range of side effects (for example non-steroidal anti-inflammatory drugs [NSAIDs]) or a narrow therapeutic range (for example digoxin) - who have symptoms suggestive of an adverse reaction - where non-compliance is suspected or known to be a problem. • People who have special needs, for example: - older people - residents in care homes - people with learning difficulties - people with sensory impairment such as poor sight or hearing difficulties - people with physical problems – for example arthritis, inability to swallow - people with mental states such as confusion, depression, anxiety, serious mental illness - people with communication difficulties and literacy or language difficulties - people from minority ethnic groups, refugees and asylum seekers. The GDG therefore agreed that health professionals should consider medication review for some patient groups where a clear purpose has been identified. These may include: • people taking multiple medicines (polypharmacy) • people with chronic or long-term conditions • older people
Trade-off between benefits and harms	The evidence reviewed for medication review shows improved outcomes over usual care or no difference to usual care. The GDG noted the meta-analyses of 8 studies that showed that medication reviews resulted in patients having more hospitalisations compared with usual care (low quality evidence). However, the GDG was aware that it was not clear if the hospitalisations were medicines-related or not because other co-morbidities of the patient population were included in the analysis. The GDG discussed which health professional should carry out medication reviews. The interventions were predominantly carried out by trained pharmacists but some involved multidisciplinary teams. Only 1 study involved a physician-led medication review. The GDG considered the resources required and services that are already in existence that offer medication reviews as part of the service for certain target groups (for example, care home pharmacists and practice-based nurses for long-term conditions to support clinicians). As the evidence was mixed the GDG agreed that the most appropriate health professional to undertake an identified medication review would need to be determined locally based on the knowledge and skills (competence) of the professional to carry out the review. The GDG discussed and agreed by consensus that competencies include effective communication skills, and technical knowledge of medicine processes and therapeutic knowledge for medicines use.

	The medication review may be profession-led or carried out as part of a multidisciplinary team.
Consideration of health benefits and resource use	The cost-effectiveness evidence was considered by the GDG. The GDG found that medication review carried out by community or hospital pharmacists was not cost-effective. However, the GDG was aware that the studies had short follow-ups (6 months) and 1 study involved the community pharmacists carrying out the medication reviews in the patient's home. The GDG discussed and agreed that focused medication reviews in some patient groups (i.e. those at higher risk of medication errors) are more likely to be cost-effective as these patients have a greater scope for benefit. The GDG was aware that there was no evidence for medication reviews carried out by primary care pharmacists or other health professionals. As the evidence presented (both cost effectiveness and the majority of clinical effectiveness) was limited to pharmacist-led reviews the GDG had to draw upon their own experience and expertise of medication reviews by other healthcare professionals. The GDG considered the simple cost-analysis that was provided to them to compare the cost of medication reviews when undertaken by various healthcare professionals. The GDG recognised that there was no data to compare the relative effectiveness or longer term cost-consequences of medication reviews when carried out by health professionals other than pharmacists. The GDG discussed that resources will vary locally to carry out medication reviews. They agreed that medication reviews carried out by the most competent health professional (determined locally) with a relatively low unit cost was the most cost-effective approach.
Quality of evidence	No evidence was found on medication reviews for children and also no evidence was on medicines use reviews. Most evidence was in patients aged over 60 years with polypharmacy and co-morbidities who lived in their own homes or in care homes. It included practice-based medication reviews in a GP surgery, community pharmacy or hospital, and domiciliary medication reviews. Some studies did not describe what 'usual care' involved, which made it difficult to determine whether there was overlap between medication review and usual care. The included studies varied in quality and were carried out in Europe, Australia, Canada or USA. The GDG was aware of the limitations relating to the applicability of some of these studies to the UK setting given the differences in healthcare systems and processes and populations. The evidence identified for this review question consisted of different types or levels of medication review that covered a wide range of activity. The outcomes reported in some studies were poor. Some numerical figures were not available or not reported in graphs and some studies were not powered to detect significance due to low recruitment numbers and high dropout rates. Most studies included small numbers of patients.
Other considerations	The GDG agreed that it is essential that the patient is informed and

involved in the decision making about changes to their medicines and is provided with opportunity to discuss and give feedback about how they feel about their medicines.

Other reviews of medicines take place in practice that can support medicines optimisation, including:

- medicines-use review (MUR) carried out by community pharmacists with the patient present
- new medicines service (NMS) carried out by community pharmacists with the patient (this may be in person or over the telephone).

The GDG were aware that the National service framework for older people (2001) and Room for Review – A guide to medication review: the agenda for patients, practitioners and managers (2002) highlight core areas that a detailed medication review should cover. Tools have also been developed to support medication review, such as the NO TEARS tool (Need/indication, Open questions, Tests, Evidence, Adverse effects, Risk reduction, Simplification/switches) and the STOPP and START criteria (Screening Tool of Older Person's potentially inappropriate Prescriptions and Screening Tool of Alert doctors to the Right Treatment). The GDG was aware of the guidance on Managing medicines in care homes (NICE social care guideline 1) that outlines what needs to be discussed during a medication review for residents in care homes, and agreed that the same points could be considered when reviewing medicines in all settings. The GDG discussed and agreed by consensus the following to be taken into account during a medication review:

- the person's (and/or the family members or carers, as appropriate) views and understanding about their medicines
- the person's (and/or their family members' or carers') concerns, questions or problems with the medicines
- all prescribed, over-the-counter and complementary medicines that the person is taking or using, and what these are for
- how safe the medicines are, how well they work, how appropriate they are, and whether their use is in line with national guidance
- any monitoring tests that are needed.
- .

The GDG discussed that the frequency of medication reviews may depend on the patient's condition and preference. There may continue to be a place for other types of review in the intervals between face-to-face medication reviews and/or for patients with less complex needs.

The GDG requested that the developer contact the Health and Social Care Information Centre (HSCIC) for information that they may hold for medication reviews to identify if this information would support the decision making process when developing recommendations. The GDG found that the HSCIC do not currently hold data that would specifically answer this review question. In addition, there is no information relating to the outcomes or actions taken following the reviews just the number of reviews carried out. The GDG agreed that it was not worth pursuing this data further as it would not add anything more to the decision making process.

8.7 Recommendations and research recommendations

Medication review can have many different interpretations and there are also different types which vary in their quality and effectiveness. In this guideline medication review is defined as 'a structured, critical examination of a person's medicines with the objective of reaching an agreement with the person about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste'.

27. **Consider carrying out a medication review for some patient groups when a clear purpose for the review has been identified. These groups may include:**

   - people taking multiple medicines (polypharmacy)
   - people with chronic or long-term conditions
   - older people.

28. **Determine locally the most appropriate health professional to carry out a medication review, based on their knowledge and skills, including all of the following:**

   - technical knowledge of processes for managing medicines
   - therapeutic knowledge on medicines use
   - effective communication skills.

   The medication review may be led, for example, by a pharmacist (professional-led) or by an appropriate health professional who is part of a multidisciplinary team.

29. **During a medication review, take into account:**

   - the person's (and/or the family members or carers, as appropriate) views and understanding about their medicines
   - the person's (and/or their family members' or carers') concerns, questions or problems with the medicines
   - all prescribed, over-the-counter and complementary medicines that the person is taking or using, and what these are for
   - how safe the medicines are, how well they work, how appropriate they are, and whether their use is in line with national guidance
   - any monitoring tests that are needed.

9 Self-management plans

9.1 Introduction

In 2001, the Department of Health launched The Expert Patients Programme, which aims to improve patients' quality of life when living with a long-term condition. The Expert Patients Programme stated that these patients are often considered to be 'in the best position to know what they want in managing their own condition'. The programme acknowledges that there has already been a shift from patients being only the recipient of their care to wanting to be involved in decisions about their care and treatment. Furthermore, it highlights that self-management approaches can be designed individually to reduce the severity of symptoms and improve patients' confidence in managing their condition, although this depends on the patient's desire to be involved and engaged in their health care.

The NHS improvement plan: putting people at the heart of public services (2004) encouraged the move of services from secondary care to primary care to increase self-management. The plan also supported the move towards promoting better self-management and treatment in community settings or in people's own homes, avoiding the need for people to go into hospital if possible. The National Service Framework for long-term conditions (2005) supports an approach to enable people to live independently at home, by managing their condition themselves. Additionally, Patient experience in adult NHS services (NICE clinical guideline 138) recommends that health professionals 'hold discussions in a way that encourages the patient to express their personal needs and preferences for care, treatment, management and self-management.'.

People with long-term conditions regularly use healthcare services. As the NHS faces increasing demand for its services, the role that people take in managing their long-term condition will become more important. Increasing the knowledge and support for people living with a long-term condition can empower them to be involved in and manage their own condition and become 'expert patients'. This includes people taking action to improve their own health and wellbeing, along with working with their health professionals to become more able to manage the day-to-day issues they face.

A self-management plan is a person-centred approach for these expert patients in managing their medicines, usually for those with long-term conditions. By empowering the patient to be confident in managing their symptoms themselves, they can make the most effective use of their medicines and treatments to achieve the best possible outcomes. Chronic obstructive pulmonary disease (COPD) (NICE clinical guideline 101) provides an example of using a self-management plan. The guideline advises patients on self-management strategies when managing exacerbations of their condition.

Self-management plans can have many definitions. In this guideline they are defined as 'structured, documented plans that are developed to support an individual patient's self-management of their condition'. Many different terms exist to describe the approach of self-management plans, including: action-planning, self-care, self-monitoring and self-management programmes. They are often used for patients with specific long-term conditions, such as asthma, COPD, pain and diabetes. Self-management plans can be patient-led or profession-led (for example initiated by the clinician).

A self-management plan is one of the approaches used by patients and health professionals to make shared decisions about managing conditions and treatments. Various forms of self-management plans exist. They are developed jointly for patients with their health professional and contain information, advice and support to help patients make appropriate choices to adapt to the changes in their condition. Additionally, a self-management plan can describe how to stay well, how to cope when the condition worsens and what to do when problems occur.

Organisations and health professionals can help improve patient engagement by tailoring support to meet an individual's needs. A self-management plan can be used to support the care a patient is receiving from a carer or advocate. Some patients may have more carer, family or health professional support than others, and some may wish to take a more active and involved role in their healthcare than others.

In general, it is thought that patients who are actively involved in their health tend to manage their condition more effectively. They are also likely to view their condition more positively and may benefit from an improved patient experience. Patients who are less engaged in managing their healthcare may have limited self-management skills. Introducing a self-management plan without this understanding may reduce patient confidence and future engagement in their care.

Self-management plans are a person-centred approach that can be used to support shared-decision-making with patients to optimise the use of their medicines. This review question aimed to find out if self-management plans for medicines improved patient outcomes from medicines.

9.2 Review question

What is the effectiveness and cost-effectiveness of using self-management plans to improve patient outcomes from medicines, compared to usual care?

9.3 Evidence review

For the purpose of this review question, self-management plans are defined as 'structured, documented plans that are developed to support an individual patient's self-management of their condition'. Self-management plans are often used for patients with long-term conditions, such as asthma, chronic obstructive pulmonary disease (COPD) or diabetes. In this guideline, the term 'self-management plans' includes action plans, individual plans and self-monitoring, and they may be patient-led or profession-led.

A systematic literature search was undertaken (see appendix C.1) that identified 5310 references. After removing duplicates, the references were screened on their titles and abstracts, and 111 full paper references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol (see appendix C.2.5).

Studies that looked at multifaceted interventions in which a self-management plan is combined with other elements such as an education programme, an exercise programme or outreach visits were excluded.

Self-management plans support patients to manage their condition themselves and may involve medicines or other interventions. The focus of this review question, however, was to look at the effectiveness of medicines-related self-management, monitoring or action plans.

The following were excluded from the review:
- Studies that looked at educational programmes and action plans (that involved medicines) compared with educational programmes and no action plans.
- Studies that compared one self-management plan (involving medicines) with another type of self-management plan (involving medicines) (the review protocol states the comparator as usual care).
- Studies that did not involve medicines as part of the self-management plan.
- Studies that looked at self-monitoring of medicines, if dose adjustment was not considered or if patients were verbally instructed to adjust their dose with no written plan.

Overall, 98 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C.5.5. Of the excluded studies, 8 were systematic reviews of studies (RCTs and observational). References included in these systematic reviews were sifted on their titles and abstracts, to identify any further studies that met the eligibility criteria as set out in the review protocol.

A total of 14 studies met the eligibility criteria, 13 studies had been identified from the original search and 1 study was identified from sifting through the systematic reviews. Of the included studies, 2 studies had additional papers identified from the systematic reviews reporting on outcomes in more detail and these were also included as part of the analyses.

All 14 included studies were RCTs investigating the effect of self-management plans compared with usual care or standard care. The included studies reviewed the self-management of long-term conditions (such as hypertension, asthma, COPD and type 2 diabetes) or self-monitoring. The self-monitoring studies included anticoagulation medicines and involved patients adjusting the dose themselves according to their written plan or algorithm. Studies selected to address this review question included training and education for using the self-management and self-monitoring plans.

The studies were quality assessed using the NICE methodology checklists for systematic reviews and RCTs (see NICE guidelines manual 2012). Appraisal of the quality of the study outcomes was carried out using GRADE.

See appendix D.1.5 for evidence tables of included studies.

See appendix D.2.5 for GRADE profiles.

Table 25 Summary of included studies

Study	Population	Intervention	Comparison	Key critical outcomes
Agrawal (2005) *India*	Aged 5-12 years with moderate persistent asthma	Individualised action plans (home-management plan)	Usual care	• Acute asthma event • Symptom score • Nocturnal awakening
Christenson (2006) *Denmark*	Aged 18 and over and prescribed oral anticoagulation	Self-monitoring with a coagulometer and dosage adjustment	Usual care	• Time within therapeutic INR range
Cromcheecke (2000) *Amsterdam*	Outpatients, mean age 42 years receiving long-term anticoagulation (phenprocoumon or acenocumarol)	Home self-testing using Coaguchek® to self-monitor prothrombin time and self-dosing	Usual care	• Better control of anticoagulation • Adverse events • Patient satisfaction
Ducharme (2011) *Canada*	Aged 1-17 years with asthma	Recording management instructions on a written action plan with prescription (WAP-P)	Usual care	• Patient adherence • Asthma control • Patient adherence
Fitzmaurice (2002) *England*	Ambulatory patients (most receiving warfarin for atrial fibrillation). Self-management group mean age of 63 years, control group mean age 69 years	Self-testing and self-dosing using Coaguchek® device to self-monitor INR	Usual care	• Percentage of time within therapeutic INR range • Haemorrhage
Fitzmaurice (2005) *England*	Ambulatory patients, mean age 69 years, who were receiving long-term anticoagulation (warfarin)	Self-testing and self-dosing using Coaguchek® device to self-monitor INR	Usual care	• Percentage of time within therapeutic INR range • Haemorrhage • Thromboembolism
Grunau (2011) *Canada*	Aged 18 years and over	Self-monitoring of INR at community laboratories. Patients adjusting their warfarin doses independently using provided nomograms	Usual care	• INR control • Thromboembolic and bleeding events
Guerci (2003)	Aged 40-75 years, with a	Self-monitoring of blood glucose	Patients received	• HbA$_{1c}$ level

Study	Population	Intervention	Comparison	Key critical outcomes
France	diagnosis of type 2 diabetes	using discmeter device	a conventional laboratory work-up based solely on laboratory measurement of HbA_{1c} every 12 weeks	• Hypoglycaemic events • Change in blood pressure
McGeoch (2006) *New Zealand*	People with COPD. Intervention group mean age was 69 years; control group mean age was 72 years	Use of a self-management plan	Usual care	• Health utilisation • COPD self-management
McManus (2010) *England*	Aged 35-85 years receiving treatment for hypertension with 2 or fewer antihypertensive medicines	Self-monitoring of blood pressure and dose adjustments	Usual care	• Change in blood pressure • Number of primary care consultations • Patient experiences
Menendez-Jandula B (2005) *Spain*	Aged 18 years or older receiving long-term anticoagulant therapy for at least 3 months	Self-monitoring using portable coagulometer weekly and self-adjusting treatment	Usual care	• Percentage of time of INR values within the target range • Thromboembolic or haemorrhagic complications
Siebenhofer (2008) *Austria*	Aged 60 years or over on long-term anticoagulation	Self-managing oral anticoagulation and recording in their diaries	Usual care	• Combined endpoints of all thromboembolic events and major bleeding complications • Anticoagulation control
Sunderji (2004) *Canada*	Aged 18 years and over on warfarin	Self-monitoring using point of care device and adjusting their warfarin doses using a nomogram	Usual care	• Percentage of time in target range • Adverse events
Thoonen (2003) *Netherlands*	Aged 16-60 years with asthma	Self-management programme	Usual care	• Asthma control
Abbreviations: COPD, chronic obstructive pulmonary disease; INR, international normalised ratio				

9.4 Health economic evidence

Summary of evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies evaluating the use of patient self-management plans to improve patient outcomes from medicines. This search identified 3354 records, of which 3288 were excluded based on their title and abstract. The full papers of 66 records were assessed and 61 were excluded at this stage. The excluded studies and reasons for their exclusion are provided in appendix C.6.5.

One systematic review of studies was identified including potentially relevant studies (Connock et al. 2007). This systematic review could not be included in full because some included studies either did not include usual care as a comparator, or measured the effectiveness of interventions that were multifaceted. References included in this systematic review were screened to identify any individual studies that met the inclusion criteria. One cost-effectiveness study was identified and included (Jowett et al. 2006). This study was not identified from the systematic literature search because there was no mention of a self-management plan or action plan in the free text or medical subject headings.

The 6 studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. At this stage, 2 studies were deemed not applicable to the guidance and excluded from further analysis. De Asis et al. (2004) undertook a cost-effectiveness study set in USA and WAS based on RCT data from 1997. Because a more relevant Dutch cost–utility analysis on the same patient population met the inclusion criteria, the study by De Asis et al. was excluded. Fitzmaurice et al. (2002) undertook a cost-comparison alongside an RCT comparing self-management of oral anticoagulants with usual care. Cost–utility analyses in this patient population had already been identified and as such the study by Fitzmaurice et al. was considered not applicable to the guidance. The 4 included studies are summarised in table 26.

All 4 included studies consisted of a cost–utility analysis built on RCT data. Connock et al. (2007) and Jowett et al. (2006) compared patient self-management of anticoagulation therapy with usual care from a UK NHS perspective. Kaambwa et al. (2013) compared self-management in the control of hypertension with usual care from a UK NHS perspective, and Schermer et al. (2002) compared self-management of inhaled steroids for asthma with usual care from a Dutch healthcare system perspective.

All 4 studies were considered to be partially applicable to guidance because the study population in each was a subgroup of the whole guidance population. The studies by Connock et al. (2007), Jowett et al. (2006) and Kaambwa et al. (2013) were all from a UK healthcare system perspective, whereas the study by Schermer et al. (2002) was from a Dutch healthcare system perspective. Connock et al. (2007) based their cost–utility analysis on systematic review data and was judged to have minor limitations. The remaining 3 studies all had potentially serious limitations. Both Jowett et al. (2006) and Schermer et al. (2002) had a short time horizon, whereas Kaambwa et al. (2013) populated their model with assumptions in which the timeframe went beyond that of the corresponding RCT.

The study evidence tables for the included studies are shown in appendix E.1.5.

This topic was not identified as a priority for health economic modelling by the GDG because published cost-effectiveness analyses already exist in the disease areas in which self-management is a feasible option.

Table 26 Economic evidence profile – Patient self-management

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost effectiveness	
Connock et al. (2007) (UK, CUA)	Minor limitations	Partially applicable[1]	Study employed cost-utility analysis over a 10-year time horizon Intervention: patient self-management of oral anticoagulation Comparator: usual care	£100,393[2]	1.577[3]	£63,655 per QALY	44% probability of being cost effective at a £30,000 per QALY threshold Scenario analysis using pooled data: £19,617 per QALY[4]
Jowett et al. (2006) (UK, CUA)	Potentially serious limitations[5]	Partially applicable[1,6]	An RCT including cost-utility analysis over a 1-year time horizon Intervention: patient self-management of oral anticoagulation Comparator: usual care	£294.44[7]	0.009[7]	£32,716 per QALY	30% probability of being cost effective at a £20,000 per QALY threshold
Kaambwa et al. (2013) Patient self-management in the control of hypertension (UK, CUA)	Potentially serious limitations[8]	Partially applicable[1,9]	Study employed cost-utility analysis over a life-time horizon (35 years) Intervention: patient self-management of hypertension Comparator: usual care	£383[10] £576[11]	0.24[10] 0.11[11]	£1,624 per QALY[10] £4,923 per QALY[11]	99% cost-effective at a £20,000 per QALY threshold for men and women
Schermer et al. (2002) Patient self-management of inhaled steroids for asthma (Holland, CUA)	Potentially serious limitations[12,13]	Partially applicable[1,14,15]	An RCT including cost-utility analysis over a 2-year time horizon Intervention: patient self-management of inhaled steroids for asthma Comparator: usual care	£9.34	0.015	£11,268 per QALY	Sensitivity analysis took a societal, rather than healthcare, prospective

[1] Study population is a small subgroup of the whole guidance population

[2] Incremental costs per 100 patients after 10 years

[3] Incremental QALYs per 100 patients after 10 years

[4] Scenario analysis based on all data identified in the authors' clinical review. This included observational studies that did not meet the inclusion criteria for clinical evidence for this guideline. In these studies patient testing of INR was conducted less frequently and therefore the costs of self-management were lower

[5] Short time horizon in the base case (1 year). When a longer time horizon was considered, outcomes from the corresponding RCT (resource use, health related QoL) were assumed to remain constant for both the self-management and usual care arms

[6] No discounting was undertaken for scenario analyses with time horizon greater than 1 year

[7] Incremental analysis per patient per year

[8] QALY and cost values used to populate the model beyond the timeframe of the corresponding RCT were assumptions

[9] QALY estimates were derived from the published literature. It is unclear if these were obtained directly from patients and/or their carers

[10] Per male patient

[11] Per female patient

[12] Short time horizon (2 years) may not have fully captured the effects of the intervention

[13] No sensitivity analysis was carried out from a healthcare system prospective

[14] Valuation in changed in utility were obtained from patients themselves rather than a representative sample of the general public

[15] Study was carried out from a Dutch healthcare system and societal perspective (results reported separately)

[16] Per patient

[17] Costs were converted into pounds sterling using the appropriate purchasing power parity

Abbreviations: ICER, incremental cost-effectiveness ratio; INR, international normalised ratio; QALY, quality-adjusted life year; RCT, randomised controlled trial; CUA, Cost-utility analysis

9.5   Evidence statements

Clinical evidence

Anticoagulation

Eight studies (low-quality evidence) looked at the control of anticoagulation between self-management and usual care groups. Three studies showed that the percentage of time within target International Normalised Ratio (INR) range was significantly higher in the self-management groups compared with usual care. Five studies showed no significant difference between the 2 groups.

Five studies looked at the adverse events of bleeding and thrombosis. There was no significant difference in the number of bleeding or thrombotic events between the self-management group and usual care group (low-quality evidence). Two studies showed that the risk of bleeding or thrombotic complications was significantly lowered in the self-management group compared with usual care group (low/moderate-quality evidence). One study showed no significant difference between the self-management group and usual care group for mortality and hospitalisations (low-quality evidence).

One study showed that the patient satisfaction outcome significantly favoured the self-management group for general treatment satisfaction, self-efficacy and reduced anxiety, distress and strain over usual care (moderate-quality evidence).

Three studies reported quality of life as an outcome. Two of these studies found no significant difference between self-management and usual care groups in quality of life improvement. One study looked at treatment-related quality of life and showed that there was significantly greater improvement in self-efficacy in the self-management group compared with the usual care group; however, there was no significant difference in the anxiety scores between the 2 groups (low-quality evidence).

Asthma

Three studies looked at the effectiveness of adding a self-management plan for asthma over usual care. All 3 studies showed that the overall control of asthma was significantly better in the self-management group compared with usual care (low-quality evidence). One study significantly favoured the self-management plan for improving patient adherence to asthma medicines and attending follow-up visits over usual care (low-quality evidence).

Two studies looked at patient health-related quality of life as an outcome measure and found that there was no significant difference between the self-management and usual care group for this outcome (low-quality evidence). One of the studies also reported care-giver quality of life and found no significant difference in improvement between the groups (low-quality evidence).

Blood pressure

One study (moderate-quality evidence) looked at self-management of blood pressure and found a significant improvement in systolic blood pressure in the self-management group compared with the usual care group. A qualitative study on patient experience found that patients were confident in the self-monitoring of blood pressure but lacked confidence to increase their medicine(s) without consulting with their GP. There was no significant difference in quality of life between the 2 groups.

COPD

One study (moderate-quality evidence) looking at the self-management of COPD found no significant differences in healthcare use, health-related quality of life and hospital-related

anxiety and depression between the self-management and usual care groups. There were significant differences between the self-management and usual care groups for COPD self-management knowledge and capacity to act for all stages of the COPD action plan, favouring the self-management group.

Diabetes

One study (low-quality evidence) looked at self-monitoring of type 2 diabetes and found that the self-management group had a significant improvement in HbA_{1c} (glycated haemoglobin) levels (indicated by a lower value) than the usual care group. There was a significant difference in hypoglycaemic events between the 2 groups showing higher asymptomatic hypoglycaemic events in the self-monitoring group.

Economic evidence

Partially applicable evidence from one study with minor limitations built on RCT data suggests that the cost effectiveness of self-management of oral anticoagulation is above the implied NICE threshold. This is supported by partially applicable evidence from one study with potentially serious limitations.

Partially applicable evidence from one study with potentially serious limitations suggests that patient self-management in the control of hypertension is cost effective at a threshold of £5000 per QALY gained.

Partially applicable evidence from one study with potentially serious limitations suggests that patient self-management of inhaled steroids for asthma is cost effective at a threshold of £20,000 per QALY gained.

9.6   Evidence to recommendations

Table 27 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG discussed the outcomes resulting from the different conditions for which the self-management plans were used for. There were 8 studies on the self-management of anticoagulation, 3 studies on the self-management of asthma and 1 study each on the self-management of type 2 diabetes, COPD and hypertension that were presented to the GDG.
	The GDG noted that the clinical outcomes resulting from the self-management of anticoagulation were mixed –either self-management was favoured, or there was no significant difference between patients' self-managing or receiving usual care. The GDG also discussed the clinical outcomes from other included studies. They agreed that self-management plans for asthma, COPD, hypertension and type 2 diabetes improved some clinical outcomes, but there was limited evidence to make a strong recommendation advocating the use for self-management plans in all patients with long-term conditions.
	The GDG agreed that the use of a self-management plan to manage medicines may improve clinical outcomes for some long-term conditions but not others, because of the difficulty in managing some long-term conditions. The self-management plan therefore needs to be tailored to the individual patient, allowing them to self-manage their condition and medicines in line with their own health needs.
	The GDG was aware that when patients want to be involved in decisions about their medicines they prefer to self-manage. The GDG

considered the evidence favouring self-management plans for patient-reported outcomes, including confidence in self-managing, patient satisfaction and knowledge about self-management. The GDG discussed and agreed that these outcomes would affect a patient's willingness and ability to self-manage. The GDG also discussed and agreed that self-management may be favoured by some groups of patients who are confident and competent in managing their condition themselves when provided with a written plan to follow. However, the GDG was aware that some patients (or their carer or advocate) may lack the confidence to manage their condition and adjust their medicines themselves and may prefer to receive usual care (that is, health professionals managing their care). The GDG also discussed that patients should be empowered to make decisions about their healthcare in partnership with their health professional and that a self-management plan is an example of how shared decision-making can be put into practice, allowing a patient to take ownership for managing their medicines. The GDG discussed and agreed by consensus that self-management may be considered as an option for patients who wish to be involved in decision making about their medicines and who are willing and able to self-manage.

The GDG found evidence showing no significant difference between patients self-managing their condition and those receiving usual care for the quality-of-life outcome. They were also aware that the duration of the included studies may not have been sufficient to address this outcome appropriately.

Trade-off between benefits and harms	The overall evidence reviewed for self-management showed that it either improved outcomes over usual care or showed no difference compared with usual care. The GDG found no evidence of significant harm resulting from the use of self-management plans. However, the GDG recognised that the length of the included studies may not have been sufficient to show potential harms.
	The GDG discussed that self-management plans need to be discussed and used safely by health professional and patients; defining boundaries and having two-way communication is vital to ensure safe and effective use. The GDG discussed and agreed by consensus that the benefits and risks should be considered by the health professional and the patient when deciding to use a self-management plan and that the shared responsibilities of the health professional and the patient should be agreed and clearly documented.
	The GDG found that in the included studies, all study participants who were assessed as competent for self-managing their condition and medicines had some training and education. The GDG discussed that it is the health professional's responsibility to ensure that the patient is capable of using the plan appropriately. The GDG agreed that patients need to be adequately supported and that training and education is important to ensure that patients are capable of self-managing their condition and medicine(s). The GDG therefore agreed that the health professional should explain to the patient how to use the self-management plan before agreeing to start it and that it is the health professional's responsibility to ensure that the patient has the knowledge and skills to use a plan appropriately; a risk assessment may be used. The GDG also agreed that health professionals should consider providing support to the patient to manage their condition and medicines in line with their self-management plan. This should be reviewed on a regular basis to

	ensure the patient does not have problems using or following it.
	The GDG considered and discussed the resource implications when using self-management or self-monitoring plans. The GDG was aware of the potential costs associated with the use of coagulometers, blood glucose monitors and testing strips to the NHS. During discussions, the GDG heard that patients who self-manage their INR sometimes test their INR more frequently (requiring more testing strips) than they would if they were attending an anticoagulation clinic, therefore incurring additional costs for the testing strips.
	The GDG considered other costs to the NHS such as staff to carry out INR testing, equipment needed and location of testing. The GDG was also aware that since the studies were conducted, several services have now moved from the secondary care setting to primary care setting in the form of outreach clinics. Therefore the costs outlined in the study may now not be reflective of current practice.
	The GDG also discussed the costs incurred to the patient when receiving usual care for managing their anticoagulation, which can involve transport costs and time off work (if employed) to attend the anticoagulation clinic. The costs incurred to the patient receiving usual care would depend on the frequency of visits the patient would have to make. Patients with stable anticoagulation readings that are within the target range, where less frequent monitoring is needed, would incur less travel costs and time off work. The GDG was aware that in some cases the patient would have to purchase equipment needed to self-manage their condition.
	The GDG also considered the resources needed to train and educate patients to safely and effectively self-manage their medicines, and agreed that the resources needed would need to be locally determined.
Consideration of health benefits and resource use	The GDG discussed the cost-effectiveness of self-managing oral anticoagulation and acknowledged that the likelihood of this being cost-effective at the implied NICE threshold depended on the frequency of testing undertaken by patients. Experiences of the GDG suggested that when patients self-manage they have a tendency to over test and are likely to test weekly (as shown in the UK RCT in which the identified cost-effectiveness models were based). Therefore, the GDG was concerned that self-managing would not be a cost-effective use of NHS resources and agreed for the intervention to be considered only where the frequency of testing would be monitored by a health professional. The GDG felt that through appropriate training and education relating to medicines for patients and ongoing support and management, patients would be less likely to over test.
	The GDG discussed how self-management in patients willing to self-manage may free up NHS resources due to reduced visits to doctors and other health professionals. Economic evidence showed that this reduction in resource use led to patient self-management plans being a cost-effective use of resources in several disease areas. The GDG judged that the potential savings would be the greatest where patients are willing and choose to be involved in managing their condition and medicines.
Quality of evidence	The GDG found that the included clinical studies were carried out in

	European countries, Canada, India, or New Zealand. The study quality varied from low to moderate. The GDG was aware of the limitations relating to the applicability of some of the studies to the UK setting, given the differences in healthcare systems, processes and populations.

The majority of the included studies were carried out in an adult population. Two studies looking at self-management plans for asthma were carried out in adults and children. There was 1 study that looked at self-management plans for asthma in children only.

The GDG found that where dose adjustment was carried out by the patient or the health professional in self-management plans, there was variation within the studies.

The economic evidence was partially applicable with minor limitations and potential serious limitations. |
| Other considerations | The GDG noted that the outcomes reported were from studies that looked at the use of self-management plans in patients with single or less complex long-term conditions and not in patients who have co-morbidities. The GDG discussed that the evidence for the use of self-management plans was limited only to patients with a single long-term condition where management was not complex.

The GDG was aware that there are some long-term conditions that are difficult to control and that the management and treatment options presented to the patients as part of their self-management plan may be more complex. For example, managing hypertension requires blood pressure to be monitored and dose of tablets to be adjusted ('a proactive management plan') and subsequently response to the dose adjustment may take time. Whereas, managing asthma requires monitoring of symptoms and knowing when to take a reliever inhaler to provide immediate relief ('reactive management plan').

The GDG discussed how a patient's ability to self-manage and the nature of their condition should be assessed in light of benefits and risks, when deciding where a self-management plan is appropriate and in the patient's best interests. The GDG discussed and agreed by consensus that the health professional should take steps to ensure that the patient is self-managing in accordance with their individualised written plan for example monitoring prescription requests for inhalers that are part of the person's asthma self-management plan. A regular review of the patient and their self-management plan should be carried out to address any change or update in the management of the condition and use of medicines.

The GDG was aware that using self-management plans when prescribing 'when required' medicines for some long-term conditions, such as chronic pain, may provide an opportunity to provide the patient with more information about their condition and medicines, particularly around dosing and under what circumstance to take what dose. The GDG discussed that by prescribing 'when required' medicines, this is already committing patients to manage their medicines themselves. The principles of prescribing medicines with a direction of 'when required' puts the responsibility of self-managing on the patient. These principles are consistent with other clinical decisions for patients when self-managing their medicines. |

	The GDG was aware that the purpose of this review question was to look at the effectiveness of self-management plans rather than looking into the details of what the self-management plan actually consisted of. They acknowledged from an earlier discussion that self-management plans should be individualised and tailored to the patient's needs. This led the GDG to discuss what key information needs to be considered in any self-management plan, in addition to thinking about personalised medicines management and the patient's wishes, beliefs and needs. The GDG was aware of the regulations for clinical management plans used by supplementary prescribers. The GDG agreed that some details in these management plans could be adapted and used when agreeing the criteria for a self-management plan. The GDG discussed and agreed by consensus that a self-management plan should consider the following: • the plan's start and review dates (review the plan on a regular basis to ensure the person does not have problems using or following it) • the condition(s) being managed • a description of medicines being taken under the plan • any strength or dose restrictions or limitations of a medicine that may be taken under the plan, how long a medicine may be taken for, or what medicines that may be self-administered under the plan are being used • the person's allergies and intolerances to medicines • the arrangements for the person to report suspected or known adverse reactions to any medicines • the circumstances in which the person should refer to, or seek the advice from, a health professional • the individual responsibilities of the health professional and the person • any other instructions the person needs to safely and effectively self-manage their medicines. •

9.7 Recommendations and research recommendations

Self-management plans can be patient-led or profession-led and they aim to support people to be empowered and involved in managing their condition. Different types of self-management plan exist and they vary in their content depending on the needs of the individual person. In this guideline self-management plans are structured, documented plans that are developed to support an individual person's self-management of their condition using medicines.

30. **When discussing medicines with people who have chronic or long-term conditions, consider using an individualised self-management plan to support people who want to be involved in managing their medicines. Discuss all of the following:**

   • the person's knowledge and skills needed to use the plan, using a risk assessment if needed

   • the benefits and risks of using the plan

   • the person's values and preferences

   • how to use the plan

   • any support the person needs

Record the discussion in the person's medical notes.

31. **When developing an individualised self-management plan for a patient, consider including:**

- the plan's start and review dates (review the plan on a regular basis to ensure the person does not have problems using or following it)
- the condition(s) being managed
- a description of medicines being taken under the plan
- any strength or dose restrictions or limitations of a medicine that may be taken under the plan, how long a medicine may be taken for, or what medicines that may be self-administered under the plan are being used
- the person's allergies and intolerances to medicines
- the arrangements for the person to report suspected or known adverse reactions to any medicines
- the circumstances in which the person should refer to, or seek the advice from, a health professional
- the individual responsibilities of the health professional and the person
- any other instructions the person needs to safely and effectively self-manage their medicines.

10 Patient decision aids used in consultations involving medicines

10.1 Introduction

Shared decision-making is an essential component of evidence-based medicine, which seeks to use the best available evidence to guide decisions about the care of an individual patient, taking into account their needs, values and preferences (Greenhalgh et al. 2014; Sackett et al. 1996). NICE guidance on Medicines adherence (NICE clinical guideline 76) and Patient experience in adult NHS services (NICE clinical guideline 138) highlights the importance of enabling patients to actively participate in their care. In 2013, the General Medical Council published Good practice in prescribing and managing medicines and devices, which also emphasises the need to 'reach agreement with the patient on the treatment proposed, explaining the likely benefits, risks and burdens, including serious and common side effects'.

A Cochrane review on patient decision aids (Stacey et al. 2014) described them as 'an intervention designed to support patients' decision-making by providing information about treatment or screening options and their associated outcomes', compared with usual care and/or alternative interventions. The decision aids describe the options available and help people to understand these options as well as the possible benefits and harms. This allows patients to consider the options from a personal view and prepares them to participate with their health professional in making a decision. Patient decision aids may be electronic or paper-based tools.

The International Patient Decision Aids Standards (IPDAS) Collaboration describes patient decision aids as 'tools designed to help people participate in decision making about health care options. They provide information on the options and help patients clarify and communicate the personal value they associate with different features of the options'.

Patient decision aids can be a useful tool to support shared decision-making. They present evidence-based estimates of the benefits and risks of the available treatment options in sufficient detail that people are better able to judge their value (Stacey et al. 2014). In contrast to health education materials, which simply provide broad background information, patient decision aids are tailored to a specific person's health status and help them to make informed, value-based decisions about their treatment with their health professional.

Patient decision aids are not essential to deliver effective shared decision-making, but where high-quality patient decision aids exist, they can facilitate patient engagement and can be used before, during or after a consultation to enable patient participation, and may help to improve a person's knowledge of the options and outcomes and give them more realistic expectations (Stacey et al. 2014). Patient decision aids should not advise patients to choose an option over another, or replace the consultation between the patient and their health professional. More importantly, they are intended to supplement or support the interaction.

The aim of patient decision aids is to improve the quality of decisions. Decision quality is the extent to which patients choose and/or receive healthcare interventions that are consistent with their informed and considered values. The features of options that patients value may include the health states that might be affected by the decision, their attitudes towards the chances associated with the relevant options, their willingness to make trade-offs over time and other issues relevant to the decision, including beliefs about the acceptability of particular interventions.

Although patient decision aids can support better decisions, this depends on the attitudes and skills of health professionals supporting patients to make well-informed choices that are

consistent with the patient's values and preferences (Stacey et al. 2014). The values and perceptions of individual people, and their attitudes to risk, may be different from those of their health professional ([Thornton H 2003](#)).

Patient decision aids are used for complex decisions that need more detailed information and more careful consideration. Complex decisions have multiple options with features that people value differently. Sometimes the scientific evidence about options is limited. Therefore, the best choice depends on the personal value that an individual person places on the benefits, harms and scientific uncertainties.

A wide range of different patient decision aids of variable quality have been developed that address many different treatment decisions, including:

- Screening decisions, such as prostate cancer, breast cancer and prenatal screening
- Surgical decisions, such as mastectomy, hysterectomy and prostatectomy
- Decisions about medicines, such as statins, anticoagulants and hormone replacement therapy.

IPDAS has developed criteria for judging the quality of patient decision aids, which cover 3 domains of quality: content, development process and evaluation of its effectiveness. NICE recommends that patient decision aids are offered to patients if suitable high-quality decision aids are available (NICE clinical guideline 138).

Patient decision aids are used variably in practice, the aim of this review question was to identify if, in a consultation about medicines, they improve patient outcomes.

10.2 Review question

What is the effectiveness and cost-effectiveness of using patient decision aids in consultations involving medicines use to improve patient outcomes, compared to usual care or other intervention?

10.3 Evidence review

The aim of this review question was to review the effectiveness and cost effectiveness of using patient decision aids in consultations involving medicines use. This includes:

- Patient decision aids.
- Shared decision aids.
- Decision grids.
- Option grids.

The use of patient decision aids in which participants were not making an active treatment decision that included a medicine as one of the options, such as patient decision aids for screening, surgical treatments or diagnostic tests, were not included in this review. Patient decision aids can be used at any point before, during or after a consultation. Patient decision aids that were either self-completed or completed with a health professional were included, provided that the intervention involved a consultation or discussion with a healthcare provider. Furthermore, interventions that included other components, such as healthcare provider training workshops to support use of the patient decision aid were also included.

This review question did not aim to compare the effectiveness of other interventions to support patients, such as compliance aids, patient information leaflets and health education materials. Therefore, studies assessing the effectiveness of these interventions were not included.

A systematic literature search was conducted (see appendix C.1), which identified 3519 references. After removing duplicates, the references were screened on their titles and abstracts, and 25 references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol (appendix C.2.6).

Overall, 3512 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion are provided in appendix C.5.6.

Seven RCTs met the eligibility criteria and were included. In addition, studies included in a Cochrane review on patient decision aids (Stacey et al. 2014) that was identified in the scoping search were also screened on their titles and abstracts, to identify any further studies that met the eligibility criteria. Twenty-one additional RCTs were included. These studies were not identified in the original systematic literature search because the search only identified those records that included 'patient decision aid' and 'medicine' components in either the medical subject headings or free text.

Twenty-three RCTs compared patient decision aids with usual care, which included studies in which the control group received general information, such as an information leaflet on menopause. Six RCTs compared patient decision aids with another intervention; these included studies in which the control group received specific information about risks and benefits of a medicine(s). One study (Kennedy 2002) included 3 arms; patient decision aid plus structured interview, patient decision aid alone and usual care.

A total of 28 RCTs investigated patient decision aids used in a range of patient populations:
- Cardiovascular disease (including primary prevention; 5 studies*)
- Type 2 diabetes (5 studies)
- Menorrhagia (4 studies*)
- Women considering hormone replacement therapy (4 studies)
- Osteoporosis (2 studies)
- Schizophrenia (2 studies*)
- Cancer (breast cancer and advanced colorectal cancer; 2 studies)
- Atrial fibrillation (1 study)
- Benign prostatic hypertrophy (1 study)
- Multiple sclerosis (1 study)
- Women considering labour analgesia (1 study)

* Includes 2 published studies reporting data from a single RCT.

All studies involved medicines use in adults; no studies that investigated the use of a patient decision aid in children or their carers were identified that met the eligibility criteria.

The included studies investigated the use of written and computerised patient decision aids in different formats or combination of formats, including:
- Information booklets, with and without pictures
- Interactive worksheets
- Video recordings
- Audio recordings
- Interactive multimedia programme with booklet and printed summary

Seven out of the 28 studies were conducted in the UK. Sixteen studies were conducted in Canada or USA. Available data were extracted into detailed evidence tables (see appendix D.1.6) and are summarised in the tables below.

Table 28 Summary of included studies – Patient decision aid compared with usual care

Study	Population	Intervention	Comparison	Key critical outcomes
Branda (2013) *USA*	Type 2 diabetes	Statin or diabetes patient decision aid	Usual care	• Patient knowledge • Decisional conflict • Participation in decision-making • Patient satisfaction • Medicines adherence
Hamann (2006)[1] *Germany*	Schizophrenia	Schizophrenia treatment patient decision aid (booklet)	Usual care	• Patient knowledge • Participation in decision-making • Patient satisfaction
Hamann (2007)[1] *Germany*	Schizophrenia	Schizophrenia treatment patient decision aid (booklet)	Usual care	• Medicines adherence
Kasper (2008) *Germany*	Multiple sclerosis	MS patient decision aid (booklet and interactive worksheet)	Usual care (standard information)	• Participation in decision-making
Kennedy (2002) *UK*	Menorrhagia	Menorrhagia patient decision aid (booklet and videotape)	Usual care	• Patient satisfaction • Patient health status • Hysterectomy rates
Leighl (2011) *Canada and Australia*	Advanced colorectal cancer	Colorectal cancer patient decision aid (take home booklet with audio recording)	Usual care (standard medical oncology consultation)	• Patient knowledge • Decisional conflict • Patient satisfaction • Participation in decision-making • Cancer therapy QoL
Mann (2010) *USA*	Diabetes patients	Statin patient decision aid	Usual care (printed materials from ADA)	• Patient knowledge • Decisional conflict • Medicines adherence
Mathers (2012) *UK*	Type 2 diabetes	Type 2 diabetes patient decision aid used in a single consultation	Usual care (standard medical consultation)	• Patient knowledge • Decisional conflict • Participation in decision-making
Montori (2011) *USA*	Postmenopausal women	Osteoporosis patient decision aid	Usual care (standard	• Patient knowledge

Study	Population	Intervention	Comparison	Key critical outcomes
		(pictographic format)	brochure)	• Decisional conflict • Patient satisfaction • Participation in decision-making • Medicines adherence
Morgan (2000) *Canada*	Cardiovascular disease	CVD patient decision aid (video programme)	Usual care	• Patient knowledge • Participation in decision-making • Patient satisfaction • General health status
Mullan (2009) *USA*	Type 2 diabetes	Type 2 diabetes medication choice patient decision aid (n=48)	Usual care (information pamphlet)	• Patient knowledge • Decisional conflict • Participation in decision-making • Medicines adherence • General health status
Murray (2001[a]) *UK*	Women considering hormone replacement therapy	HRT patient decision aid (interactive multimedia programme with booklet and printed summary)	Usual care	• Decisional conflict • Participation in decision-making • General health status
Murray (2001[b]) *UK*	Benign prostatic hypertrophy	BPH patient decision aid (interactive multimedia programme with booklet and printed summary)	Usual care	• Decisional conflict • Participation in decision-making • General health status • Prostatectomy rates
Oakley (2006) *UK*	Women with osteoporosis or high risk of osteoporosis	Patient decision aid (information booklet, audio cassette and worksheet)	Usual care	• Decisional conflict • Patient satisfaction • Medicines adherence
Protheroe (2007) *UK*	Menorrhagia	Menorrhagia computerised patient decision aid plus written information	Usual care (written information)	• Decisional conflict • Patient knowledge • Menorrhagia specific QoL
Sheridan (2006) *USA*	Cardiovascular disease (primary prevention)	CVD prevention computerised patient decision aid	Usual care (list of CVD risk factors)	• Participation in decision-making
Sheridan (2011)[2]	Cardiovascular disease	CVD primary prevention computerised	Usual care	• Medicines adherence

Study	Population	Intervention	Comparison	Key critical outcomes
USA	(primary prevention)	patient decision aid plus 3 tailored medicines adherence reminders		
Sheridan (2014)[2] *USA*	Cardiovascular disease (primary prevention)	CVD primary prevention computerised patient decision aid plus 3 tailored medicines adherence reminders	Usual care	• Patient knowledge • Decisional conflict • Participation in decision-making
Thomson (2007) UK	Atrial fibrillation	Antithrombotic computerised patient decision aid	Usual care (following evidence-based guidelines)	• Patient knowledge • Decision conflict • Participation in decision-making
Vuorma (2003)[3] *Finland*	Women with menorrhagia or fibroids	Menorrhagia patient decision aid (booklet)	Usual care	• Patient knowledge • Patient satisfaction • Hysterectomy rates
Vuorma (2004)[3] *Finland*	Women with menorrhagia or fibroids	Menorrhagia patient decision aid (booklet)	Usual care	• Patient satisfaction • General health status
Weymiller (2007) *USA*	Type 2 diabetes	Statin choice patient decision aid	Usual care (information pamphlet	• Patient knowledge • Decisional conflict • Medicines adherence
Whelan (2003) *Canada and USA*	Women with lymph node-negative breast cancer	Adjuvant chemotherapy in breast cancer patient decision aid	Usual care (medical consultation only)	• Patient knowledge • Patient satisfaction • Participation in decision-making

[1] Hamann 2006 and Hamann 2007 are the same RCT, different outcomes reported in the 2 published studies

[2] Sheridan 2011 and Sheridan 2014 are the same RCT, different outcomes reported in the 2 published studies

[3] Vuorma 2003 and Vuorma 2004 are the same RCT, different outcomes reported in the 2 published studies

Abbreviations: ADA, American Diabetes Association; BPH, benign prostatic hypertrophy; CVD, cardiovascular disease; HRT, hormone replacement therapy; MS, multiple sclerosis; QoL, quality of life; RCT, randomised controlled trial

Table 29 Summary of included studies – Patient decision aid compared with other intervention

Study	Population	Intervention	Comparison	Key critical outcomes
Deschamps (2004)	Peri- and post-	HRT patient decision aid with follow-up	Pharmacist consultation, with	• Decisional conflict

Study	Population	Intervention	Comparison	Key critical outcomes
Canada	menopausal women considering HRT	physician consultation	follow-up physician consultation	• Participation in decision-making • Patient satisfaction • Medicines adherence
Kennedy (2002) *UK*	Menorrhagia	Menorrhagia patient decision aid (booklet and videotape) sent to patients	Menorrhagia patient decision aid (booklet and videotape) sent to patients plus a pre-consultation structured interview	• Patient satisfaction • General health status • Hysterectomy rates
Lalonde (2006) *Canada*	Patients on lipid-lowering or antihypertensive therapy	Cardiovascular health patient decision aid (booklet and personal worksheet)	Cardiovascular health personal risk profile	• Patient knowledge • Decisional conflict • Patient satisfaction
Légaré (2003) *Canada*	Post-menopausal women (aged 45 to 69 years) considering HRT	Self-administered HRT patient decision aid (audio-tape, booklet and worksheet)	Information pamphlet on risks and benefits of HRT	• Decisional conflict
Raynes-Greenow (2010) *Canada*	Primiparous women ≥ 37 weeks gestation	Labour analgesia patient decision aid in 2 formats (booklet only and booklet plus audio guide)	Information pamphlet on risks and benefits of labour analgesia	• Patient knowledge • Decisional conflict • Participation in decision-making • Patient satisfaction • Labour and birth outcomes
Schapira (2007) *USA*	Post-menopausal women considering HRT	HRT computerised patient decision aid	Information pamphlet on risks and benefits of HRT	• Patient knowledge • Decisional conflict • Patient satisfaction
Abbreviation: HRT, hormone replacement therapy				

10.3.1 Analysis

The RCTs were quality assessed using the NICE methodology checklist for RCTs. Nine studies were found to be of high quality, 12 studies were found to be moderate quality and 7 studies were found to be low quality.

Two separate analyses were conducted:
1. Patient decision aid compared with usual care.
2. Patient decision aid compared with other intervention.

Characteristics of the comparators in the 2 analyses

Studies in which the comparator arm was no intervention or the provision of general patient information were included in the 'usual care' analysis. Studies in which the comparator arm was another active intervention or the provision of specific patient information about the risks and benefits of treatments were included in the 'other intervention' analysis. Comparators included in the patient decision aid compared with other intervention analysis were:

- pharmacist consultation (1 RCT)

- patient decision aid plus a pre-consultation structured interview (1 RCT)

- cardiovascular health personal risk profile (1 RCT)

- information pamphlet on risks and benefits of treatment (3 RCTs).

A large number of different critical outcomes were reported across the studies, not all of which could be included in the analyses. Therefore, the GDG prioritised some key critical outcomes for the analyses, which were most commonly measured in the included studies and consistent with the IPDAS criteria and outcomes in pooled analyses in the Cochrane review on patient decision aids.

Key critical outcomes relating to the use of patient decision aids in consultations about medicines that were prioritised by the GDG were:
- patient knowledge
- decisional conflict
- participation in decision-making
- patient satisfaction
- medicines adherence
- patient-oriented clinical outcomes.

Outcomes were measured at the first follow-up visit, unless otherwise stated.

Studies were pooled where possible when similar outcomes were measured and the effects were not dependent on the specific content of the patient decision aid. Some studies did not present sufficient data to allow pooling in the meta-analyses. Mean differences were calculated for continuous outcomes and risk ratios for dichotomous outcomes, as well as the corresponding 95% confidence intervals (CIs), if sufficient data were available. Data were analysed with a fixed-effects model. If there was potentially moderate or substantial heterogeneity between studies, analysis with a random-effects model was also conducted.

The evidence across outcomes was appraised using the GRADE framework and forest plots are presented where appropriate (see appendix D.2.6).

10.3.2 Key critical outcomes

Patient knowledge

Patient knowledge was measured by the number of questions answered correctly in a patient knowledge questionnaire. Different questionnaires were used across the studies, depending on the topic covered in the patient decision aid. However, the patient knowledge score was converted to a percentage score so data could be pooled across studies (that is, the number of questions answered correctly/the total number of questions multiplied by 100).

Six RCTs (total n=678) investigating patient decision aids with usual care that reported patient knowledge were included in a meta-analysis. In the meta-analysis, patient knowledge was increased with a patient decision aid, compared with usual care; mean difference 10.21, 95%CI 7.27 to 13.14 (see appendix D.2.6 for GRADE profile and forest plot). A further 8 presented data that could not be included in the pooled outcome; 4 of these studies reported increased patient knowledge with a patient decision aid, compared with usual care, whereas 3 studies reported no difference between groups; and 1 study (Sheridan 2014) measured patient knowledge in the intervention group only, before and after use of the patient decision aid. The findings of these studies are shown in table 30 below.

Two RCTs (total n=773) investigating patient decision aids with other intervention that reported patient knowledge were included in a meta-analysis. In the meta-analysis, there was no difference in patient knowledge with patient decision aids, compared with other intervention (information booklet describing risks and benefits of treatment); mean difference 2.60, 95%CI −0.54 to 5.75. Patient knowledge increased in Raynes-Greenow (2010) (mean difference 8.60, 95%CI 3.82 to 13.38), whereas there was no difference reported in Schapira (2007) (mean difference −2.00, 95%CI −6.18 to 2.18). See appendix D.2.6 for GRADE profile and forest plot. Because there was substantial heterogeneity between studies, a random-effects analysis was conducted that also showed no difference in patient knowledge with patient decision aids, compared with other intervention; mean difference 3.23, 95%CI −7.15 to 13.62.

A further RCT presented data that could not be included in the pooled outcome. The findings of this study are shown in table 30 below.

Table 30 Summary of studies reporting patient knowledge not providing adequate data for meta-analysis

Study	Findings
Patient decision aid (PDA) vs usual care	
Hamann (2006)	Insufficient data presented in paper for analysis. Study found patient knowledge was significantly increased in the PDA group, compared with usual care
Leighl (2011)	Median and range of values only were presented in paper. Study found patient knowledge was significantly increased in the PDA group, compared with usual care
Mann (2010)	Insufficient data presented in paper for analysis. Study found no significant difference in patient knowledge between groups
Mathers (2012)	Insufficient data presented in paper for analysis. Study found patient knowledge was significantly increased in the PDA group, compared with usual care (based on 2 knowledge questions)
Sheridan (2014)	Patient knowledge was assessed in the intervention group only. Study found patient knowledge was significantly increased following the PDA intervention, compared with baseline
Vuorma (2003)	Insufficient data presented in paper for analysis. Study found no significant difference in patient knowledge between groups
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a

Study	Findings
	forest plot which showed patient knowledge was significantly increased following the PDA intervention, compared with the control group; mean difference 2.4, 95%CI 1.5 to 3.3
Thomson (2007)	Insufficient data presented in paper for analysis. Study found no significant difference in patient knowledge between groups
PDA vs other intervention	
Lalonde (2006)	Insufficient data presented in paper for analysis. Study found no significant difference in patient knowledge between groups

Decisional conflict

Decisional conflict is the personal uncertainty about which course of action to take. The decisional conflict scale (DCS) was used in all studies that investigated decisional conflict. It measures personal perceptions of: uncertainty in choosing options; modifiable factors contributing to uncertainty such as feeling uninformed, unclear about personal values and being unsupported in decision-making; and effective decision-making. The DCS consists of a total score plus 5 separate subscale scores:

- uncertainty subscore
- informed subscore
- values clarity subscore
- support subscore
- effective decision-making subscore.

In some studies, the DCS point score was converted to a 1–100 point score so data could be pooled across studies, in line with the Ottawa Hospital Research Institute user manual. Lower decisional conflict scores indicate less decisional conflict.

Decisional conflict scale – total score

Seven RCTs (total n=936) investigating patient decision aid with usual care that reported DCS total score were included in a meta-analysis. In the meta-analysis, mean DCS total score was lower with patient decision aids, compared with usual care; mean difference –6.41, 95%CI –8.22 to –4.60 (see appendix D.2.6 for GRADE profile and forest plot). Because there was substantial heterogeneity between studies, a random-effects analysis was conducted that also showed that mean DCS total score was lower with patient decision aid, compared with usual care; mean difference –6.57, 95%CI –10.29 to –2.84.

A further 5 RCTs presented data that could not be included in the pooled outcome; 2 of these studies reported lower DCS total score with patient decision aids, compared with usual care, whereas 1 study reported no difference between groups; and 2 studies measured DCS total score in the intervention group only, before and after use of the patient decision aid. The findings of these studies are shown in table 31 below.

Four RCTs (total n=980) investigating patient decision aids with other interventions that reported DCS total score were included in a meta-analysis. In the meta-analysis, there was no difference in mean DCS total score with patient decision aids, compared with other interventions; mean difference –1.08, 95%CI –2.71 to 0.55 (see appendix D.2.6 for GRADE profile and forest plot). A further study presented data that could not be included in the pooled outcome. The findings of these studies are shown in table 31 below.

Table 31 Summary of studies reporting mean DCS total score not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Leighl (2011)	Median and range of values only were presented in paper. Study found no significant difference in DCS total score between groups
Oakley (2006)	DCS total score was assessed in the intervention group only. Study found DCS total score was significantly lower following the PDA intervention, compared with baseline
Sheridan (2014)	DCS total score was assessed in the intervention group only. Study found DCS total score was significantly lower following the PDA intervention, compared with baseline
Thomson (2007)	Insufficient data presented in paper for analysis. DCS total score was significantly lower in the PDA group immediately after the consultation, compared with the control group
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a forest plot which showed DCS total score was significantly lower following the PDA intervention, compared with the control group; mean difference –10.6, 95%CI –15.4 to –5.9
PDA vs other intervention	
Deschamps (2004)	Insufficient data presented in paper for analysis. Study found no significant difference in DCS total score between groups
Note: Lower decisional conflict scores indicates less decisional conflict	
Abbreviations: DCS, decisional conflict scale; PDA, patient decision aid	

Decisional conflict scale – uncertainty subscore

Three RCTs (total n=463) investigating patient decision aids with usual care that reported DCS uncertainty subscore were included in a meta-analysis. In the meta-analysis, mean DCS uncertainty subscore was lower with patient decision aids, compared with usual care; mean difference –8.33, 95%CI –12.25 to –4.41 (see appendix D.2.6 for GRADE profile and forest plot). A further study presented data that could not be included in the pooled outcome. The findings of this study are shown in table 32 below.

Two RCTs (total n=200) investigating patient decision aids with other interventions that reported DCS uncertainty subscore were included in a meta-analysis. In the meta-analysis, there was no difference in mean DCS uncertainty subscore with patient decision aids, compared with other interventions; mean difference –3.34, 95%CI –7.69 to 1.02 (see appendix D.2.6 for GRADE profile). Because there was substantial heterogeneity between the 2 studies, a random-effects analysis was conducted. In this analysis, there was no difference in mean DCS uncertainty subscore with patient decision aids, compared with other interventions; mean difference –4.64, 95%CI –13.66 to 4.37.

Table 32 Summary of studies reporting mean DCS uncertainty subscore not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a forest plot which showed DCS uncertainty subscore was significantly lower following the PDA intervention, compared with the control group; mean difference –12.8, 95%CI –18.4 to –7.3
Note: Lower decisional conflict scores indicates less decisional conflict	
Abbreviations: DCS, decisional conflict scale; PDA, patient decision aid	

Decisional conflict scale – informed subscore

Three RCTs (total n=402) investigating patient decision aids with usual care that reported DCS informed subscore were included in a meta-analysis. In the meta-analysis, mean DCS informed subscore was lower with patient decision aids, compared with usual care; mean difference –6.35, 95%CI –9.58 to –3.13 (see appendix D.2.6 for GRADE profile and forest plot). A further 2 studies presented data that could not be included in the pooled outcome. The findings of these studies are shown in table 33 below.

One small RCT (n=24) investigating patient decision aids with other interventions reported DCS informed subscore. There was no difference in mean DCS informed subscore with patient decision aids, compared with other interventions (personal risk profile); mean difference 7.00, 95%CI –2.12 to 16.12 (see appendix D.2.6 for GRADE profile). A further study presented data that could not be included in the pooled outcome. The findings of these studies are shown in table 33 below.

Table 33 Summary of studies reporting mean DCS informed subscore not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a forest plot which showed DCS informed subscore was significantly lower following the PDA intervention, compared with the control group; mean difference –17.3, 95%CI –22.6 to –12.0
Thomson (2007)	Insufficient data presented in paper for analysis. DCS informed subscore was significantly lower in the PDA group immediately after the consultation, compared with the control group
PDA vs other intervention	
Deschamps (2004)	Insufficient data presented in paper for analysis. Study found no significant difference in DCS informed subscore between groups
Note: Lower decisional conflict scores indicates less decisional conflict Abbreviations: DCS, decisional conflict scale; PDA, patient decision aid	

Decisional conflict scale – values clarity subscore

One RCT (n=167) investigating patient decision aids with usual care reported DCS values clarity subscore. Mean DCS values clarity subscore was lower with patient decision aids, compared with usual care; mean difference –10.00, 95%CI –14.97 to –5.03 (see appendix D.2.6 for GRADE profile). A further 2 studies presented data that could not be included in the analysis. The findings of these studies are shown in table 34 below.

One small RCT (n=24) investigating patient decision aids with other intervention reported DCS values clarity subscore. There was no difference in mean DCS values clarity subscore with patient decision aids, compared with other interventions (personal risk profile); mean difference 2.00, 95%CI –7.54 to 11.54 (see appendix D.2.6 for GRADE profile).

Table 34 Summary of studies reporting mean DCS values clarity subscore not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a forest plot which showed DCS values clarity subscore was significantly reduced following the PDA intervention, compared with the control group; mean difference –8.5, 95%CI –15.7 to –1.3
Thomson (2007)	Insufficient data presented in paper for analysis. DCS values clarity subscore was significantly lower in the PDA group immediately after the consultation,

Study	Findings
	compared with the control group
Note: Lower decisional conflict scores indicates less decisional conflict	
Abbreviations: DCS, decisional conflict scale; PDA, patient decision aid	

Decisional conflict scale – support subscore

Two RCTs (total n=317) investigating patient decision aids with usual care that reported DCS support subscore were included in a meta-analysis. In the meta-analysis, mean DCS support subscore was lower with patient decision aids, compared with usual care; mean difference –3.89, 95%CI –6.99 to –0.80 (see appendix D.2.6 for GRADE profile and forest plot). A further 2 studies presented data that could not be included in the pooled outcome. The findings of these studies are summarised in table 35 below.

One small RCT (n=24) investigating patient decision aids with other interventions reported DCS support subscore. There was no difference in mean DCS support subscore with patient decision aids, compared with other interventions (personal risk profile); mean difference 1.50, 95%CI –8.93 to 11.93 (see appendix D.2.6 for GRADE profile).

Table 35 Summary of studies reporting mean DCS support subscore not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Branda (2013)	Insufficient data presented in paper for analysis. Study found no significant difference in DCS total score between groups
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a forest plot which showed DCS support subscore was significantly reduced following the PDA intervention, compared with the control group; mean difference –9.4, 95%CI –14.8 to –3.9
Note: Lower decisional conflict scores indicates less decisional conflict	
Abbreviations: DCS, decisional conflict scale; PDA, patient decision aid	

Decisional conflict scale – effective decision-making subscore

Three RCTs (total n=463) investigating patient decision aids with usual care that reported DCS effective decision-making subscore were included in a meta-analysis. In the meta-analysis, mean DCS effective decision-making subscore was lower with patient decision aids, compared with usual care; mean difference –6.84, 95%CI –9.21 to –4.47 (see appendix D.2.6 for GRADE profile and forest plot). A further 2 studies presented data that could not be included in the pooled outcome. The findings of these studies are shown in table 36 below.

Two RCTs (total n=198) investigating patient decision aids with other interventions that reported DCS effective decision-making subscore were included in a meta-analysis. In the meta-analysis, there was no difference in mean DCS effective decision-making subscore with patient decision aid, compared with other interventions; mean difference −0.39, 95%CI –3.92 to 3.19 (see appendix D.2.6 for GRADE profile).

Table 36 Summary of studies reporting mean DCS effective decision-making subscore not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Branda (2013)	Insufficient data presented in paper for analysis. Study found no significant difference in DCS total score between groups
Weymiller (2007)	Insufficient data presented in paper for analysis. Data was presented as a forest plot which showed DCS effective decision subscore was significantly reduced following the PDA intervention, compared with the control group;

Study	Findings
	mean difference –10.0, 95%CI –15.0 to –5.0

Note: Lower decisional conflict scores indicates less decisional conflict
Abbreviations: DCS, decisional conflict scale; PDA, patient decision aid

Participation in decision-making

Participation in decision-making was measured by patients' preferred method of decision-making (control preference scale):

- Patient controlled (autonomous) decision-making
- Shared decision-making (between patient and health professional)
- Health professional controlled decision-making

Participation in decision-making was also measured using the OPTION scale score in some studies, which is a validated tool designed to assess the overall shared decision-making process in consultations. Higher OPTION scale scores indicate greater patient involvement.

Participation in decision making – patient controlled decision-making

Four RCTs (total n=736) investigating patient decision aids with usual care that reported patient controlled decision-making preference were included in a meta-analysis. In the meta-analysis, the number of patients adopting a patient controlled decision-making role was higher with patient decision aids, compared with usual care; risk ratio 1.20, 95%CI 1.07 to 1.35 (see appendix D.2.6 for GRADE profile and forest plot). Because there was substantial heterogeneity between studies, a random-effects analysis was conducted. In this analysis, there was no difference in the number of patients adopting a patient controlled decision-making role with a patient decision aid, compared with usual care; risk ratio 1.25, 95%CI 0.90 to 1.72.

One RCT (n=596) investigating patient decision aids with other interventions reported patient controlled decision-making preference. There was no difference in the number of patients adopting a patient controlled decision-making role with a patient decision aid, compared with other interventions (information pamphlet describing risks and benefits of treatment); risk ratio 0.95, 95%CI 0.87 to 1.04 (see appendix D.2.6 for GRADE profile). A further study presented data that could not be included in the analysis. The findings of this study are shown in table 37 below.

Participation in decision making – shared decision-making

Five RCTs (total n=896) investigating patient decision aids with usual care that reported shared decision-making preference were included in a meta-analysis. In the meta-analysis, the number of patients adopting a shared decision-making role was lower with patient decision aids, compared with usual care; risk ratio 0.85, 95%CI 0.75 to 0.97 (see appendix D.2.6 for GRADE profile and forest plot). Because there was moderate heterogeneity between studies, a random-effects analysis was conducted. In this analysis, there was no difference in the number of patients adopting a shared decision-making role with patient decision aids, compared with usual care; risk ratio 0.84, 95%CI 0.71 to 1.00.

One RCT (n=596) investigating patient decision aids with other interventions reported shared decision-making preference. There was no difference in the number of patients adopting a shared decision-making role with patient decision aids, compared with other interventions (information pamphlet describing risks and benefits of treatment); risk ratio 1.23, 95%CI 0.87 to 1.74 (see appendix D.2.6 for GRADE profile). A further study presented data that could not be included in the analysis. The findings of this study are shown in table 37 below.

Participation in decision making – health professional controlled decision-making

Five RCTs (total n=907) investigating patient decision aids with usual care that reported health professional controlled decision-making preference were included in a meta-analysis. In the meta-analysis, the number of patients adopting a health professional controlled decision-making role was lower with patient decision aids, compared with usual care; risk ratio 0.60, 95%CI 0.39 to 0.93 (see appendix D.2.6 for GRADE profile and forest plot).

One RCT (n=596) investigating patient decision aids with other interventions reported health professional controlled decision-making preference. There was no significant difference in the number of patients adopting a health professional controlled decision-making role with patient decision aids, compared with other interventions (information pamphlet describing risks and benefits of treatment); risk ratio 0.85, 95%CI 0.20 to 3.51 (see appendix D.2.6 for GRADE profile). A further study (Deschamps 2004) presented data that could not be included in the analysis. The findings of this study are shown in table 37 below.

Participation in decision making – patient involvement (OPTION scale)

Three RCTs (total n=194) investigating patient decision aids with usual care that reported patient involvement (measured by the OPTION scale score) were included in a meta-analysis. In the meta-analysis, patient involvement was increased with patient decision aids compared with usual care; risk ratio 22.09, 95%CI 17.23 to 26.94 (see appendix D.2.6 for GRADE profile and forest plot).

A further 5 RCTs presented data that could not be included in any of the pooled outcomes for participation in decision-making. The findings of these studies are shown in table 37 below.

Table 37 Summary of studies reporting patient knowledge participation in decision-making outcomes not providing adequate data for meta-analysis

Study	Findings
PDA vs usual care	
Hamann (2006)	COMRADE score used to measure patient involvement and data could not be classified into 3 preferences. Study found patient involvement was significantly increased in the PDA group, compared with usual care
Leighl (2011)	Insufficient data presented in paper for analysis. Study found no significant difference in patients achievement of their involvement preferences between groups
Morgan (2000)	Insufficient data presented in paper for analysis. Study found no significant difference in shared decision-making between groups
Sheridan (2006)	Data could not be classified into 3 preferences. Patient knowledge was assessed in the intervention group only. Study found no significant differences between groups
Thomson (2007)	Insufficient data presented in paper for analysis and data could not be classified into 3 preferences. Study found significant increase in patient perception that they were more important in decision-making
PDA vs other intervention	
Deschamps (2004)	Insufficient data presented in paper for analysis. Study found no significant differences between groups
Abbreviation: PDA, patient decision aid	

Patient satisfaction

Patient satisfaction was measured by patient responses to a questionnaire; higher scores indicate greater patient satisfaction. In some studies, patient satisfaction score was converted to a 1–100 point score. Different patient satisfaction questionnaires were used for a range of outcome measures, including satisfaction with:

- treatment choice
- treatment outcome

- knowledge transfer
- the decision-making process
- preparation for decision-making
- opportunities to participate in decision-making.

Ten RCTs investigating patient decision aids with usual care reported a range of measures of patient satisfaction, such as satisfaction with the decision-making process, satisfaction with treatment outcome, satisfaction with knowledge transfer and satisfaction with the consultation. No data could be pooled. Overall, there were no differences between patient decision aids and usual care for most of the patient satisfaction outcomes (see appendix D.2.6 for GRADE profile). One RCT (Kennedy 2002) that compared a patient decision aid plus structured interview with usual care found an increase in 2 measures of patient satisfaction with patient decision aid plus interview. One study (Oakley 2006) reported patient satisfaction after the intervention in the patient decision aid group only.

Five RCTs studies investigating patient decision aids with other intervention also reported a range of measures of patient satisfaction. Data from 2 RCTs measuring patient satisfaction with the decision were pooled. No data from other outcomes could be pooled. Across all studies, there were no differences between patient decision aids and other interventions for any patient satisfaction outcomes (see appendix D.2.6 for GRADE profile).

Medicines adherence

Eight RCTs investigating patient decision aids with usual care reported medicines adherence. No data could be pooled. There was no difference in medicines adherence with patient decision aids compared with usual care in 5 RCTs. Three RCTs reported a difference between groups, with 2 studies being in favour of patient decision aids and 1 study being in favour of usual care (see appendix D.2.6 for GRADE profile).

One RCT investigating patient decision aids with usual care reported medicines adherence. There was no difference in medicines adherence with patient decision aids compared with other interventions (pharmacist consultation) (see appendix D.2.6 for GRADE profile).

Patient-oriented clinical outcomes

Six RCTs investigating patient decision aids with usual care reported general health status. No data could be pooled. There was no difference in general health status with patient decision aids compared with usual care across all studies (see appendix D.2.6 for GRADE profile).

Two RCTs (total n=763) investigating patient decision aids with usual care that reported hysterectomy rates were included in a meta-analysis. In the meta-analysis, there was no difference in hysterectomy rates with patient decision aids compared with usual care; risk ratio 1.04, 95%CI 0.90 to1.20 (see appendix D.2.6for GRADE profile). One RCT also reported data for patient decision aids plus structured interview compared with usual care; there was no difference in hysterectomy rates between groups.

One RCT investigating patient decision aids alone with patient decision aids plus structured interviews reported hysterectomy rates. Hysterectomy rates were lower with patient decision aid plus structured interviews, compared with patient decision aids alone; rate ratio 0.80, 95%CI 0.64 to 0.99 (see appendix D.2.6 for GRADE profile).

One RCT investigating patient decision aids with usual care reported menorrhagia quality of life. There was no difference in menorrhagia quality of life with patient decision aids compared with usual care (see appendix D.2.6 for GRADE profile).

One RCT investigating patient decision aids with usual care reported menorrhagia specific utility scale score. Menorrhagia specific utility scale score improved in the patient decision aid group, compared with usual care (see appendix D.2.6 for GRADE profile).

One RCT investigating patient decision aids with usual care reported cancer therapy quality of life. There was no difference in cancer therapy quality of life with patient decision aids compared with usual care (see appendix D.2.6 for GRADE profile).

One RCT investigating patient decision aids with usual care reported prostatectomy or referral for prostatectomy. There was no difference in prostatectomy or referral for prostatectomy with patient decision aids compared with usual care. One RCT (Raynes-Greenow 2010) investigating patient decision aids with usual care reported labour and birth outcomes. There was no difference in labour and birth outcomes with patient decision aids compared with usual care (see appendix D.2.6 for GRADE profile).

10.4 Health economic evidence

Summary of evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies evaluating patient decision aids used in consultations to improve patient outcomes from medicines. This search identified 2879 records, of which 2866 were excluded based on their title and abstract. The full papers of 13 studies were assessed and all 13 were excluded at this stage. The excluded studies and reason for their exclusion are shown in appendix C.6.6.

A Cochrane review of studies was identified separately from the scoping search (Stacey et al. 2014). This could not be included in full because many of the included studies used patient decision aids to make decisions unrelated to medicines, did not involve a consultation or contact with a clinician, or included no economic analysis. References included in this systematic review were screened to identify any studies that met the inclusion criteria. Four cost-effectiveness studies were identified and included. These studies were not identified in the systematic literature search because the search only identified those records that included 'patient decision aid' and 'medicine' components in either the medical subject headings or free text. The 4 studies identified from the Cochrane review did not include the term 'medicine' within the free text or medical subject headings.

The 4 studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. At this stage, the study by Vuorma et al. (2004) was judged not applicable to the guidance because it was set in Finland and studies of the same patient group with a UK NHS perspective had already been included in the review and were therefore more relevant to the guidance. This study was excluded from any further analysis. The 3 included studies are summarised in table 38.

The study by Kennedy et al. (2002) included a cost–consequence analysis comparing patient information to aid treatment decision with patient information plus a structured interview to aid treatment decisions and with usual care. Patients in this study had menorrhagia and were using decision aids to choose between treatment options. Murray et al. (2001[a] and 2001[b]) compared an interactive multimedia decision aid with usual care in both patients considering hormone replacement therapy (Murray et al. 2001[a]) and patients with benign prostatic hypertrophy (Murray et al. 2001[b]).

All 3 included studies were built on RCT data to provide a cost–consequence analysis for the duration of the trial (therefore each considered a short time frame). Quality of life was reported directly from the patients and the studies were set in the UK NHS, with costs also from this perspective. Each of the 3 studies was considered to be a subgroup of the guideline

population. The 3 studies were therefore judged to be partially applicable to the guidance with potentially serious limitations.

The study evidence tables for the included studies are shown in appendix E.1.6.

This area was not identified as an area for health economic modelling by the GDG, given the variation in practice likely to exist in the use of patient decision aids in consultations about medicines.

Table 38 Economic evidence profile – Patient decision aids

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost effectiveness	
Kennedy et al. (2002) (UK, CCA)	Potentially serious limitations[1]	Partially applicable[2,3]	An RCT including cost consequence over a 2-year time horizon Interventions: Patient menorrhagia decision aided via information pack Patient menorrhagia decision aid via information pack plus structured interview Comparator: Usual care	−£463.16[4] −£761.84[5] −£302.63[6]	Equal[7] Improved QoL[8] Improved QoL[9]	Cost saving[4] Dominant[5] Dominant[6]	Limited scenario analysis resulted in no change in direction of results
Murray et al. (2001)[a] (UK, CCA)	Potentially serious limitations[1]	Partially applicable[2,3]	An RCT including cost consequence over a 9-month time horizon Intervention: Patient decision aid consisting interactive multimedia programme Comparator: Usual care	£215.50[10]	Equal[11]	Cost incurring	Narrow confidence interval around incremental costs suggests low uncertainty
Murray et al. (2001)[b] (UK, CCA)	Potentially serious limitations[1]	Partially applicable[2,3]	An RCT including cost consequence over a 9-month time horizon Intervention: Patient decision aid consisting interactive multimedia	£405.40[12]	Equal[11]	Cost incurring	Wide confidence interval around incremental costs suggests high uncertainty

			programme			
			Comparator: Usual care			

[1] Sensitivity analysis was limited, however given that the analysis were based on a corresponding RCT there is likely to be high internal validity

[2] Short time horizon may mean that long-term costs and QALYs were not captured

[3] Study population is a small subgroup of the whole guidance population and the study is relatively old

[4] Patient decision aid compared with usual care

[5] Patient decision aid plus structured interview compared with usual care

[6] Patient decision aid plus structured interview compared with patient decision aid

[7] No significant difference on any dimension of SF-36 between patient decision aid and usual care

[8] Significant improvement in physical dimension of SF-36 and no significant difference in any other dimension between patient decision aid plus structured interview and usual care

[9] Significant improvement in physical dimension of SF-36 and no significant difference in any other dimension between patient decision aid plus structured interview and patient decision aid

[10] 95% CI £203.10 to £228.00. The incremental cost varies slightly from the cost difference between the two interventions as reported in the publication because of rounding

[11] No significant difference from baseline to final assessment between the 2 groups in the SF-36, EQ-5D or MenQoL

[12] 95% CI −£58.90 to £302.00. The incremental cost varies slightly from the cost difference between the two interventions as reported in the publication because of rounding

Abbreviations: CI, confidence interval; QALYs, quality-adjusted life years; QoL, quality of life; RCT, randomised controlled trial; CCA, Cost-consequence analysis

10.5 Evidence statements

Clinical evidence

High-quality evidence from 6 RCTs showed that a patient decision aid used in a consultation about medicines was effective in improving patient knowledge, compared with usual care.

Moderate-quality evidence from 7 RCTs showed that a patient decision aid used in a consultation about medicines was effective in improving overall decisional conflict, compared with usual care.

Moderate-quality evidence from 5 RCTs showed that a patient decision aid used in a consultation about medicines reduced the number of patients who wanted their health professional to make the decision for them, compared with usual care.

Moderate-quality evidence from 3 RCTs showed that a patient decision aid used in a consultation about medicines was effective in increasing patient involvement during the consultation, compared with usual care.

Low-quality evidence from 1 RCT showed that a patient decision aid was effective in improving patient satisfaction with decision-making, compared with usual care. One RCT showed that a patient decision aid was not effective in improving patient satisfaction with decision-making.

Low-quality evidence from 8 RCTs showed that a patient decision aid used in a consultation about medicines did not appear to improve medicines adherence, compared with usual care.

Economic evidence

Partially applicable evidence from three studies with potentially serious limitations built on RCT data suggests that the cost effectiveness of using patient decision aids in consultations about medicines depends on the scope of the patient decision aid in use and potentially the patient population using the patient decision aid.

Robust evidence from one study suggests that the use of a low-cost paper-based patient decision aid for women with menorrhagia is cost-saving over usual care, whereas evidence from a second study suggests electronic patient decision aids in patients considering hormone replacement therapy are cost-incurring compared with usual care. More uncertain evidence from one study suggests that the use of an electronic patient decision aid used in patients with prostatic hypertrophy is cost-incurring compared with usual care.

No evidence was available for the cost effectiveness of patient decision aids in any other patient populations.

10.6 `Evidence to recommendations

Table 39 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG discussed the relative importance of the outcomes and agreed that mortality, patient-reported outcomes, clinical outcomes as reported in the study, and health and social care utilisation were critical in decision-making. Medicines-related problems and health and social care related quality of life were considered important for decision-making, but not critical. A large number of different critical outcomes were reported across the studies, including patient knowledge, different measures of decisional conflict, different measures of patient satisfaction, medicines adherence and a wide

range of clinical outcomes. Therefore, the GDG prioritised some key critical outcomes for the analyses, which were most commonly measured in the included studies and consistent with the IPDAS criteria and outcomes included in pooled analyses in a Cochrane review on patient decision aids (Stacey et al. 2014). Key critical outcomes relating to the use of patient decision aids in consultations about medicines prioritised by the GDG were:

- patient knowledge
- decisional conflict
- participation in decision making
- patient satisfaction
- medicines adherence
- patient-oriented clinical outcomes.

Trade-off between benefits and harms	**Patient involvement in decision-making about medicines** The GDG agreed that using a patient decision aid is only one component of shared decision-making and should not replace an effective shared decision-making consultation with a patient. A patient decision aid can support health professionals to have a shared decision-making approach as part of a wider shared decision-making process, but is not sufficient on its own. The evidence reviewed by the GDG found that a patient decision aid did not appear to be more effective than other active interventions that present the risks and benefits of the available options to patients, although evidence was limited. The GDG agreed that patient decision aids can support people to become involved in decision-making and encourage them to play a more active role. The evidence showed that the number of people wanting the health professional to make the decision for them significantly reduced after a patient decision aid was used, compared with usual care. The GDG recognised that most people want to have some involvement in decisions about their medicines. Very few people want the health professional solely to make the decision. However, the GDG recognised that many patients do not receive an effective shared-decision making consultation about their medicines in practice. The GDG recognised that it was important for the health professional to determine the patient expectations about what level of involvement in decisions they would like. They were aware that health professionals often make assumptions about this, and these assumptions may be incorrect. The GDG discussed the principles of shared decision-making and agreed that there are many different perceptions of shared decision-making. The agreed that this was an important aspect of undergraduate curricula but this was outside the scope of this guideline. The GDG recognised that shared decision-making brings together the best available evidence and the health professional's own clinical expertise, while always taking account of an individual patient's values and preferences. The GDG was aware that the values and preferences of an individual patient, and their attitudes to risk, may be different from those of health professionals. The GDG recognised that shared decision-making should not be a 'rules-based' application of evidence-based medicine, and that the patient's values and preferences should be considered. The patient consultation is a 2-way communication process and should not be dominated by the health professional.

The GDG concluded that health professionals should apply the principles of evidence-based medicine during consultations when discussing the available options with an individual patient. They should carefully use the best available evidence when making decisions with or for individual patients, together with their own clinical expertise and the patient's values and preferences.

The GDG concluded that all patients should be offered the opportunity to be involved in making decisions about their medicines. The health professional should find out what level of involvement in decision-making the patient would like and should avoid making their own assumptions about this.

The GDG concluded that health professionals should find out about a patient's values and preferences by discussing what is important to them about managing their condition(s) and their medicines. They should ask open questions to understand the patient's ideas, concerns and expectations. The GDG agreed that it was also important to recognise that the patient's values and preferences may be different to those of the health professional, and to avoid making assumptions about them.

The role of patient decision aids

The available evidence (high to moderate quality) suggests that patient decision aids used in consultations about medicines are effective in improving patient knowledge and reducing decisional conflict associated with decision-making, compared with usual care. However, the GDG recognised that using a patient decision aid is not a 'quick fix' and is not a replacement for a skilled consultation between a patient and a health professional. They agreed that a patient decision aid can help to allow a shared decision-making approach and help patients to consider the risks and benefits of the available options. It gives patients an opportunity to consider their options and allows health professionals to explore their responses to information. They also agreed that it may help to reduce variation in the consultation process.

The evidence identified for this review included studies investigating some specific topics including cardiovascular disease, type 2 diabetes, menorrhagia, menopause and osteoporosis. The GDG recognised that some topics are more suitable for a patient decision aid than others. They are particularly beneficial when patients are making a preference-sensitive decision where there are a number of trade-offs between benefits and harms, and where there is therapeutic uncertainty about the most appropriate option.

The GDG was aware that health professionals may need more time in consultations to use a patient decision aid and allow for effective shared decision-making. They recognised that it may be appropriate to take more than one consultation and that continued patient support was important. The GDG also agreed that this may provide further opportunity to seek out the patient's values and preferences to make an informed decision over a period of time. Although the GDG agreed that the process may take longer when they use a patient decision aid, it may help to alter the power dynamic of the consultation in favour of the patient. The GDG also recognised that a patient's decisions may change over time – for example, as they become older and their baseline risk increases – and their decisions may need to

be readdressed. The GDG agreed that patient decision aids should not be used to impose a health professional's view on the decision they think the patient should make.

The GDG discussed the use of patient decision aids in patient consultations about medicines, compared with patients being given a patient decision aid to take away and self-administer. The evidence review only considered studies that included a consultation. The GDG recognised that a patient may want to take the patient decision aid home to read further or discuss with a family member or carer. However, they agreed that patient decision aids are intended to be used in consultations to encourage better informed, patient-focused decision-making between the patient and health professional.

Following its discussions, the GDG concluded that patients should be offered the opportunity to use a patient decision aid in a consultation about medicines, where one is available to help them make a preference-sensitive decision that involves trade-offs between benefits and harms. Health professionals should ensure that the patient decision aid is appropriate in the context of the consultation as a whole.

A patient decision aid should not be used to replace discussions with a patient in a consultation about medicines. It should be used as a tool to support patients when they are considering the available options as part of an effective shared decision-making consultation. The GDG also concluded that it was important to recognise that it may be appropriate to have more than one consultation to ensure that a patient can make an informed decision about their medicine(s). Patients should be given the opportunity to review their decision, as appropriate, as this may change over time.

Supporting the use of patient decision aids
The GDG recognised the importance of health professionals familiarising themselves with the content of a patient decision aid thoroughly before using it. The GDG also discussed the skills and expertise needed by health professionals to be competent in using them effectively in consultations with patients about their medicines. They recognised the importance of training health professionals in this area and agreed some core knowledge, skills and expertise that are needed. The GDG was also aware that patient decision aids may be used as a tool to support health professional education, but this is outside the scope of this guideline.

The GDG acknowledged that using patient decision aids is not currently routine practice. Developing a patient decision aid is only part of the process, and ensuring that health professionals use them appropriately and consistently in their practice is much more difficult. The GDG agreed by consensus that the large-scale production of a wide range of patient decision aids is not appropriate. A more targeted approach of prioritising a few key patient decision aids and supporting people to use them appropriately and consistently, would be more beneficial. The GDG agreed that these discussions should take place locally so that patient decision aids are prioritised for use according to local health needs in line with pathways. The GDG agreed by consensus that local medicines decision-making groups may want to enable this process as part of their governance arrangements.

The GDG agreed that all relevant health professionals and stakeholders across the local health economy need to be aware of patient decision aids being used locally, to ensure there is a consistent approach. The GDG also recognised the importance of having an appropriate education and training in place, but recognised there are resource implications associated with this.

Following its discussions, the GDG concluded that health professionals should ensure they have the necessary knowledge, skills and expertise to carry out an effective shared decision-making consultation about medicines. This includes:

- relevant clinical knowledge
- effective communication and consultation skills, especially eliciting patients' values and preferences
- effective numeracy skills, including explaining the risks and benefits in natural frequencies, and relative and absolute risk
- explaining the trade-offs between particular benefits and harms which each individual may weigh differently.

Before using a patient decision aid in a consultation about medicines, health professionals should read and understand its content, paying particular attention to its limitations and the need to adjust discussions according to the patient's baseline risk.

Commissioners and providers should consider adopting a locally agreed, targeted approach to prioritise the use of key patient decision aids that are offered to patients in a local health economy, according to the health needs of the population. This may be facilitated by a local medicines decision-making group as part of local governance arrangements. These patient decision aids should also be included in the appropriate patient pathway(s) and their use reviewed regularly.

The GDG also concluded that patient decision aids that are prioritised locally should be disseminated to all relevant health professionals and stakeholders. Training and education needs should also be considered to support people in developing the skills needed to use patient decision aids effectively in consultations about medicines.

Consideration of health benefits and resource use	The GDG considered the economic evidence on patient decision aids used in consultations about medicines and were concerned about the age of the included studies (studies were published in 2001 and 2002). The GDG discussed the relevance of this evidence, in particular around the use of patient decision aids on hormone replacement therapy. The GDG acknowledged that although the patient decision aids for this topic may be of limited relevance to the current clinical practice within the NHS, the results of the study may be generalisable to similar patient decision aids in other (more relevant) topics. The GDG was also aware of the short time frame of the economic evidence and that longer term costs and benefits would not have been captured within the analysis.
	The GDG was aware that the economic evidence suggested that more costly patient decision aids, for example those using multimedia platforms, were less likely to be cost-effective than cheaper patient decision aids (for example, paper-based tools). The GDG felt that the content of the patient decision aid – that is, the inclusion of relevant evidence-based information with graphical representations and option grid – was more important than the platform on which the aid was provided.
Quality of evidence	The quality of the evidence for studies that investigated using patient decision aids compared with usual care was high to moderate for

	most of the outcomes analysed. The evidence was low quality for the medicines adherence outcome. The quality of the evidence for studies that investigated patient decision aids compared with other active intervention was generally lower quality overall. For outcomes where it was possible to pool data in a meta-analysis, a fixed effects model was used. When heterogeneity between studies was potentially moderate or substantial, the GDG asked for a further analysis with a random effects model to be conducted.
Other considerations	Information was presented to the GDG by an expert co-opted witness to provide context. This allowed the GDG to ask questions and discuss the interpretation of the evidence into recommendations.
	The GDG recognised that not all patients may understand or want to use a patient decision aid. However, the GDG agreed that age or health literacy was not an acceptable reason to not offer using a patient decision aid. Some patients may need additional support but this should not be a factor in whether the patient should participate in decision-making.
	NICE published its first patient decision aid on atrial fibrillation in June 2014. The GDG was aware that many different patient decision aids exist, produced by a number of different providers. Some websites collate examples of patient decision aids, but it is not always clear whether the development process followed the IPDAS criteria. There is currently no single repository where health professionals can access high-quality patient decision aids.
	The evidence review did not investigate the quality of the patient decision aids, but some studies did state that they were developed according to IPDAS criteria. The GDG was not able to determine if the quality of the patient decision aids would influence the reported outcomes. The GDG was concerned that if poor quality patient decision aids were used that did not reflect the best available evidence then the decision has the potential to lead to patient harm.
	The GDG agreed that the quality of patient decision aids can vary and this was an important issue for consideration. The agreed by consensus that the IPDAS criteria were the gold standard for developing patient decision aids. This process includes:
	• clearly defining the scope, such as describing the health condition, the decision being considered and the target audience
	• establishing a steering group with clearly defined membership criteria that includes patients, health professionals and relevant experts
	• declaring conflicts of interest, if appropriate
	• finding out patient and practitioners' views on decision support needs
	• describing the media and format, with supporting rationale
	• describing the intended setting, including its introduction into the care pathway, how and when the patient decision aid will be disseminated to patients and/or practitioners
	• appraising and summarising clinical evidence relevant to the decision and options, including describing the methods for evidence review
	• describing prototype development
	• testing for comprehensibility and usability with patients and practitioners
	• finding out patient and practitioners' views of the feasibility of using the patient decision aid in practice

• peer review by experts external to the development process

The GDG also recognised that the format and presentation of patient decision aids can vary. Many different formats are available with various levels of interactivity. The GDG was not able to recommend a particular format but discussed and agreed some principles that were important.

The GDG concluded that only high-quality patient decision aids that have followed a robust and transparent development process are used in patient consultations, in line with the IPDAS criteria.

10.7 Recommendations and research recommendations

Many people wish to be active participants in their own healthcare, and to be involved in making decisions about their medicines. Patient decision aids can support health professionals to adopt a shared decision-making approach in a consultation, to ensure that patients are able to make well-informed choices that are consistent with their values and preferences.

32. **Offer all people the opportunity to be involved in making decisions about their medicines. Find out what level of involvement in decision-making the person would like and avoid making assumptions about this.**

33. **Find out about a patient's values and preferences by discussing what is important to them about managing their condition(s) and their medicines. Recognise that the patient's values and preferences may be different from those of the health professional and avoid making assumptions about them.**

34. **Apply the principles of evidence-based medicine when discussing the available treatment options with a person in a consultation about medicines. Use the best available evidence carefully when making decisions with or for individual patients, together with clinical expertise and the patients' values and preferences.**

35. **In a consultation about medicines, offer the person the opportunity to use a patient decision aid (when one is available), to help them make a preference-sensitive decision (a decision based on the patient's preferences and personal values of each treatment option presented) that involves trade-offs between benefits and risks. Ensure the patient decision aid is appropriate in the context of the consultation as a whole.**

36. **Do not use a patient decision aid to replace discussions with a person in a consultation about medicines.**

37. **Recognise that it may be appropriate to have more than 1 consultation to ensure that a person can make an informed decision about their medicines. Give people the opportunity to review their decision, as appropriate, because this may change over time (for example, a person's baseline risk may change).**

38. **Ensure that patient decision aids used in consultations about medicines have followed a robust and transparent development process, in line with the IPDAS criteria.**

39. **Before using a patient decision aid with a person in a consultation about medicines, read and understand its content, paying particular attention to its limitations and the need to adjust discussions according to the patient's [baseline risk](#).**

40. **Have the necessary knowledge, skills and expertise, when using a patient decision aid, including:**

    - relevant clinical knowledge
    - effective communication and consultation skills, especially when finding out patients' values and preferences
    - effective numeracy skills, especially when explaining the risks and benefits in natural frequencies, and relative and absolute risk
    - explaining the trade-offs between particular benefits and risks.

41. **Consider training and education needs to support health professionals and patients in developing the appropriate skills and expertise to use patient decision aids effectively in consultations about medicines.**

42. **Organisations should consider identifying and prioritising which patient decision aids are needed for their patient population through, for example, a local medicines decision-making group. Agree a consistent, targeted approach in line with local pathways and review the use of the patient decision aids regularly.**

43. **Organisations should ensure that patient decision aids prioritised for use locally are disseminated to all relevant health professionals and stakeholders.**

11 Clinical decision support

11.1 Introduction

Evidence-based medicine is founded on the idea that decision-making in healthcare should incorporate the best available evidence in conjunction with the experience of the clinician and the views of the patient (Sackett et al. 1996). In clinical practice, one way to implement this approach is to use information technology and a clinical decision support 'system' or 'tool' along with evidence-based medicine and clinical experience.

For the purpose of this guideline, clinical decision support is an active, computerised intervention that occurs at the time and location of prescribing, to support prescribers with decision-making. The term 'active' in this definition is a form of 'interruptive alert' that interrupts the health professional's workflow because they need to act on the alert generated at the point of care. There are a variety of clinical decision support systems available to support prescribers when they are clinically managing a patient's condition(s).

Clinical decision support systems match the characteristics of an individual patient to a computerised knowledge base and with software algorithms applied can, depending on the individual system, generate:

- alerts
- prompts to adhere to local or national guidelines
- patient-specific recommendations, such as dosage and alternative medication suggestions
- duplicate therapy warnings, or
- drug–drug and drug–allergy interaction checking.

Clinical decision support is incorporated within clinical IT systems that are used in everyday clinical practice, such as in GP practices, community pharmacies or hospital settings. Clinical decision support is available for use as a stand-alone system that can be integrated into the clinical IT system.

Various clinical decision support systems are used across all healthcare settings. For example, software can be used to:

- provide dosing instructions for warfarin based on the international normalised ratio (INR)
- select a medicine based on local formulary or national guidelines for a specific condition
- alert the prescriber that there is a potential drug-drug interaction when a new medicine has been initiated.

When considering the implementation of clinical decision support systems, high cost and resource implications need to be balanced. Furthermore, although the use of electronic systems for prescribing are encouraged to reduce the risk of medication errors, there has been variable uptake of their use in England and Wales. The aim of this review question was to identify the effectiveness of clinical decision support to optimise the use of medicines to improve patient outcomes.

11.2 Review question

What is the effectiveness and cost-effectiveness of using clinical decision support to reduce sub-optimal use of medicines and improve patient outcomes from medicines, compared to usual care or other intervention?

11.3 Evidence review

A systematic literature search was carried out (see appendix C.1), which identified 5631 references. The review protocol and subsequent search strategy included references published in the year 2000 and later. The GDG reviewed and discussed this publication date limit before receiving the search results and on reflection they recognised that there have been many technological advances within clinical decision support systems over the past 5 years. The GDG agreed that the principles of decision support (clinical and computerised) would be adequately captured in more recent studies (that is from 2009 onwards). There was discussion as to whether this time period was sufficient. The GDG requested that a high-level review of the included studies published in 2007 and 2008 be carried out. This would identify any additional evidence that would contradict or change the interpretation of the evidence from 2009 and onwards. The review of these 6 studies from 2007 and 2008 did not identify additional evidence that would contradict or change the outcomes of the included studies for 2009 and onwards. The GDG therefore agreed to only include studies that were published in 2009 and onwards for this review question; the underlying principles of decision support were thought not to have changed over the years. Sufficient evidence dating back to 2009 would provide more up-to-date evidence for the GDG to consider with regard to the advancement of decision support systems.

After removing duplicates the references were screened on their titles and abstracts and 222 references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol (appendix C.2.7). There were 57 systematic reviews that were identified from the 222 references. The systematic reviews could not be included in full because not all individual studies met the inclusion criteria. Therefore, the studies included in each systematic review were sifted and the full text of an additional 34 studies were requested for review.

Overall, 20 randomised controlled trials (RCTs) were included that were published from 2009 to 2014. There were 202 excluded studies that did not meet the eligibility criteria. In addition, the 34 studies identified from the systematic reviews did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C.5.7.

Many types of decision support systems, clinical or non-clinical, were identified during the sifting process. For this review question, only clinical decision support systems were included. Some studies looked at clinical decision support systems being a tool to ensure adherence to national guidelines; where these studies met the inclusion criteria, they were included. Several studies looked at process outcomes to assess the uptake and use of clinical decision support systems; these studies were also excluded (see below).

Included studies looked at clinical decision support systems that used alerts, reminders and drug-dosage calculations; for example based on kidney function. The included studies involved the use of clinical decision support when medicines were initiated or efficacy and safety were being reviewed in a variety of patient groups with different conditions. The clinical decision support system was integrated into electronic healthcare records. The types of clinical decision support systems varied and consisted of:

- national guidelines
- algorithms
- targeted medicines for specific conditions, for example, anticholinergic use in dementia
- drug-drug interactions
- electronic forms for the prescriber to populate to get patient-tailored decision support.

These clinical decision support systems were active or interactive and selectively provided information relevant to the characteristics or circumstances of a clinical situation. There was also an included study that used clinical decision support embedded within a personal digital

assistant device that could be used at the point of prescribing (see appendix D.1.7 for more information).

Studies that looked at non-active or non-interactive clinical decision support systems were excluded; for example, a prescriber proactively using guidelines embedded in their clinical system. Also studies looking at patient-facing decision support systems, such as computerised software providing patient information on treatment, were excluded because the focus of this review question was on decision support for prescribers. Decision support systems that were used for process measures, providing monitoring support, care reminders, or follow-up appointments or for providing performance feedback on quality indicators were also excluded. Software that calculated dosing based on a medicine that had already been initiated, for example calculating dosing of warfarin based on the international normalised ratio (INR), was not included as a clinical decision support system for the purpose of this review question.

The studies were quality assessed using the NICE methodology checklists for RCTs (see NICE guidelines manual 2012). Appraisal of the quality of the study outcomes was carried out using GRADE.

See appendix D.1.7 for evidence tables summarising included studies.

See appendix D.2.7 for GRADE profiles.

Table 40 Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Bell LM (2010) *USA*	Children aged 2–18 years with persistent asthma	Decision support to improve asthma care	Usual care	• Proportion of children with persistent asthma with at least 1 prescription for a controller medication
Bosworth (2009) *USA*	Patients had a mean age of 63 years and 98% male, 40% African American with a diagnosis of hypertension	Decision support to control blood pressure	• Reminder control • Patient behavioural intervention • Decision support & Patient behavioural intervention	• Estimated percentage blood pressure control
Bourgeois (2010) *USA*	Aged 18 years and under presenting with a diagnosis of ARI	An acute respiratory infection-interactive template (ARI-IT) was embedded into the electronic health records	Usual care	• Antimicrobial use
Boustani (2012) *USA*	Hospitalised older adults (at least 65 years) with cognitive impairment	Decision support to suggest discontinuation of the use of anticholinergics	Usual care	• Healthcare utilisation • Mortality • Discontinuation of potentially inappropriate anticholinergic medicines
Chen (2009) *USA*	Aged 20–79 years	Interactive point of care electronic medical record disease management tool for managing hyperlipidaemia	Usual care	• Proportion of high-risk patients with an low density lipoprotein-cholesterol ≥130 mg/dl who were prescribed lipid-lowering medicines
Eaton (2011) *USA*	Patient criteria not specified in the study	Personal digital assistant-based decision support tool for managing hyperlipidaemia	Personalised digital assistant without the decision support tool	• Proportion of patients screened and treated according to National Cholesterol Education Program Adult Treatment Panel III guidelines (ATP-III) on lipid management goals
Field (2009) *Canada*	Patients with renal insufficiency (average age 86 years)	Decision support for prescribing medicines in patients with renal impairment	Usual care	• Proportions of alerts that led to an appropriate final order of medicine
Fiks (2009)	Children and adolescents	Vaccine alerts	Usual care	• Rates of captured opportunities for

Study	Population	Intervention	Comparison	Outcomes
USA	with asthma aged 60 months or over and under 20 years			influenza vaccination (visit level analysis)
Fortuna (2009) *USA*	Population characteristics not specified in the study, only clinician characteristic specified	Decision support for use of hypnotics	• Usual care • Decision support system plus educational sessions	• Proportion of prescriptions for hypnotic medicines that were heavily marketed medicines
Gill (2011) *USA*	People at high risk for non-steroidal anti-inflammatory drugs related gastrointestinal complications (mean age not reported in the study)	Decision support on adherence to guidelines for use of non-steroidal anti-inflammatory drugs	Usual care	• Proportion of patients who received guideline concordant care
Khan (2013) *USA*	Aged 65 years or over, transferred to the intensive care unit and had cognitive impairment at the time of admission to the hospital	Decision support to suggest discontinuation of the use of anticholinergics	Usual care	• Mortality • Healthcare utilisation • Order to discontinue use of anticholinergics
Linder (2009) *USA*	Not specified, all patients visiting for potential ARI	An ARI smart form embedded into the electronic health records	Usual care	• Healthcare utilisation • Antibiotic prescribing rate for ARI visits
McGinn (2013) *USA*	Median age of patients included was 46 years presenting with pneumonia or streptococcal pharyngitis	Decision support on management for pneumonia or streptococcal pharyngitis	Usual care	• Healthcare utilisation • Changes in provider patterns of ordering antibiotics
O'Connor (2011) *USA*	Adults with type 2 diabetes, aged 18–75 years	Decision support on type 2 diabetes care	Usual care	• Change in HbA_{1c} • Change in blood pressure • Change in low density lipoprotein–cholesterol
Saenz (2012) *Spain*	Patients (average age 68 years) with type 2 diabetes mellitus on: • insulin therapy • insulin therapy plus oral antidiabetics	Decision support to aid in decision-making process at start of and during treatment in type 2 diabetes	Usual care	• Change in HbA_{1c}

Study	Population	Intervention	Comparison	Outcomes
	• oral antidiabetics			
Schwarz (2012) *USA*	Females aged 18–50 years with no evidence of sterilisation, menopause or infertility	'Simple' decision support (standard alert) to promote safe prescribing to women of reproductive age	• Usual care • Multifaceted decision support (patient tailored alert)	• Change in percentage of prescriptions of teratogenic medicines
Strom (2010) *USA*	Not specified	Decision support to alert a trimethoprim-sulfamethoxazole or warfarin interaction	Usual care	• Proportions of 'desired responses' (not reordering the alert-triggering drug within 10 minutes after alert firing)
Tamblyn (2012) *Canada*	Aged 65 years or over	Decision support for psychoactive medicines	Usual care	• Injury risk from psychoactive medicines
Terrell (2009) *USA*	Aged 65 and over who were being discharged from the emergency department	Decision support for inappropriate medicines prescribed in elderly	Usual care	• Proportion of emergency department visits by seniors that resulted in one or more prescriptions for an inappropriate medication
Terrell (2010) *USA*	Aged 18 years and over who had a creatinine clearance level below the threshold for dosage adjustment	Clinical decision support provided dosing recommendations (via alerts) for targeted medicines for use in kidney impairment	Usual care	• Proportion of target medicines that were excessively overdosed
Abbreviation: ARI, acute respiratory infection				

11.4 Health economic evidence

Summary of evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies evaluating the use of clinical decision support to improve patient outcomes from medicines. This search identified 2725 records, of which 2683 were excluded based on their title and abstract. The full papers of 42 records were assessed and 39 were excluded at this stage. The excluded studies and reason for their exclusion are provided in appendix C.6.7.

The 3 studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. At this stage, 2 studies were excluded. The study by Subramanian et al. (2012) was considered not applicable to the guidance because it is a US cost-comparison study and a US cost-utility study had already been identified. The study by Kofoed et al. (2009) was considered partially applicable to the guidance, despite consisting of a cost-benefit analysis rather than cost-utility analysis, because the study was conducted from a Danish healthcare perspective and was therefore judged to be more relevant to the current NHS than the US studies. However, when quality assessed in terms of internal validity, the study was considered to have major limitations. This was largely because the effectiveness of the intervention was based on hypothetical evidence rather than clinical evidence. Therefore, neither study was included in any further analyses.

Therefore, following quality assessment, 1 study was judged to be suitable for inclusion. This is summarised in table 41. This study by Gilmer et al. (2012) includes a cost-utility analysis undertaken from a US healthcare system perspective comparing a clinical decision aid wizard in prescribing for patients with type 2 diabetes with usual care. The analysis is built on RCT data. The study was judged to be partially applicable to the guideline because the study population was a subgroup of the guideline population and a US healthcare system perspective was taken. The study had minor methodological limitations.

The study evidence tables for the included studies are shown in appendix E.1.7.

Clinical decision support to reduce sub-optimal use of medicines and improve patient outcomes from medicines was not identified as a priority for health economic modelling by the GDG because of the difficulties in attributing improvements in patient outcomes from medicines resulting from the use of clinical decision support to those that were because of other confounding factors, such as knowledge acquired previously or advice received from colleagues.

Table 41 Economic evidence profile – Clinical decision support

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	**Effects**	**Cost effectiveness**	
Gilmer et al. (2012) (US, CUA)	Minor limitations[1]	Partially applicable[2,3]	Study employed cost-utility analysis over a 40-year time horizon based on RCT data. Intervention: Clinical decision support system (Wizard) for patients with diabetes. Comparator: usual care.	£71[4,8]	0.04[5]	£1930 per QALY[8]	99% probability of being cost effective at a £31,983 per QALY threshold. 92% probability of being cost effective at £15,992 per QALY threshold. Model was sensitive to intervention effect over time and costs incorporated[6,7,8]

[1] Model structure is for patients newly diagnosed with type 2 diabetes, while patients in RCT on which the model was built had been diagnosed for mean of 10 years. Study authors noted that A1c level were similar between the two model population and RCT patients, however

[2] Study population is a subgroup of the whole guidance population

[3] US healthcare system perspective with discounting at 3% for both costs and health effects (consistent with US guidelines)

[4] Incremental costs per patient over 40-year time horizon. Standard error=£422

[5] Incremental QALYs per patient over 40-year time horizon. Standard error=£0.01

[6] When the effects of the intervention cease after 1 (2) years, ICER=£41,872 (£25,805) per QALY

[7] When costs include drug costs not supported by the clinical decision aid (of which benefits were not included in model) and additional outpatient costs, ICER=£13,874

[8] Costs were converted into pounds sterling using the appropriate purchasing power parity

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; RCT, randomised controlled trial; CUA, Cost-utility analysis.

11.5 Evidence statements

Clinical evidence

For this review question, there were 4 critical outcomes identified: mortality, clinical outcomes as reported in the study, health and social care utilisation and patient-reported outcomes. The included studies did not report on any patient-reported or social care utilisation outcomes.

Two studies (high- and moderate-quality evidence) showed no significant difference in mortality rates between patients who received care from their prescriber using clinical decision support and patients who received usual care.

Clinical outcomes were reported by 3 studies. One study (moderate-quality evidence) showed that clinical decision support significantly improved glycated haemoglobin levels (HbA_{1c}) and systolic blood pressure control in patients with type 2 diabetes compared with patients for whom clinical decision support was not used. There was no significant difference found between the 2 groups for low-density lipoprotein cholesterol. Another study (high-quality evidence) looking at HbA_{1c} levels in type 2 diabetes found a significant reduction in HbA_{1c} levels in the group who were managed by a prescriber using clinical decision support compared with in those who received usual care. One study (high-quality evidence) found no significant differences in the amount of change in blood pressure control in each of the intervention groups (decision support, patient behavioural intervention and combined decision support plus patient behavioural intervention) compared with the control group.

Five studies reported on healthcare utilisation (high/moderate-quality evidence) using different outcome measures. There was no significant difference found between the groups who received clinical decision support or usual care, but 1 of the studies favoured clinical decision support for having fewer patients revisiting study clinics for acute respiratory infections within 30 days of originally being seen compared with usual care when calculated using the Z-test in review manager (the published study reported no significant difference, p=0.32 using chi-squared test).

Thirteen studies reported on suboptimal prescribing using different outcome measures. Eight studies (1 high-quality, 4 moderate-quality, 2 low-quality and 1 very low-quality evidence) showed that clinical decision support significantly improved suboptimal prescribing compared with usual care. Five studies (4 moderate-quality and 1 low-quality evidence) showed no significant difference between the groups who received clinical decision support or usual care.

Four studies reported on medicine-related problems using different outcome measures. Two studies (high- and moderate-quality evidence) showed that clinical decision support significantly reduced potential medicines-related problems compared with usual care. Two studies (high- and low-quality evidence) showed no significant difference between the groups who received clinical decision support or usual care.

Economic evidence

Partially applicable evidence from one study with minor limitations built on RCT data suggests that use of a clinical decision aid in patients with diabetes is a cost-effective use of NHS resources. This clinical decision aid worked alongside existing electronic medical records to inform clinical care.

No relevant evidence was identified informing the cost effectiveness of the use of clinical decision aids in other patients or where electronic medical records are not in use.

No relevant evidence from a UK NHS perspective was identified.

11.6 Evidence to recommendations

Table 42 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG was aware that the included studies reported study outcomes using different measures and for analysis they were grouped under the critical and important outcomes as agreed for this review question. The GDG was also aware that there was no evidence reporting patient-reported outcomes or social care utilisation.
	The GDG considered that mortality was the most critical outcome for this review question. Only 2 studies had reported on this outcome, and they showed no significant difference in the groups that received clinical decision support compared with usual care. The GDG was presented with mixed evidence for clinical outcomes, and found that in some studies clinical decision support improved clinical outcomes, such as type 2 diabetes control and management of hypertension (improved systolic blood pressure only) compared with usual care. However, another study showed no improvement in clinical outcomes. The GDG also found that clinical decision support had no effect on healthcare utilisation when compared with usual care.
	Other outcomes regarded as important by the GDG were suboptimal prescribing and medicines related problems.
Trade-off between benefits and harms	The GDG was aware of 1 study where a clinical decision support system used for alerting prescribers to a drug interaction precipitated clinically important treatment delays in 4 patients. This study was therefore stopped a month early. The GDG discussed the evidence in great depth and agreed that although the study was of very low quality evidence, the clinical decision support system used had flagged up important interactions that had the potential to cause greater harm than that of delayed therapy and that clinical decision support needs to be applied appropriately in all patients.
	The GDG considered integrated clinical IT systems – for example, EMIS web, that are widely used in GP practices across the UK. The GDG was aware that clinical decision support systems are one component of this clinical IT system used. The GDG was also aware of the different types of clinical decision support (for example, alerting prescribing in accordance with national guidelines or in line with local formulary) that are available for use and that the systems will not necessarily 'know' all the comorbidities and medicines indications for a given patient. The GDG briefly discussed the use of PRODIGY, which was decision support software integrated into clinical IT systems and used previously by GPs in the UK. However, this type of decision support was considered to be proactive rather than interactive and therefore these were not included in the evidence review. The GDG was aware that clinical decision support also has functionality around other aspects of care other than medicines. The GDG discussed and agreed that clinical decision support cannot determine the risks and benefits of prescribing a medicine to an individual patient. The GDG felt strongly that such systems may be helpful to support clinical decision making and prescribing but they should not ever replace clinical judgment. The GDG considered clinical judgement to include observation of and taking a history from the patient (or family/carer) where possible. Assessing and evaluating a patient's clinical condition though direct conversation with them can

	elicit subtle, but very important, information about their care and management which could otherwise be missed. Therefore the use of clinical decision support should always be used in conjunction with clinical judgement.
	The GDG felt that clinical decision support is used as a guide for prescribers, particularly in reducing inappropriate prescribing caused by poor knowledge or error. The GDG felt that there would be no clinical harm to patients in using clinical decision support provided that clinical judgement was used to assess each individual situation.
	The GDG agreed that clinical decision support could be considered to support clinical decision making and prescribing but it should not be used to replace clinical judgement.
Consideration of health benefits and resource use	The GDG acknowledged that the health economic evidence consisted of 1 study which was carried out from a US perspective. In this study, it appeared that a clinical decision support system for patients with type 2 diabetes was a cost-effective use of resources. The GDG was aware that the model assumed a 40-year effect (that is, the lifetime of the patients) of the intervention on changes to medicines and therefore patient outcomes reflected this in the base case. The GDG considered that the intervention had to create clinical outcome benefits for at least 2 years following the use of the clinical decision support in order for the intervention to be cost-effective at the implied NICE threshold.
	The GDG was also aware that the incremental costs and benefits over a 40-year time horizon between the intervention and comparator arms of the model were very small. Given that costs were calculated from a US healthcare system perspective the GDG discussed and agreed that this small cost difference may have been negligible or even reversed if the model had been conducted from a UK, NHS perspective.
	The GDG was concerned that the clinical data included in the model were taken from a recent US RCT and a UK-based RCT, using data from 20 years ago (UKPDS study), and therefore may not be relevant to the current NHS setting. The GDG discussed that, given this and the small cost differences measured from a US perspective, their recommendations could not be based on this evidence.
	The GDG was mindful that large resources may be needed to implement clinical decision support systems and keep systems up-to-date with the most relevant information. For this reason, the GDG discussed and agreed that discussions may need to take place locally to determine if the costs associated with implementing and maintaining clinical decision support systems are feasible. The available economic evidence and experience of the GDG suggests that health benefits may occur as a result of implementing clinical decision support systems and that these benefits may outweigh the cost of implementing such systems if systems are focused on alerts that identify important safety issues. The GDG agreed that by highlighting these important safety issues, greater potential health benefits exist.
Quality of evidence	The evidence for this review question varied from low to high quality. There were no identified RCTs carried out in the UK. All the studies were RCTs carried out in the USA (17 studies), Canada (2 studies) and Spain (1 study) in mixed populations ranging from children to

	adults. The GDG was aware of the following limitations of the evidence: • not fully applicable to the UK healthcare setting • studies used discrete software designed for specific patient groups • usual care not defined in the studies therefore not comparable to UK usual care • included studies did not focus specifically on the safe use of clinical decision support.
Other considerations	The GDG discussed the importance of involving patients (and/or their family members or carers) when using clinical decision support to make decisions about medicines during a consultation about medicines. The GDG agreed that discussions between the patient (and/or their family members or carers) and the health professional would explain why certain medicines were being reviewed or why they were not being given to them. The GDG was aware that patients may feel unsettled if regular medicines were changed without justification for change. The GDG felt that prescribers should make the clinical decision first then clinical decision support should be used to facilitate the shared decision- making process. The GDG acknowledged the limitations of the evidence reviewed for the use of clinical decision support but were aware that in the UK, clinical decision support is currently used as part of clinical IT systems, mainly in GP practices and less commonly in secondary care. The GDG recognised that such systems are costly to implement. However, as clinical IT systems are widely used in UK practice, the GDG felt that such systems have several recognised health benefits and that clinical decision support integrated into existing systems can contribute to these benefits. The GDG was aware that service providers such as GP practices were already in the process of acquiring electronic prescribing systems that may have some type of clinical decision support integrated into them. On the basis of the evidence reviewed, the GDG felt that it would be more appropriate to make recommendations that would inform the safe use of clinical decision support. The GDG discussed that some clinical decision support systems use alerts that appear as a 'pop-up window' that often appear too frequently – for example, theoretical drug–drug interactions – at the point of prescribing. The GDG felt that prescriber responses may become automatic ('alert fatigue') when overriding alerts and there may be a risk that clinically significant important alerts may not be acted on depending on the type of clinical decision support used. The GDG discussed having a process for overriding and for acknowledging important alerts. Examples include alerts categorised according to their risk, such as 'red alerts' for alerting high risk medicines safety information to the prescriber, or a system that requires an additional authorisation to prevent overriding for medicines-related 'never events'. The GDG discussed the importance of clinical decision support having the ability to include alerts that are mandatory for the prescriber to acknowledge. The GDG suggested that these risks could be reduced if the prescriber has undertaken the appropriate training (either locally or provided by the supplier of clinical decision support software) and has the skills and expertise to understand what the clinical decision support is informing them about and when it is appropriate to override these alerts. There was no evidence looking at the skills and knowledge needed to use clinical

decision support. The GDG therefore discussed and agreed by consensus that health professionals using clinical decision support at the point of prescribing should have the necessary knowledge and skills (competence) to use the system, including understanding its limitations.

The GDG considered the safety role of clinical decision support, including where it can provide prompts for the prescriber to consider for uncommon events that they may not encounter every day in practice. This could include, for example, potential consequences to consider and discuss with the patient when starting a medicine that requires frequent or complex monitoring because of its potential side effects. The GDG highlighted that clinical decision support should support clinical decision making and not be a barrier to it. The GDG recognised that clinical decision support would need to be kept up-to-date in terms of clinical information and software versions and be applicable to local healthcare needs. The GDG discussed and agreed by consensus that information integrated into clinical decision support should:

- identify important safety issues
- include a system for health professionals to acknowledge the alert (for mandatory alerts) which is not customisable for alerts relating to medicines-related 'never events'
- reflect the best available evidence
- contain useful clinical information that is relevant to the health professional to reduce 'alert fatigue'
- be up-to-date and has the ability to be updated.

The GDG considered the governance arrangements for using clinical decision support, including an assessment of benefits and harms relating to its use. The GDG discussed and agreed by consensus that robust and transparent local governance arrangements should be in place for developing, using, reviewing and updating computerised clinical decision support systems.

No evidence was identified for the use of clinical decision support in UK settings. Although the GDG felt that they could extrapolate from the evidence that was predominately carried out in the USA, the GDG was aware that the term 'usual care' was not adequately described in the studies. The GDG discussed that provision of 'usual care' in the studies would not have necessarily been the same as 'usual care' provided in the UK where clinical decision support is widely used in GP practices (but not so often in secondary care). The GDG therefore agreed that a research recommendation should be made to allow research to be carried out on the use of clinical decision support within the UK setting to support with the medicines optimisation agenda.

11.7 Recommendations and research recommendations

Clinical decision support software is a component of an integrated clinical IT system providing support to clinical services, such as in a GP practice or secondary care setting. These integrated clinical IT systems are used to support health professionals to manage a person's condition. In this guideline the clinical decision support software relates to

computerised clinical decision support, which may be active or interactive, at the point of prescribing medicines.

44. Consider computerised clinical decision support systems (taking account of existing systems and resource implications) to support clinical decision-making and prescribing, but ensure they do not replace clinical judgement.

45. When using a computerised clinical decision support system to support clinical decision-making and prescribing, ensure that it:

- identifies important safety issues
- includes a system for health professionals to acknowledge the alert (for mandatory alerts) which is not customisable for alerts relating to medicines-related 'never events'
- reflects the best available evidence
- contains useful clinical information that is relevant to the health professional to reduce 'alert fatigue', where a prescriber's responsiveness to a particular type of alert declines as they are repeatedly exposed to that alert over time.
- is up-to-date.

46. Ensure that robust and transparent processes are in place for developing, using, reviewing and updating computerised clinical decision support systems.

47. Ensure that health professionals using computerised clinical decision support systems at the point of prescribing have the necessary knowledge and skills to use the system, including an understanding of its limitations.

11.7.1 Research recommendation

To be read in conjunction with the NICE Research recommendations process and methods guide

Uncertainties

This review question looked at the clinical and cost-effectiveness of using clinical decision support to reduce suboptimal use of medicines and improve patient outcomes from medicines, compared to usual care or other intervention. The systematic review found no evidence for the use of clinical decision support systems in UK settings and the GDG agreed that there was uncertainty about this.

Uncertainties include: clinical effectiveness of medicines for patients, cost-effectiveness of clinical decision support systems used to reduce suboptimal use of medicines or patient-reported outcomes relating to medicines.

Reason for uncertainty

Studies may have been undertaken in this area however the searches did not identify any randomised controlled trials to answer the review question that are relevant to the UK.

Existing evidence is available and the research into the question has been undertaken, but the results cannot be applied to the population in question as the included studies were carried out mainly in the USA. Although the GDG felt that they could extrapolate from the evidence carried out in the USA, the GDG was aware that the term 'usual care' was not adequately described in the studies. The GDG discussed and agreed that the provision of

'usual care' in the studies would not necessarily have been the same as 'usual care' provided in the UK where clinical decision support is widely used – for example, in GP practices.

Key uncertainties

The key uncertainty is whether the use of clinical decision support in the UK setting can reduce sub-optimal use of medicines and improve patient outcomes from medicines compared to usual care in a UK setting. Usual care will need to consider different care settings including primary and secondary care. Research into this area will help to identify if clinical decision support is a clinically and cost-effective intervention in relation to medicines.

The research will identify if these clinical decision support systems have benefit and values to patients (in reducing suboptimal use of medicines) and will therefore provide guidance to organisations who commission them and health professionals who may use them in their clinical practice.

Recommendation

1. **What is the clinical and cost effectiveness of using clinical decision support systems to reduce the suboptimal use of medicines and improve patient outcomes from medicines, compared with usual care, in the UK setting?**

Randomised controlled trials should consider the use of clinical decision support systems to improve outcomes and safety for medicines, in the UK setting compared to usual care. A follow up period (ideally longer than 2 years) would capture longer term outcomes. Outcomes for this research question should include patient reported outcomes, clinical outcomes, medicines related problems and cost effectiveness. The research can be carried out in all populations that use services where clinical decision support systems can be used. The research could also look at process measures for using clinical decision support systems, for example the clinical effectiveness of such systems can depend on the end users of the system and their interpretation of the active information provided on the screen.

Rationale

Clinical decision support systems (defined as 'an active, computerised intervention that occurs at the time and location of prescribing, to support prescribers with decision-making') are widely used in some primary care settings, such as in GP practices, but they may also be used in secondary care (in specialist units, for example renal units). There are many types of clinical decision support system available and they vary, from providing clinical decision support for general medicines use to highlighting specific drug interactions. As different types of clinical decision support systems are used already in some UK healthcare settings, the GDG agreed that research needs to be carried out to identify if using clinical decision support systems is a clinical- and cost-effective intervention to reduce the suboptimal use of medicines and improve patient outcomes from medicines compared with usual care, in the UK setting.

PICO format:

Criterion	Explanation
Population	All people taking medicines
Intervention	Clinical decision support systems. Defined in the review protocol as 'an active, computerised intervention that occurs at the time and location of prescribing, to support prescribers with decision-making'

Comparator(s)	Usual care
	'Usual care' in the primary care setting for example in a GP practice use clinical decision support systems which may highlight for example choice of formulary medicines or drug interaction to the prescriber, however 'usual care' in secondary care may be different where such clinical decision support systems may or may not be available to use.
Outcome	The following outcomes should be considered:
	• patient-reported outcomes (for example satisfaction, medicines adherence)
	• quality of life
	• clinical outcomes
	• medicines-related problems (for example adverse drug reactions).
	An appropriate length of follow-up would be 2 years or more for the outcomes to be externally valid.
	Process measures may also be considered for this research question to see what impact clinical decision support systems has on the training on use of systems, updating systems, and 'alert fatigue'.
Study Design	RCT
Timeframe	Follow-up outcomes of 2 years or more

12 Medicines-related models of organisational and cross-sector working

12.1 Introduction

In 2010, the government set out in <u>Equity and excellence: Liberating the NHS</u> an aim to 'simplify and extend the use of powers that enable joint working between the NHS and local authorities'. To support implementation of this in England, several outcome frameworks were produced for the NHS, adult social care and public health. The NHS outcomes framework aims to drive up quality by focusing on a culture and behaviour of health outcomes rather than processes.

The <u>Health and Social Care Act</u> was passed in 2012, leading to the establishment of different commissioning organisations from April 2013. The Act aims to improve quality and efficiency of NHS services by reforming organisations that commission, regulate and support health and social care services. Commissioning organisations now include clinical commissioning groups, local authorities and NHS England. The Act places emphasis on health and social care sectors working jointly or collaboratively. The Act also established Health and wellbeing boards to bring together local leaders of health and social care to improve the health and wellbeing of their local population and reduce health inequalities.

Over several years legislation has also been passed to allow more flexibility in how services are commissioned and structured, particularly when prescribing, supplying and administering medicines.

Background to the medical model

Historically, a doctor (or dentist) would identify that a medicine(s) was needed as part of the care pathway and <u>prescribe</u> a medicine for the patient. A pharmacist (or dispensing doctor) would then <u>dispense</u> the medicine(s) against the prescription and <u>supply</u> the medicine(s) to the patient.

This traditional 'medical model' changed in the years after publication of the final Crown report <u>Review of prescribing, supply and administration of medicines</u> in 1999. Legal frameworks were developed that have allowed services to be redesigned and health professionals to work more flexibly for the benefit of patients. In particular, prescribing responsibilities have been extended to enable other health professionals to complete additional training and qualify as <u>non-medical prescribers to improve a patient's access to medicines</u>.

As a result of these changes, there are now several legal options for prescribing and supplying medicines. These include:

- Independent prescribing – the prescriber (a doctor, dentist or non-medical independent prescriber) takes responsibility for the clinical assessment of the patient, establishing a diagnosis, the clinical management needed and prescribing.

- <u>Supplementary prescribing</u> – a voluntary partnership between a doctor or dentist and a <u>supplementary prescriber</u>, to prescribe within an agreed patient-specific <u>clinical management plan</u> with the patient's agreement.

- Patient Group Directions (PGDs) - PGDs provide a legal framework that allows the supply and/or administration of a specified medicine(s), by named, authorised, registered health professionals, to a pre-defined group of patients needing prophylaxis or treatment for a condition described in the PGD, without the need for a prescription or an instruction from a prescriber. Using a PGD is not a form of

prescribing. See Patient Group Directions (NICE medicines practice guideline 2) for more information.

- Patient Specific Directions (PSDs) – written instructions, signed by a doctor, dentist, or non-medical prescriber for a medicine to be supplied and/or administered to a named patient after the prescriber has assessed the patient on an individual basis. Writing a PSD is a form of prescribing.

- Exemptions from medicines legislation; see The Human Medicines Regulations 2012 for full details.

These options provide organisations with opportunities for considering different models of care for patients receiving the medicines they need in the safest and most appropriate way.

Profession-led models of care

Organisations have started to consider alternative models of care for patients to optimise their medicines. They have considered their service design and reviewed services based on the needs of their local patient population. As part of this review, the medical model has evolved allowing other health professionals to further develop their roles and responsibilities, supporting doctors in their clinical roles. For example, in primary care, some GP practices have nurse-led asthma clinics and pharmacist-led care home medicine review services; in secondary care, anticoagulation clinics are overseen by consultants but managed by pharmacist or nurse professionals.

Joint working – primary and secondary care

Patient experience in adult NHS services (NICE clinical guideline 138) outlines how patients should be seen as individuals in the healthcare system. Services need to be tailored to respond to the needs, preferences and values of the person and should be individualised as much as possible. To enable seamless care to be provided, integration between all care settings is required; however, different models may exist to meet the needs of the local population. For example, when a patient is receiving end of life care, they may start their treatment in secondary care, but the patient may wish to receive subsequent care at home, requiring their care to be transferred to a primary care or outreach service.

Joint working – health and social care

In 2012, the White paper Caring for our future: reforming care and support outlined the need to 'dissolve the traditional boundaries that lie between the third sector, private organisations, local authorities and individuals'. The paper focused on 2 key principles to:

- prevent, postpone and minimise people's need for formal care and support by promoting people's independence and wellbeing

- encourage joint working with local authorities, the NHS and others to provide high-quality, integrated services built around the needs of individuals.

Integration of healthcare with social care has led to different models of care being used to provide care and treatment to patients. One example is when a patient has been discharged from hospital but requires rehabilitation before they are ready to return to their own home, which could be provided in a social care setting. This helps provide seamless care between different care settings allowing health and social care practitioners to work together to improve patient outcomes, particularly when ensuring appropriate medicines use and shared-decision making.

Joint working – pharmaceutical industry and other commercial organisations

[Best practice guidance for joint working between the NHS and the pharmaceutical industry](#) was published by the Department of Health in 2008. The aim of this guidance was to encourage and support joint working between the NHS, pharmaceutical industry and other relevant commercial organisations, giving advice about the responsibilities of all parties on entering into a joint working arrangement. To further support this, [Moving beyond sponsorship: Interactive toolkit for joint working between the NHS and the pharmaceutical industry was published in 2010](#).

In 2011, the Department of Health published [Innovation Health and Wealth – Accelerating Adoption and Diffusion in the NHS](#). This policy set out measures to support the adoption and diffusion of innovation across the NHS. The policy outlines the challenges the NHS faces with a growing population, advances in technology and increasing expectations of the public. It also states that industries, such as the pharmaceutical industry, often work in partnership with the NHS to support a constant supply of new medicines. Academic health Science Networks were established to link the system with the NHS and scientific communities, academia, third sector and local authorities to support and share innovation.

Overall

Ensuring that people receive high-quality care relies on a complex set of responsibilities and relationships between practitioners, provider organisations, commissioners, service users and regulators. There are many different models of care, between health and social care and with the pharmaceutical industry and other commercial organisations. Joint working has been a challenge in the NHS for a long time. Organisations across the country have different working models between NHS England, clinical commissioning groups, commissioning support organisations and social enterprises to name a few. These models of care are commissioned on the needs of the population nationally and locally. There are examples in practice of primary and secondary care services working together and GPs and local medicines optimisation teams again utilising a model to support the best outcomes for patients, sometimes supported by working jointly with the pharmaceutical industry.

Joint working between health and social care practitioners in different care settings still needs to improve to provide the safest, most efficient service to patients. This can be challenging with, for example, different IT infrastructures, separate budgets for health and social care, changes that affect other budgets, information sharing and integrated teams with different employers, resources, performance outcomes or remits.

With all the challenges that exist for health and social care in working together more effectively and efficiently, this review question aimed to review which models of care can lead to improved patient outcomes specifically for the suboptimal use of medicines.

12.2 Review question

What models of organisational and cross-sector working are effective and cost effective in reducing the suboptimal use of medicines and improving patient outcomes from medicines, compared to usual care, or other intervention?

12.3 Evidence review

A systematic literature search was conducted (see appendix C.1) that identified 2885 references. After removing duplicates, the references were screened on their titles and abstracts, after which 131 references were obtained and reviewed against the inclusion and exclusion criteria as described in the review protocol (appendix C.2.8).

Studies that looked at the effect, impact or role of a particular health professional were excluded because the focus of this review question was to identify the way in which care was delivered to optimise medicines. Also, studies that did not involve medicines as part of the model were excluded. The included studies looked at professional-led models and collaborative care models. There were no studies identified that looked at cross-sector working.

Overall, 120 studies were excluded because they did not meet the eligibility criteria. A list of excluded studies and reasons for their exclusion is provided in appendix C.5.8.

Eleven studies met the eligibility criteria and were included. Of the excluded studies, 17 were systematic reviews of studies (RCTs and observational studies) that could not be included in full. References included in these systematic reviews were screened on their titles and abstracts to identify any further studies that met the eligibility criteria. Seven additional RCTs were identified and included.

All 18 studies included were RCTs investigating the effect of the collaborative care model on the management of chronic diseases, diabetes and hypertension, care of older people, or professional-led models of care for depression, hypertension, diabetes, hyperlipidaemia and transition of care for older people. The included studies on professional-led models of care were all pharmacist-led (see appendix D.1.8 evidence tables for details).

The studies were quality assessed using the NICE methodology checklists for systematic reviews and RCTs (see NICE guidelines manual 2012). Appraisal of the quality of the study outcomes was carried out using GRADE.

See appendix D.1.8 for evidence tables summarising included studies.

See appendix D.2.8 for GRADE profiles.

Table 43 Summary of included studies

Study	Population	Intervention	Comparison	Key critical outcomes
Al Mazroui (2009) *UAE*	People with type 2 diabetes mellitus (mean age 48 years) and receiving medicines for diabetes	The clinical pharmacist-led management of type 2 diabetes	Usual care	• Change in clinical parameters • Medicines adherence
Capoccia (2004) *USA*	People (mean age 38 years) diagnosed with a new episode of depression and started on antidepressant medicines	Bi-monthly, the clinical pharmacist and the study psychiatrist review individual cases or have informal discussion sessions regarding treatment or counselling	Usual care	• Depression symptoms • Healthcare utilisation • Medicines adherence • Patient satisfaction
Carter (2008) *USA*	Aged 21–85 years with a diagnosis of hypertension	The clinical pharmacist-led management of hypertension	Usual care	• Blood pressure control • Medicines adherence
Choe (2005) *USA*	People with type 2 diabetes (mean age 51 years)	The clinical pharmacist-led management of type 2 diabetes	Usual care	• Change in HbA_{1c} level
Crotty (2004a) *Australia*	Older adults (mean age 82 years)	Pharmacist transition coordinator	Usual care	• Healthcare utilisation • Patient-reported outcomes
Crotty (2004b) *Australia*	Nursing home residents	Case conferences involving the resident's GP, a geriatrician, a pharmacist, residential care staff and a representative of the Alzheimer's Association of South Australia	Usual care	• Change in residents behaviour
Edelman (2010) *USA*	People with diabetes and hypertension (mean age 60 years)	Group medical clinics comprised 7 to 8 patients and a care team that consisted of a primary care general internist, a pharmacist, and a nurse or other certified diabetes educator	Usual care	• Healthcare utilisation • Diabetes control • Blood pressure control
Finley (2003) *USA*	People started on antidepressant therapy (mean age 54 years)	Collaborative care model consisted of clinical pharmacy specialists providing medicines maintenance	Usual care	• Healthcare utilisation • Clinical and functional outcomes • Medicines adherence
Hogg (2009) *Canada*	Aged 50 years or over, at risk of functional decline, physical	A multidisciplinary team. One pharmacist and 3 nurse practitioners	Usual care	• Healthcare utilisation • Chronic disease management

Study	Population	Intervention	Comparison	Key critical outcomes
	deterioration, or experiencing an event requiring emergency services	were added to the family practice		score
Hunt (2008) *USA*	People with hypertension (mean age 68 years)	Pharmacist-led management of hypertension	Usual care	• Blood pressure control • Self-management • Medicines adherence • Healthcare utilisation • Patient satisfaction
Jacobs (2012) *USA*	Aged 18 years or over with type 2 diabetes	Clinical pharmacist-led management of type 2 diabetes	Usual care	• Diabetes control • Blood pressure control • Lipid control
Jameson (2010) *USA*	Aged 18 years or over with type 2 diabetes	Pharmacist-led review of medicines and changes to medicines after approval from patient's physician	Usual care	• Diabetes control
Jareb (2012) *Jordan*	Aged 18 years or over with type 2 diabetes	A clinical pharmacist-led management of type 2 diabetes	Usual care	• Diabetes control • Medicines adherence • Blood pressure control • Lipid control
Krass (2007) *Australia*	People with type 2 diabetes	A community pharmacist review type 2 diabetes	Usual care	• Diabetes control • Blood pressure control
Lee (2009) *Hong Kong*	Aged 18 years or over and were taking one or more lipid-modifying agents for dyslipidaemia	Pharmacist-led review of medicines for dyslipidaemia	Usual care	• Lipid control
Magid (2013) *USA*	Aged 18–79 years with hypertension	Pharmacist-led management of medicines for hypertension	Usual care	• Blood pressure control • Healthcare utilisation • Medicines adherence
Pape (2011) *USA*	People with high cholesterol and diabetes mellitus (mean age 62 years)	Clinical pharmacist-led management of high cholesterol	Usual care	• Lipid control • Blood pressure control • Diabetes control

Study	Population	Intervention	Comparison	Key critical outcomes
Rothman (2005) *USA*	Aged 18 years and over with type 2 diabetes	Clinical pharmacist-led management of type 2 diabetes	Usual care	• Blood pressure control • Diabetes control • Healthcare utilisation

12.4   Health economic evidence

Summary of evidence

A systematic literature search (appendix C.1) was undertaken to identify cost-effectiveness studies evaluating models of organisational or cross-sector working to reduce the suboptimal use of medicines. This search identified 1975 records, of which 1907 were excluded based on their title and abstract. The full papers of 68 records were assessed and 55 were excluded at this stage. A list of excluded studies and reasons for their exclusion is provided in appendix C.6.8.

The 3 studies meeting the inclusion criteria were quality assessed using the NICE quality assessment checklists for cost-effectiveness studies. At this stage, the study by Saokaew et al. (2009) was judged not applicable to the guidance because it was a cost–comparison study based in Thailand (a non-OECD country). It was therefore excluded from any further analysis. The 2 included studies are summarised in table 44.

The study by Ghatnekar et al. (2013) included a cost–utility analysis comparing the Lund integrated medicines management (LIMM) model, which aimed to optimise medicines through medicines reconciliation and review delivered by a multidisciplinary team with usual care. The study had a short time horizon, was based in Sweden, used assumptions to generate utilities (not from patients or clinicians directly) and was populated with clinical data from an observational study. This study was therefore judged to have potentially serious limitations and to be only partially applicable to the guidance.

The second included study (Karnon et al. 2008) provided a cost–benefit analysis comparing an intervention of pharmacists joining ward rounds with no intervention. Other interventions were also considered; however, these were outside of the scope of this review question. Some costs included in this analysis were from a US, rather than a UK, perspective and no discounting was done. Again, the clinical data were not drawn from an RCT. Utility values were drawn from litigation costs and assumptions. This study was therefore also judged to have potentially serious limitations and to be only partially applicable to the guidance.

The study evidence tables for the included studies are shown in appendix E.1.8.

Models of organisational and cross-sector working in reducing the suboptimal use of medicines and improving patient outcomes from medicines was not identified as an area for health economic modelling by the GDG, given the variation in practice likely to exist in this area.

Table 44 Economic evidence profile – models of organisational and cross-sector working

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	**Effects**	**Cost effectiveness**	
Ghatnekar et al. (2013) (Sweden, CUA)	Potentially serious limitations[1,2,3]	Partially applicable[4,5]	Study employed a cost-utility analysis over a 3-month time horizon Intervention: LIMM model – optimise drug treatment through medication reconciliation and review delivered by a multidisciplinary team Comparator: usual care	−£289[16]	0.005 QALYs	Dominant	98% cost effective[6]
Karnon et al. (2008) (UK, CBA)	Potentially serious limitations[3,8]	Partially applicable[9,10]	Study employed a cost-benefit analysis over a 5-year time horizon Intervention: Pharmacists joining ward rounds[7] Comparator: usual care	£0.21m to £0.37m[11]	146 pADEs £6.043m[12]	Net benefit: £27.256m[13] −£0.154m[14]	Results uncertain[15]

[1] Short time horizon means that long-term costs and quality-adjusted life years (QALYs) were not captured

[2] Utility values were populated with assumptions

[3] The model was populated with clinical evidence that did not meet the inclusion criteria for the clinical evidence review

[4] Utility values were not derived from patients or their carers directly

[5] Swedish healthcare system perspective

[6] At a threshold of 0 euros per QALY gained, therefore intervention has probability of 98% of being at least as effective and at least as cheap

[7] Other interventions were also considered; however these are outside the scope of this review question

[8] A number of assumptions were made around the use of NHS litigation claims, the external validity of US data and the relationship between errors and pADEs. These could change the conclusions about cost-benefits

[9] No discounting was undertaken

[10] Not all costs were from a UK NHS and PSS perspective; this was acknowledged by the authors and the validity questioned

[11] Cost (95% confidence interval) of intervention=£0.21–0.37m and control=£0 for a 400-bed hospital over a 5-year time horizon

[12] Cost (95% confidence interval) of pADEs for intervention=£11.711m (£2.854m to £27.835m) and control=£17.754m (£4.4m to £42.095) over a 5-year time horizon for a 400-bed

hospital

[13] Net benefit including treatment and health benefit costs. 95% confidence interval is reported as £5.623m to £69.52m over a 5-year time horizon for a 400-bed hospital

[14] Net benefit including treatment costs (no health benefit costs). 95% confidence interval is reported as −£0.601m to −£0.451m over a 5-year time horizon for a 400-bed hospital

[15] The large confidence intervals generated through Monte Carlo simulation of the model (20,000 iterations) each time sampling a new set of input parameters indicates uncertainty in the results

[16] Costs were converted into pounds sterling using the appropriate purchasing power parity

Abbreviations: LIMM, Lund integrated medicines management; pADEs, preventable adverse drug events; PSS, personal social services; QALY, quality-adjusted life year; CUA, cost-utility analysis; CBA, cost-benefit analysis.

12.5 Evidence statements

Clinical evidence

Collaborative (multidisciplinary) models of care

One study (moderate-quality evidence) showed there was no significant difference in the change in residents' behaviour compared with usual care, where a collaborative care model for the care of older people was used (consisted of the resident's GP, a geriatrician, a pharmacist, residential care staff and a representative of the Alzheimer's Association of South Australia).

One study (low-quality evidence) significantly favoured collaborative care model consisting of a pharmacist and 3 nurse practitioners over usual care on overall quality of disease management. There was no significant difference found between collaborative care and usual care in the number of hospitalisations and visits to the emergency department.

One study (low-quality evidence) looking at managing diabetes and hypertension showed no significant difference between the collaborative care model (consisted of a primary care general internist, a pharmacist and a nurse or other certified diabetes educator) and usual care for reduction in HbA_{1c}, adherence to medicines and reduction in hospitalisations. The collaborative care model was significantly favoured over usual care for the following outcomes: reduction in blood pressure, perceived competence scores, and reduction in primary care and emergency care visits.

Professional-led models of care

Fifteen studies looked at professional-led models of care for diabetes, hypertension, depression, hyperlipidaemia and transitions of care. All models in these studies were led by a pharmacist (mainly clinical pharmacists) providing care for patients with long-term conditions. Details can found in the evidence tables in appendix D.1.8.

Six of these studies (low-quality evidence). favoured the pharmacist-led care model for reducing HbA_{1c} levels over usual care. One study (moderate-quality evidence) showed no significant difference between the pharmacist-led care and usual care in reducing HbA_{1c}.

One study (low-quality evidence) showed no significant difference between the pharmacist-led care and usual care in reducing HbA_{1c}, however there was a significant difference favouring the pharmacist-led model of care for patient treatment satisfaction over usual care.

Pharmacist-led models of care in 2 studies (low-quality evidence), were significantly favoured for improvement in diabetes knowledge and 2 studies (low-quality evidence) also favoured the pharmacist-led care model for improving medicines adherence over usual care.

One study(moderate-quality evidence) favoured the pharmacist-led care model over usual care for better control of blood pressure and 2 studies (low/moderate-quality evidence) favoured the pharmacist-led care model over usual care for attaining target blood pressure.

Three studies (moderate/low-quality evidence) showed no significant difference in improving adherence to medicines when comparing pharmacist-led model with usual care.

One study (low-quality evidence) showed no significant difference in improving self-management after receiving pharmacist-led care or usual care. The number of hypertension-related clinic visits was significantly lower in the usual care group compared with the pharmacist-led care group in 1 study (moderate-quality evidence).

One study (low-quality evidence) showed no significant difference between the pharmacist-led care model and usual care in healthcare utilisation.

Two studies (low-quality evidence),showed no significant difference in change in depressive symptoms, change in functional status and healthcare utilisation between pharmacist-led care model and usual care . Patient satisfaction was reported in both studies, in which 1 study (low-quality evidence) significantly favoured the pharmacist-led care model over usual care and the other study (low-quality evidence) showed no significant difference between the pharmacist-led care model and usual care. One of these studies (low-quality evidence). showed that the pharmacist-led care model significantly improved adherence to medicines compared with usual care during the continuation phase of the study; there was no significant difference during the early phase of the study.

Two studies (low/moderate-quality evidence) looked at pharmacist-led models of care for hyperlipidaemia and found that the pharmacist-led care model significantly reduced low-density lipoprotein cholesterol (LDL-C) in patients compared with usual care

One study (low-quality evidence).showed that the pharmacist-led care model was significantly favoured for the following outcomes over usual care: reduction in pain and healthcare utilisation.. No significant difference was found between the pharmacist-led care model and usual care for other clinical outcomes (falls, worsening mobility, worsening behaviours and increased confusion).

Economic evidence

Partially applicable evidence from one study with potentially serious limitations populated with observational study data suggests that multidisciplinary team delivery of a multifaceted intervention designed to optimise medicines use during hospital stays is dominant compared with usual care.

Partially applicable evidence from one study with potentially serious limitations populated with published data (non-RCT-based) and expert opinion suggests that there is a net benefit when pharmacists are introduced into hospital ward rounds. These results are highly uncertain.

12.6 Evidence to recommendations

Table 45 Linking evidence to recommendations (LETR)

Relative values of different outcomes	The GDG considered all the different models of care that were presented to them and discussed the outcomes of each one. The included studies all compared the model of care with usual care only. There were no studies comparing 1 model of care with another.
	The GDG discussed the relative importance of the outcomes and agreed that mortality, patient-reported outcomes, clinical outcomes as reported in the study, and health and social care utilisation were critical outcomes for this review question. Medicines related problems, practitioner-reported outcomes, sub-optimal medicines use and health and social care related quality of life were considered as important outcomes. The GDG was aware that there was no evidence reporting mortality.
	The available clinical evidence suggests that collaborative care working in a primary care setting that involves multidisciplinary teams (consisting of a doctor, a pharmacist and/or a nurse) may improve outcomes such as clinical, patient-reported and healthcare use outcomes for specific conditions. The GDG was aware that in practice, multidisciplinary team working is more

common in secondary care, where health professionals are working in close proximity (such as in ward rounds in hospital), compared with primary care, where health professionals work in different locations. For example, doctors and practice nurses may be based in a GP practice and pharmacists may be based in a community pharmacy or part of a local medicines optimisation team. Multidisciplinary team working in primary care for specific groups of people could be determined locally – for example, having a multidisciplinary team for managing medicines for older people in care homes. The GDG considered multidisciplinary team working in intermediate care and agreed that the same principles could apply to this care setting.

The GDG found that there was a range of outcomes that significantly favoured the pharmacist-led model of care, especially disease-orientated outcomes for hypertension, diabetes and hyperlipidaemia. The GDG discussed the mixed evidence for patient-orientated outcomes such as adherence to medicines. The GDG suggested that the evidence would be comparable to that for disease-orientated outcomes as adherence to medicines is linked to improvement in clinical outcomes.

The GDG recognised that the studies that looked at pharmacist-led care models were based mainly in primary care, where the pharmacist was delivering the service from a clinic in a GP practice. Other care settings included a community pharmacy (1 study), outpatients department (2 studies) and a hospital setting (1 study). The GDG acknowledged that the pharmacists leading the model of care in the studies were all clinical pharmacists who were experienced in managing chronic diseases or had specialised within a disease area – for example, in diabetes.

The GDG discussed and agreed that a multidisciplinary approach may improve outcomes for patients who have long-term conditions and take many medicines (polypharmacy). When a patient's medicines are being reviewed and discussed, a pharmacist should be part of the multidisciplinary team. The GDG also discussed and agreed that a clinical pharmacist-led care model in primary care may be beneficial to a specific group of patients – for example, those with long-term conditions.

Trade-off between benefits and harms	The GDG discussed and agreed that both multidisciplinary team models of care and pharmacist-led model of care are beneficial and no harm to patients was identified from the evidence. The GDG discussed that where a multidisciplinary team model of care is used, there should be an overall lead in the team. This may be a GP in the primary care setting or a consultant in secondary care setting. However, this may vary and the GDG discussed and agreed by consensus that this may be determined locally. In addition, the GDG also discussed that a clinical pharmacist may be the most appropriate health professional to take lead for managing the medicines in the multidisciplinary team. However, this may vary on a case-by-case basis and the GDG discussed and agreed by consensus that this may be determined locally.
Consideration of health benefits and resource use	The GDG considered that the economic evidence on models of care was limited to 2 studies and 2 interventions. Economic evidence was available on multidisciplinary team delivery of a multifaceted intervention aimed at optimising medicines use and adding pharmacists to ward rounds. The GDG noted that both of these interventions appeared to be a cost-effective use of resources, but were aware of the limitations of both studies. Notably, the economic evidence was built on clinical evidence that did not meet the inclusion criteria of the clinical evidence review for this guideline, that is, observational studies, rather than RCTs.

	The GDG agreed that the economic evidence relating to a multidisciplinary team model of care had some methodological limitations, but felt that the lack of uncertainty in the result (evident from the probabilistic sensitivity analysis conducted) meant that this approach could be recommended. Likewise, although the evidence related to adding pharmacists to ward rounds had limitations, the GDG judged this was sufficient to recommend consideration of such interventions. The GDG discussed that both health benefits and costs savings may result from multidisciplinary or profession-led team working. Changing approaches to working may not require additional resources, but allow for better use of current resources. In addition, the improvement in skill mix gained from this type of working may lead to better outcomes to patients resulting from optimised management. The GDG therefore felt that recommending multidisciplinary team working is likely to be a good use of NHS resources. The GDG acknowledged that there was no economic evidence identified that looked at pharmacist-led care models in primary care and as such the cost-effectiveness of such interventions is unknown.
Quality of evidence	The clinical evidence varied from low to moderate quality. There were no identified studies that were carried out in the UK. The studies included were mainly carried out in the USA, some in Australia, UAE, Hong Kong, Jordon and Canada. The economic evidence was partially applicable with potentially serious limitations taken from observational studies.
Other considerations	The GDG discussed the term 'collaborative care' as a model of care and found that there are different interpretations of the term. Some GDG members thought that 'collaborative care' may involve cross-organisational communication – for example, hospital sending a discharge letter to the patient's GP to transfer care and follow-up. Others saw it as a multidisciplinary team approach consisting of health and social care practitioners delivering care together at the same time, as presented in the evidence. The GDG was aware of other models of care that have been established – for example, early intervention teams, in-reach/outreach teams, supported discharge teams, and end-of-life care teams. The GDG discussed and agreed by consensus that pharmacists should be involved in parts of the care pathway where medicines are being discussed. The GDG was aware that, based on the inclusion criteria in the review protocol, no evidence was found for professional-led models of care, other than pharmacist-led. The GDG also acknowledged that given that the guideline is focussing on medicines optimisation, this was a likely reason why evidence was primarily identified for pharmacist-led models of care. The GDG found no evidence for models of cross-organisational working between health and social care or between health and the pharmaceutical industry or homecare companies. The GDG was aware of models of care that do exist between health and social care, but there is no published evidence to show outcomes. Examples include care coordinators or keyworkers coordinating patients' care in mental health settings. These also involve social care teams that help patients manage their medicines, in addition to other care arrangements to support independence in the patient's own home. The GDG heard that social care practitioners work with patients to identify adherence-related problems and often report this back to community pharmacies. The GDG discussed and agreed that when commissioning services to optimise medicines, the type of model of care used should be

determine locally to meet the healthcare needs of the local population. As there was uncertainty around whether cross-organisational working between different sectors would improve patient reported outcomes for suboptimal use of medicines, the GDG agreed that a research recommendation should be made to identify if cross organisational working (such as between NHS and social care) can improve patient-reported outcomes for suboptimal prescribing of medicines.

The GDG was aware that although no evidence was found showing health and pharmaceutical industry working collaboratively, in practice, both sectors often have educational partnerships with regard to managing medicines. The GDG heard that there is a publication by the Department of Health on Best practice guidance for joint working between the NHS and the pharmaceutical industry to enable NHS organisations and the pharmaceutical industry to work together in the interests of patients.

The GDG discussed that several homecare companies offer a delivery service of medicines to the patient that is organised, for example, through hospitals. The GDG was aware that the Royal Pharmaceutical Society (RPS) has published the Handbook for Homecare Services in England to support the implementation of the RPS Professional Standards for Homecare Services.

12.7 Recommendations and research recommendations

The introduction of skill mixing of various health and social care practitioners to meet the needs of different patient groups has led to different types of models of care emerging across health and social care settings. Cross-organisational working further provides seamless care during the patient care pathway when using health and social care services. The type of model of care used will be determined locally based on the resources and health and social care needs of the population in relation to medicines.

48. **Consider a multidisciplinary team approach to improve outcomes for people who have long-term conditions and take multiple medicines (polypharmacy).**

49. **When medicines are being discussed at any point in the care pathway, involve a pharmacist with relevant clinical knowledge and skills.**

12.7.1 Research recommendation

To be read in conjunction with the NICE Research recommendations process and methods guide.

Uncertainties

This review question aimed to review which models of care can lead to improved patient-reported outcomes specifically for the suboptimal use of medicines. The systematic review found no evidence for models of cross-organisational working between health and social care or between healthcare and the pharmaceutical industry or homecare companies in relation to medicines optimisation. There was uncertainty around whether cross-organisational working amongst different sectors would improve patient-reported outcomes relating to suboptimal use of medicines.

Uncertainties include: clinical effectiveness of medicines for patients, cost effectiveness of models used to reduce suboptimal use of medicines to inform commissioning of services and patient-reported outcomes relating to medicines for different models of care.

Reason for uncertainty

There is no evidence available as the relevant research has not been done, or that it may have been done but not yet published.

Key uncertainties

The main key uncertainty is that it is unknown whether models of cross-organisational working between health and social care or between health and the pharmaceutical industry or homecare companies can lead to improved patient outcomes specifically for the suboptimal use of medicines.

Research in this area would identify whether cross-organisational working can provide positive patient-reported outcomes in relation to medicines optimisation. For the NHS, services can be integrated further between organisations to provide for patients the best outcomes from their medicines, which may help to reduce medicines waste. For social care, research into joint working with the NHS may highlight models which work well to optimise patients' medicines, improving outcomes and improving safety. Research into this area may also highlight the limitations and challenges that exist currently when considering cross-collaborative working and these should be addressed where appropriate.

Recommendation

2. What models of cross-organisational working, for example between NHS and social care, or primary and secondary care, improve clinical and cost effectiveness in relation to the suboptimal prescribing of medicines?

Randomised controlled trials should consider models of cross-collaborative working to improve outcomes and safety for medicines, in the UK setting compared to usual care. A follow-up period (ideally longer than 2 years) would capture longer term outcomes. Outcomes for this research question should include patient-reported outcomes, clinical outcomes, medicines-related problems and cost effectiveness. The research should be can be carried out in all populations that use services across different sectors, for example, care (relating to the use of medicines) of people may be transferred from an NHS organisation to social care, from a secondary care organisations to primary care or within secondary care, for example from one ward to another. The research could also identify benefits and challenges of cross-organisational working for suboptimal prescribing of medicines.

Rationale

The GDG was aware of pockets of good practice that involve models of care consisting of cross-organisational working relating to medicines. However, no published evidence was found to show whether or not it improves patient-reported outcomes in relation to suboptimal prescribing. This research recommendation will help to provide evidence on whether or not cross-organisational working is a cost effective model of care when improving patient-reported outcomes for suboptimal prescribing.

PICO format:

Criterion	Explanation
Population	All people taking medicines using the following care settings: NHS Social care Pharmaceutical industry Home care companies Private providers of healthcare services
Intervention	Model used to deliver cross-organisational working, for example NHS and social care working together using a model to deliver a service collaboratively for medicines.
Comparator(s)	Routine care or usual care
Outcome	The following outcomes should be considered: patient-reported outcomes (for example satisfaction, medicines adherence) quality of life clinical outcomes medicines-related problems (for example adverse drug reactions, medicines discrepancies on records). An appropriate length of follow-up would be 2 years or more for the outcomes to be externally valid. Process measures may also be considered for this research question to see what impact cross-collaborative working has on resources such as time and staffing. Process measure outcomes may include: time required to transfer medicines-related information from one care setting to another training of staff required to solve any medicines-related queries.
Study Design	RCT
Timeframe	Follow-up outcomes of 2 years or more

13 Reference list

13.1 Clinical

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14 Glossary

This glossary provides brief definitions and explanations of terms used within this guideline. Further definitions and explanation of terms can be found on the **NICE glossary page**.

Alert fatigue

Declining prescriber's responsiveness to a particular type of alert as they are repeatedly exposed to that alert over a period of time

Allied health professionals

Health professions distinct from nursing, medicine and pharmacy.

Bar coding administration systems

System that uses scanning the barcodes of medicines to improve medication administration accuracy.

Clinical Commissioning Groups, CCG

NHS organisations set up by the Health and Social Care Act 2012 to organise the delivery of NHS services in England.

Complimentary medicine

Treatments that fall outside of mainstream healthcare. These medicines and treatments range from acupuncture and homeopathy to aromatherapy.

Computerised physician order entry systems, CPOE

Electronic system used mainly in the USA to allow prescribers to enter in electronic instructions for the treatment of patients under their care. This system allows communication over a computer network to the medical staff or to the departments (for example a pharmacy) responsible for fulfilling the order.

Electronic prescribing systems

Prescribing system used to enter requests for prescriptions to be generated electronically over a computer network.

Local health economy

This includes NHS organisations for example GP practices, and voluntary and independent sector bodies involved in the commissioning, development and provision of health services for particular population groups.

High-risk medicines

Medicines that are most likely to cause significant harm to the patient, even when used as intended.

Medication-related never events

Serious, largely preventable patient safety incidents that should not occur if the available preventative measures have been implemented by healthcare providers

Medicines use reviews, MURs

Pharmacists undertaking structured adherence-centred reviews with patients on multiple medicines, particularly those receiving medicines for long term conditions.

New Medicines Service, NMS

Pharmacy service providing support for people with particular long-term conditions newly prescribed a medicine to help improve medicines adherence.

'No-blame culture'

In health and social care, this enables open and honest reporting of mistakes that are treated as an opportunity to learn to improve care.

Over-the-counter medicines

Medicines that can be bought without a prescription.

Patient's baseline risk

Patient decision aids illustrate the absolute benefits and risks of interventions, assuming a particular baseline risk. It is important to take into account the patient's likely starting or baseline risk when using a patient decision aid. Even though the relative risk is the same regardless of the patient's baseline risk, patients with a lower baseline risk than that illustrated in a patient decision aid will have a lower absolute chance of benefiting and a lower residual risk. Patients with a greater baseline risk than that illustrated will have a greater absolute chance of benefiting but also a greater residual risk

Personal digital assistant device

Handheld mobile computerised device that can store data such as guidelines.

Pharmacovigilance

Monitoring the safety of medicines

PINCER (pharmacist-led information technology intervention for medication errors)

Method for reducing a range of medication errors in general practices with computerised clinical records

Polypharmacy

Use of multiple medicines by a person

Preference-sensitive decision

Decisions about treatment made based on the persons preferences and personal values of each treatment option presented. Decisions should be made only after patients have enough information to make an informed choice, in partnership with the prescriber.

Robust and transparent

Robust and transparent processes, including sharing of information and appropriate collaboration with relevant stakeholders, aims to improve the consistency of decision-making about medicines and ensure that patient safety is not compromised. This should reduce inappropriate variation in patient care when decisions are made due to inconsistent, inadequate or unsafe processes and policies. However, even with robust and transparent processes in place, legitimate variation will remain. Organisations will make decisions within their local governance arrangements that are based on local priorities and the needs of their local population.

Superintendent pharmacist

This is a pharmacist who is appointed to act on behalf of a body corporate that wishes to conduct a retail pharmacy business