Policy Research Unit in Economic Evaluation of Health & Care Interventions (EEPRU)

ECONOMICS OF MEDICINES OPTIMISATION

January 2014
Report 016

Authors: Faria R¹, Barbieri M¹, Light K², Sculpher M².

¹ ScHARR, The University of Sheffield
² Centre for Health Economics, University of York
**Date completed:** 10\textsuperscript{th} February 2014

**Source of funding**
This research was undertaken by the Policy Research Unit in Economic Evaluation of Health and Care Interventions which is funded by the UK Department of Health Policy Research Programme.

The views expressed in this report are those of the authors and not those of the Department of Health. Any errors are the responsibility of the authors.

**Acknowledgement**
The authors would like to thank Professor Rachel Elliott, Professor Nick Barber and Professor Anthony Avery for their valuable comments and assistance in conducting this work.
# CONTENTS

1. Executive summary.................................................................................................................. 1
   1.1. Background .......................................................................................................................... 1
   1.2. Methods ............................................................................................................................... 1
   1.3. Results .................................................................................................................................. 1
   1.4. Conclusions and implications for research .......................................................................... 2
2. Background .............................................................................................................................. 1
   2.1. Scale and burden of suboptimal medicines use in the UK ..................................................... 2
3. Scoping review on effectiveness and cost-effectiveness of interventions ..................................... 7
   3.1. Methods ............................................................................................................................... 7
       Data sources and searches ....................................................................................................... 7
       Selection criteria ...................................................................................................................... 7
       Data Extraction and synthesis ................................................................................................. 8
   3.2. Results .................................................................................................................................. 8
       Systematic reviews .................................................................................................................. 10
       Economic evaluations ............................................................................................................ 15
4. Discussion .................................................................................................................................. 18
5. References ................................................................................................................................. 21
6. Appendices .................................................................................................................................. 30
   6.1. Appendix 1 Full search strategies ....................................................................................... 30
1. EXECUTIVE SUMMARY

1.1. BACKGROUND

The UK National Health Service (NHS) faces the triple challenge of improving health outcomes while coping with the increasing demand for services and achieving efficiency savings. Medicines optimisation can improve health outcomes and reduce costs. However, addressing suboptimal use of medicines in an effective and cost-effective manner requires an understanding of the size and nature of the evidence base. The objectives of this work are, firstly, to undertake a scoping review relating to the suboptimal use of medicines in the NHS, both in terms of the scale, costs and health lost; and, secondly, to review the extent of the evidence on effectiveness and cost-effectiveness of interventions to address suboptimal use of medicines.

1.2. METHODS

Systematic searches (up to February 2013) of the NHS Economic Evaluation Database, the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects are undertaken to identify for systematic reviews on the effectiveness or cost-effectiveness and for primary research on cost-effectiveness of interventions. Studies in English set in any country are included. Suboptimal use of medicines is categorised in a number of different aspects on discussions with advisors and a brief review of the area: compliance with guidelines, inappropriate prescribing, prescriptions errors, medicines reconciliation and discharge, dispensing errors, administration errors, medicines management in care homes, adherence and monitoring errors.

1.3. RESULTS

In total, 107 studies are included in the review (29 economic evaluations and 78 systematic reviews) from 646 records identified.

Systematic reviews on effectiveness of interventions

With the exception of insufficient prescribing of low cost generics and record keeping, every one of the aspects of suboptimal medicines use is addressed by the systematic reviews. The majority of the studies (51, 65%) focussed on interventions to improve adherence, either in any disease area (21; 27%) or in specific conditions (30, 38%). Randomised controlled trials (RCTs) are available for all aspects. There is considerable evidence on the different aspects of suboptimal medicines use specific to the UK setting. Most studies report intermediate outcomes: measures of adherence (53, 68%), clinical outcomes (24, 31%) and adverse drug events (16, 21%). No study reports quality-adjusted life years but four (5%) report measures of quality of life.
Economic evaluations

The majority of the studies (16, 55%) examines interventions to improve adherence, followed by prescription errors (8, 28%) and inappropriate prescribing (4, 14%). Six studies (21%) address more than one aspect of suboptimal use of medicines. Most studies (19, 66%) conduct a within-trial economic evaluation using data from a single study. Clinical outcome measures are the most frequently used (8, 28%), followed by measures of adherence (6, 21%) and appropriateness of medication (5, 17%). Quality-adjusted life years (QALYs) are used in five studies (17%).

1.4. CONCLUSIONS AND IMPLICATIONS FOR RESEARCH

There is a large body of evidence on the effectiveness of interventions to improve adherence to medication. Most are, however, specific to a particular disease area. Interventions to improve the different aspects of suboptimal prescribing form the second largest body of literature, particularly those to reduce prescription errors and inappropriate prescribing. The evidence on cost-effectiveness follows the same pattern but is much smaller in size.

Interventions to improve suboptimal use of medicines tend to be specific to a particular aspect of the pathway and/or to a particular disease area. Little consideration is made on how to improve medicines use in patients with co-morbidities and poly-medication. The medicines pathway is rarely examined holistically but in a fragmented manner, making it difficult to draw conclusions on which aspect of suboptimal use of medicines should be prioritised for investment. Decision modelling has the potential to address the evidence gaps in the literature by translating intermediate outcomes into health and costs and by integrating the evidence across the full medicines pathway.
2. BACKGROUND

The UK National Health Service (NHS) faces the triple challenge of improving health outcomes while facing increasing demand for services and achieving efficiency savings in the region of £20 billion by 2014-15 as part of the Quality, Innovation, Productivity and Prevention (QIPP) initiative. QIPP sits in the context of a wider international drive to improve quality of care and health outcomes whilst keeping costs down. Improving the use of medicines can improve health outcomes and reduce costs. In the UK, the cost from medicines waste in primary care was estimated at £300 million per year. In secondary care, hospitalisations related with adverse drug reactions may cost up to £466 million per year. Worldwide, medicines optimisation could achieve savings in the region of 8% of total global healthcare costs. The World Health Organisation (WHO) has examined the case for better use of medicines and concluded that there is a large potential for improvement in health outcomes if medicines are better used. The potential for health gains is equally impressive as more than 250,000 hospital admissions per year are attributable to adverse drug events and 16% of medication incidents have resulted in patient harm and 0.9% in death.

Medicines optimisation is clearly beneficial and uncontroversial but can be difficult to achieve. In practice, the optimal use of medicines involves getting all the steps right in the medicines pathway, namely prescribing, record keeping, dispensing, monitoring and administration. Although a perfect system is impossible, suboptimal use of medicines is often the norm for most patients and only 4%-21% may be getting the maximum benefit from medicines. The different aspects of suboptimal use of medicines relate to the different steps in the medicines management pathway. Optimal prescribing may be affected by poor compliance with best-practice guidelines, insufficient generic prescribing, inappropriate prescribing (under-, over- and misuse of medicines) and prescription errors. In addition, suboptimal prescribing may occur from misdiagnosis or failing to detect that a particular symptom is caused by another medicine. The interface between primary and secondary care is another area affected by suboptimal use of medicines, in particular at admission (medicines reconciliation) and discharge. Other causes of suboptimal medicines use are dispensing errors, administration errors, poor medicines management in care homes, under-monitoring and non-adherence. As a result, optimisation involves not only integration of the different healthcare professionals but also communication with patient and carers. Figure 1 sets out the key elements in medicines optimisation: an understanding of the patient’s experience, ensuring that the medicine use is as safe as possible, making decisions guided by evidence on effectiveness and cost-effectiveness and integrating medicines optimisation within routine practice.
Addressing these various areas of concern in an effective and cost-effective manner requires an understanding of the size and nature of the evidence base. The objectives of this work are, firstly, to undertake a scoping review relating to the suboptimal use of medicines in the NHS, both in terms of the scale, costs and health lost; and, secondly, to review the extent of the evidence on effectiveness and cost-effectiveness of interventions to address suboptimal medicines use. This will inform future research on cost-effective strategies to achieve medicines optimisation.

### 2.1. SCALE AND BURDEN OF SUBOPTIMAL MEDICINES USE IN THE UK

Table 1 summarises the recent literature on the scale and burden of suboptimal use of medicines. Suboptimal prescribing, for example, can occur from poor compliance with guidelines, inappropriate prescribing, insufficient prescribing of low cost generics, or prescription errors. It is difficult to disentangle these different issues. Poor compliance with guidelines can not only be an issue in its own, but can also result in inappropriate prescribing (as in antibiotics, antipsychotics or non-steroid anti-inflammatory medication), or insufficient prescribing of low cost generics (as in statins or renin-angiotensin drugs).

Prescription errors are another aspect of suboptimal prescribing. Errors are relatively frequent in general practice, but most are unlikely to have adverse consequences. A similar pattern emerges from secondary...
care, with error rates from 8.4% to 10.3% depending on the grades of doctor considered. However, almost all errors are intercepted by pharmacists before reaching the patient. Errors can also occur at the interface between secondary and primary care, i.e. at admission to hospital and at discharge. Such errors relate with difficulties in obtaining the patient history and in the communication of changes in medication from the hospital to the GP. Dispensing errors appear to be less frequent than prescription errors, both in community pharmacies and in hospital settings. The picture is somewhat different in care homes, with dispensing errors at 9.8%. The difference found in this study is related with the repackaging of tablets in monitored dosage systems; in particular, pharmacies whose packages did not allow enough space for all the required statutory labelling. The most frequent cause of errors in care homes is in monitoring, which is also the type of error most likely to cause harm. Monitoring errors in the community, where one in seven patients may be at risk, are in same order of magnitude as in care homes. Deficient record keeping is an aspect of suboptimal use of medicines that can result in prescription errors, in issues in medicines reconciliation and discharge, dispensing errors, administration errors, monitoring errors and medicines waste due to over-ordering of medicines. However, no studies were found on the prevalence or burden due to deficient record keeping. The final and most important hurdle for medicines optimisation is adherence. Overall, between 30%-60% of all medicines are not taken as prescribed. Non-adherence is a complex issue. Non-adherence may be non-intentional, i.e. the patient forgets to take the medication, or intentional, whereby there is a rational decision process in which the individual compares the benefits and risks from the medication. In any case, non-adherence can have a substantial impact on both costs and health outcomes. Non-adherence has been estimated to cost between £36-£196 million per year in direct costs to the NHS (2006-07 prices). The consequences in terms of health loss are more difficult to estimate, but there is evidence that non-adherence is associated with poorer outcomes in cardiovascular disease, diabetes, osteoporosis and asthma.
<table>
<thead>
<tr>
<th>Aspect of suboptimal use</th>
<th>Scale of the problem</th>
<th>Costs and health lost</th>
</tr>
</thead>
</table>
| Poor compliance with guidelines          | • Evidence of unwarranted variation of prescription rates of recommended drugs:  
  o Prescribing rates for anti-dementia drugs varied across Primary Care Trusts in England during 2010-11, between 0.1-1.3 per age- and sex-weighted population, a variation that is unlikely to be fully explained by differences in prevalence 30.  
  o Prescribing rates for Parkinson’s disease drugs across Primary Care Trusts in England during 2010-11 varied from 2.0-6.9 per age-weighted population, a variation that is unlikely to be fully explained by differences in prevalence 30.  
  o Prescribing rates of hypnotics drugs per weighted population varied fourfold across Primary Care Trusts in England during 2010-11 30.  
• Not following the guidelines in the prescription of statins, renin-angiotensin drugs, proton-pump inhibitors and clopidogrel accounted for £227 million over one year 11.  
• Insulin total net ingredient cost per patient varied from £79 to £176 in 2010-11 across Primary Care Trusts in England but this variation did not correlate with patient outcomes 30.  
• Non-insulin anti-diabetic drugs total net ingredient cost per patient varied from £65 to £180 in 2010-11 across Primary Care Trusts in England, but this variation did not correlate with patient outcomes 30.  
• Failing to follow the guidelines in the prescription of statins, renin-angiotensin drugs, proton-pump inhibitors and clopidogrel accounted for £227 million over one year 11.  
• The NHS achieved year on year savings of £395.6 million in 2008, £443.0 million in 2009 and £414.8 million in 2010 by following guidance on prescribing of low cost generics 31.  |
| Insufficient prescribing of low cost generics | • Prescribing rates in 2006 for statins prescribed as simvastatin (recommended) varied across Primary Care Trusts from around 25% to 85% 11.  
• 58% of patients referred to hospital with sore throats were prescribed an inadequate dose or an inappropriate antibiotic in primary care. Hospital doctors prescribed antibiotics contrary to guidelines in 39% of patients referred to hospital 32.  
• A threefold variation in prescribing rates of Quinolones was found across Primary Care Trusts, an antibiotic that should be reserved for resistant infections 12.  
• An evaluation of the quality of prescribing in 102 hospitals across England found that 47% were not on the appropriate anti-thrombotic prophylaxis and that 51% were incorrectly prescribed benzodiazepines 33.  
• A review of the use of antipsychotic medication in people with dementia found that 80% of patients were unlikely to derive any benefit from these drugs 34.  
• An analysis of UK patient records in 2003 found that 32.2% of elderly patients were prescribed potentially inappropriate medication and 20.5% received a potentially high risk drug 35.  
• The inappropriate use of antipsychotic medication in patients with dementia was associated with an additional 1,800 deaths and 1,620 cerebrovascular events per year 34.  
• Inappropriate prescribing of non-steroid anti-inflammatory drugs has been associated with 3,500 hospitalisations and 400 deaths per year in patients over 60 years of age 13.  
• The NHS achieved year on year savings of £395.6 million in 2008, £443.0 million in 2009 and £414.8 million in 2010 by following guidance on prescribing of low cost generics 31.  |
| Inappropriate use of antibiotics         | • 58% of patients referred to hospital with sore throats were prescribed an inadequate dose or an inappropriate antibiotic in primary care. Hospital doctors prescribed antibiotics contrary to guidelines in 39% of patients referred to hospital 32.  
• A threefold variation in prescribing rates of Quinolones was found across Primary Care Trusts, an antibiotic that should be reserved for resistant infections 12.  
• Inappropriate prescribing of non-steroid anti-inflammatory drugs has been associated with 3,500 hospitalisations and 400 deaths per year in patients over 60 years of age 13.  |
| Inappropriate prescribing               | • An evaluation of the quality of prescribing in 102 hospitals across England found that 47% were not on the appropriate anti-thrombotic prophylaxis and that 51% were incorrectly prescribed benzodiazepines 33.  
• A review of the use of antipsychotic medication in people with dementia found that 80% of patients were unlikely to derive any benefit from these drugs 34.  
• An analysis of UK patient records in 2003 found that 32.2% of elderly patients were prescribed potentially inappropriate medication and 20.5% received a potentially high risk drug 35.  
• The inappropriate use of antipsychotic medication in patients with dementia was associated with an additional 1,800 deaths and 1,620 cerebrovascular events per year 34.  
• Inappropriate prescribing of non-steroid anti-inflammatory drugs has been associated with 3,500 hospitalisations and 400 deaths per year in patients over 60 years of age 13.  |
| Prescription errors                      | • A retrospective study in 15 general practices in England (the PRACTIce study) reviewed                                                                                                               |                                                                                                                                                                                                                                                                                                                                             |
the records of 1,777 patients (6,048 prescription items) and found 247 (4.08%) prescribing errors, 55 (0.91%) monitoring errors, 427 (7.06%) cases of suboptimal prescribing and 8 legal problems. Overall, 12% of all patients and 4.9% of all prescriptions included prescription or monitoring errors. The mean prescription error rate by first year foundation trainee doctors was estimated at 8.4% per medication order, but most did not reach the patient. A study in three NHS hospitals found that 14.7% of prescription orders had an error; 16.3% in medical admission wards and 12.2% on surgical wards. A study evaluating the effectiveness of an intervention to reduce prescription or monitoring errors (the PINCER trial) found that 3% of patients were at risk of at least one prescription problem.

### Medicines reconciliation and discharge

- A report from the Care Quality Commission reviewed patients’ care following discharge from hospitals. It found that 24% of GPs do not systematically provide information on co-morbidities, allergies and drug reactions to hospital; 53% of GP practices reported that discharge summaries were received in time to be useful either “all” or “most” of the time; only 27% of GP practices reported that discharge summaries were “hardly ever” or “never” inaccurate or incomplete; and 81% of practices reported that details of prescribed medicines were incomplete or inaccurate on discharge summaries “all” or “most” of the time.
- A study in 42 NHS Trusts providing specialist mental health services found discrepancies in patients’ medication history at admission in 25% to 31% of patients.
- Another study investigated the severity of discrepancies in the patients' medication history at the time of admission and following discharge. Discrepancies occurred in 69% of the admissions and 43% of the discharges.

### Dispensing

- A systematic review estimated that the dispensing error rate in hospital pharmacies between 0.008% to 0.02%.
- A study in 20 NHS hospitals in Wales estimated an overall incident rate of dispensing errors of 1.6%, 24% of which the wrong strength, 17% the wrong drug, 13% the wrong form and 11% the wrong instructions.
- An observational study in 11 UK pharmacies found a content error in 1.7% of dispensed items and a labelling error in 1.6%; 67% of errors were unlikely to have adverse consequences.

### Administration errors

- An observational study in older people wards in four hospitals in East Anglia found that 38.4% of medication doses were given incorrectly. This study also included a review of the literature, which indicated that medication administration errors in the UK ranged between 3-8%.

### Medicines management in care homes

- A pivotal study evaluating the prevalence, types and causes of medication errors (prescribing, monitoring, dispensing and administration) in the care home setting found that 65.9% of residents had been subject to a medication error: prescribing 8.3%, monitoring 14.7% (for relevant medicines), dispensing 9.8% and administration.
### Adherence

- A longitudinal survey of patients found that 67 (30%) of 226 patients still taking their medication at 10 days and 43 (25%) of the 171 patients still taking their medication at 4 weeks were non-adherent. 40.
- A review of the literature found that 5%-20% of all prescriptions are not dispensed and 10% of repeat medications are not refilled. Overall, 30% to 60% of medicines are not taken as prescribed 23.
- A recent report estimated that the gross annual cost of NHS primary and community care prescription medicines wastage in England for 2009 is currently in the order of £300 million per year, including £90 million of unused prescription medicines in individuals’ homes, £110 million returned to community pharmacies and £50 million of unused medicines disposed of by care homes 3.
- The National Audit Office estimated in 2007 for England that the value of medicines returned unused is £100 million and that the cost of destroying them was £1.5 million 41.
- Non-adherence to diabetic medication has been associated with statistically significant increased risks for all-cause hospitalization (odds ratio=1.58) and for all-cause mortality (odds ratio=1.81) 27.

### Monitoring

- 5% (n=3,253) of the medication incidents reported to the National Patient Safety Agency in 2007 were caused by lack of or inappropriate monitoring. Of these, three lead to death and three lead to severe harm 41.
- The PINCER trial: 15% of patients were at risk of at least one monitoring problem. Specific monitoring problems were: 11% on long term angiotensin converter enzyme inhibitors or loop diuretics without urea and electrolyte monitoring; 39% on methotrexate for ≥3 months without full blood count in the past 3 months; 37% of patients on methotrexate for ≥3 months without a liver function test in the past 3 months; 7% on warfarin for ≥3 months without an international normalised ratio (INR) in the past 3 months; 49% of patients on lithium for ≥3 months without a lithium concentration measurement in the past 3 months; 49% of patients on lithium for ≥6 months without an international normalised ratio (INR) in the past 6 months 22.
- The PRACItCe study identified 55 monitoring errors in 770 prescription items reviewed that required blood monitoring (7%) 34.
3. SCOPING REVIEW ON EFFECTIVENESS AND COST-EFFECTIVENESS OF INTERVENTIONS

3.1. METHODS

Data sources and searches
In order to scope the literature on the effectiveness and cost effectiveness of interventions to address sub-optimal use of medicines, bibliographic search strategies are designed to provide an overview of the literature and identify any evidence gaps. Given that the studies of interest are systematic reviews or economic evaluations, the databases searched are the NHS Economic Evaluation Database (NHS EED), the Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of Effects (DARE). Grey literature (work published in channels other than peer-reviewed journals) is not examined. The base search strategy is constructed using The Cochrane Library and then adapted to the other resources searched. Searches were conducted in February 2013, and are limited to material published since 2000 and written in English. Appendix 1 details the search strategies.

NHS EED contains economic evaluations of health care interventions and is updated weekly. Included studies are published in the database and prioritised for abstract writing. Structured abstracts are written and independently checked by health economists. DARE contains systematic reviews of the effects of health care interventions and the delivery and organization of health services and is updated weekly; citations identified as potential systematic reviews are assessed for inclusion by two researchers. Reviews need to meet at least four of five criteria (criteria 1-3 are mandatory) to be included: (1) inclusion/exclusion criteria are reported; (2) adequate search; (3) included studies are synthesised; (4) quality of the studies is assessed; (5) there are sufficient details about the included studies. Reviews are then published in the database and prioritised for abstract writing. Structured abstracts are written by researchers and checked by a technical editor. DARE includes records of all Cochrane reviews and protocols, as well as published papers associated with Cochrane reviews.

Selection criteria
The effectiveness review includes systematic reviews of interventions to address one or more aspects of suboptimal use of medicines. Given that a small number of systematic reviews of economic evaluations is anticipated, this review includes both primary research and systematic reviews. Studies in English set in any country are included. Only full economic evaluations are included in the economic review, i.e. studies comparing two or more interventions in terms of costs and effects. Interventions to improve clinical management in the whole disease pathway, but without a specific focus on medicines use, are excluded. Titles are screened by one reviewer and confirmed with the abstracts by another.
Data Extraction and synthesis

Data are extracted from the NHS EED or DARE structured abstracts using a standardised form. Full-text papers are consulted where the structured abstract is not available or if the abstract does not contain the information required. Data extraction includes: objective, aspect(s) of suboptimal use of medicines that interventions addressed, type of intervention, target of the intervention, and outcomes. For cost-effectiveness studies, the type of analysis (within trial or model based), the setting and the source of effectiveness data are extracted. For systematic reviews, the search period, the inclusion/exclusion criteria, type of studies included, quality assessment and data synthesis are also extracted. Data are presented in tables and figures. A narrative synthesis is undertaken.

3.2. RESULTS

Figure 2 presents the flowchart of the study selection process. A full list of publications that do not meet all of the inclusion criteria, along with the reasons for their exclusion, is available on request. Briefly, 646 records are found, of which 157 abstracts are assessed for eligibility. In total, 107 studies are included in the review (29 economic evaluations and 78 systematic reviews).
Figure 2  Flow diagram for the review of systematic reviews and economic evaluations on interventions to improve the suboptimal use of medicines (adapted from Moher et al, 2009)
Systematic reviews

All systematic reviews meeting the inclusion criteria review studies on the effectiveness of intervention; none includes economic evaluations. Table 2 summarises the disease areas and the type of studies included by aspect of suboptimal medicines use. With the exception of insufficient prescribing of low cost generics and record keeping, every one of the aspects of suboptimal medicines use is addressed by the systematic reviews. The majority of the studies (51, 65%) focusses on interventions to improve adherence, either in any disease area (21; 27%) 42-62 or in specific conditions (30, 38%) 45,63-91.

Nine reviews address more than one aspect of suboptimal use of medicines:

- poor compliance with prescribing guidance and suboptimal medicines use in care homes 92, 93
- inappropriate prescribing and adherence 43
- poor compliance with guidelines and inappropriate prescribing 94,95
- prescription and dispensing errors 96
- inappropriate prescribing and medicines reconciliation and discharge 97
- prescription, dispensing and administration errors and medicines reconciliation 98
- inappropriate prescribing and dispensing errors 99.

Randomised controlled trials (RCTs) are available for all aspects covered by the reviews. The number of RCTs varies from one to 81 (median=10). Five systematic reviews (6%) included no RCTs 61,100-103. Three of these evaluate the effect of computerised prescription entry on prescription errors 100,102,103, one examines the effect of automated dose dispensing on medication safety 101 and other the effect of self-administration of medication by hospital patients on compliance errors amongst other process outcomes 61.

Table 3 indicates the country where the studies included in the systematic reviews are based. This is based on the structured abstracts, complemented with full text studies when immediately available. The systematic reviews include studies from a large number of countries. One quarter of the reviews includes studies based in the UK. Most studies are based in the US (33; 452%).
<table>
<thead>
<tr>
<th>Aspect of suboptimal medicines use</th>
<th>Number (%)</th>
<th>Disease area</th>
<th>Types of studies included</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All</td>
<td>Specific conditions or therapies</td>
</tr>
<tr>
<td>Lack of compliance with guidelines</td>
<td>6</td>
<td>8%</td>
<td>92-95, 104</td>
</tr>
<tr>
<td>Prescription errors</td>
<td>10</td>
<td>(13%)</td>
<td>95, 96, 98, 100, 102, 103, 110, 111</td>
</tr>
<tr>
<td>Medicines reconciliation and discharge</td>
<td>3</td>
<td>(4%)</td>
<td>97, 98, 114</td>
</tr>
<tr>
<td>Dispensing errors</td>
<td>3</td>
<td>(4%)</td>
<td>96, 98, 99</td>
</tr>
<tr>
<td>Administration errors</td>
<td>3</td>
<td>(4%)</td>
<td>96, 98, 101</td>
</tr>
<tr>
<td>Medicines management in care homes</td>
<td>4</td>
<td>(5%)</td>
<td>92, 93, 115, 116</td>
</tr>
<tr>
<td>Adherence</td>
<td>51</td>
<td>(65%)</td>
<td>42-62</td>
</tr>
</tbody>
</table>

* RCT – randomised controlled trial
† URTI – upper respiratory tract infection
<table>
<thead>
<tr>
<th></th>
<th>Tuberculosis</th>
<th>Asthma</th>
<th>Bipolar disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring</td>
<td>3</td>
<td>97, 99, 120</td>
<td>97</td>
</tr>
<tr>
<td>Other (any pharmacist intervention to improve patient care, any intervention to reduce medication adverse events)</td>
<td>2</td>
<td>7, 121</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>46 (59%)</td>
<td>32 (41%)</td>
</tr>
</tbody>
</table>
Table 3  Setting of primary studies included in the systematic reviews by aspect of suboptimal use of medicines (references in superscript numbers)

<table>
<thead>
<tr>
<th>Aspect of suboptimal medicines use</th>
<th>Number (%)</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor compliance with guidelines</td>
<td>6 (8%)</td>
<td>93, 93, 95, 101, 92, 93, 95, 91, 94, 105</td>
</tr>
<tr>
<td>Inappropriate prescribing (including antibiotics)</td>
<td>9 (12%)</td>
<td>43, 106, 43, 95, 107, 43, 95, 106-108, 107, 108, 94, 97, 98, 109</td>
</tr>
<tr>
<td>Prescription errors</td>
<td>10 (13%)</td>
<td>98, 110, 95, 98, 110, 95, 96, 100, 110, 112, 13, 113, 98, 110, 110, 108, 110, 96, 102, 103, 111</td>
</tr>
<tr>
<td>Medicines reconciliation and discharge</td>
<td>3 (4%)</td>
<td>98, 98, 98, 98, 98, 98, 97, 114</td>
</tr>
<tr>
<td>Dispensing errors</td>
<td>3 (4%)</td>
<td>98, 98, 98, 98, 98, 98, 98, 96, 99</td>
</tr>
<tr>
<td>Administration errors</td>
<td>3 (4%)</td>
<td>98, 98, 101, 98, 98, 98, 98, 96</td>
</tr>
<tr>
<td>Medicines management in care homes</td>
<td>4 (5%)</td>
<td>93, 116, 93, 115, 116, 92, 93, 115, 116, 93, 115, 116</td>
</tr>
<tr>
<td>Adherence</td>
<td>51 (65%)</td>
<td>43, 45, 48, 63, 71, 72, 77, 82, 84, 86, 87, 89, 90, 106, 43, 45, 48, 54, 64, 71, 72, 76, 77, 84, 86, 88, 90, 106, 43, 45, 48, 54, 64, 66-71, 72, 76, 77, 84, 86-90, 90, 106, 48, 62, 64, 77, 45, 64, 66, 71, 72, 76, 77, 84, 86, 87, 89, 42, 44, 46, 47, 48-53, 55-58, 60, 62, 65-68, 70, 73-75, 78-81, 83, 85, 86, 92, 111</td>
</tr>
<tr>
<td>Monitoring</td>
<td>3 (4%)</td>
<td>94, 97, 120</td>
</tr>
<tr>
<td>Other</td>
<td>2 (3%)</td>
<td>7, 7, 7, 121, 7</td>
</tr>
<tr>
<td>Total</td>
<td>78 (24%)</td>
<td>19 (28%), 22 (42%), 33 (42%), 13 (17%), 11 (14%), 42 (54%)</td>
</tr>
</tbody>
</table>

Figure 3 shows the type of interventions included in the systematic reviews. Most (46, 59%) interventions are educational or involve some degree of counselling or behavioural therapy (25, 32%). There is a large variety of interventions making it difficult to classify them into homogeneous categories.
The category ‘educational interventions’ includes information leaflets. The percentages do not sum to 100% because some reviews cover more than one type of intervention.

Table 4 summarises the type of measures reported in the systematic reviews. Most studies report measures of adherence (52, 67%)\textsuperscript{42-45, 47-53, 55-91, 94, 97, 114, 121}, followed by clinical outcomes (24, 31%) and adverse drug events (16, 21%)\textsuperscript{7, 94, 95, 97, 98, 100, 102, 103, 107, 109-113, 115, 121}. No study reports quality-adjusted life years but four (5%) report measures of quality of life. Clinical outcomes are reported in 17 (22%) systematic reviews of interventions to improve adherence.

<table>
<thead>
<tr>
<th>Types of outcome measures</th>
<th>Number (%)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>9 (12%)</td>
<td>7, 93, 97, 99, 102, 106, 115, 121</td>
</tr>
<tr>
<td>Healthcare resource use or costs</td>
<td>16 (21%)</td>
<td>7, 45, 50, 61, 82, 83, 90, 95, 106, 113, 121, 447</td>
</tr>
<tr>
<td>Quality of life</td>
<td>4 (5%)</td>
<td>58, 60, 62, 121</td>
</tr>
<tr>
<td>Adverse drug events</td>
<td>16 (21%)</td>
<td>7, 94, 95, 97, 98, 100, 102, 103, 107, 109-113, 121</td>
</tr>
<tr>
<td>Measure of adherence</td>
<td>52 (67%)</td>
<td>42-45, 47-53, 55-91, 94, 97, 114, 121</td>
</tr>
<tr>
<td>Clinical outcome</td>
<td>24 (31%)</td>
<td>7, 42, 44, 46, 51, 52, 54, 58, 59, 62, 64, 69, 70, 77, 78, 90, 91, 93, 95, 109, 111, 115, 121</td>
</tr>
<tr>
<td>Patient satisfaction or knowledge</td>
<td>5 (6%)</td>
<td>46, 61, 64, 97, 121</td>
</tr>
<tr>
<td>Discrepancies in medication records</td>
<td>3 (4%)</td>
<td>102, 114, 115</td>
</tr>
<tr>
<td>Measure of appropriate medication</td>
<td>9 (12%)</td>
<td>92, 93, 99, 101-107, 115, 121</td>
</tr>
<tr>
<td>Days lost from work</td>
<td>1 (1%)</td>
<td>90</td>
</tr>
</tbody>
</table>
Economic evaluations

Table 5 (next page) presents the aspects of suboptimal medicine use addressed in the included economic evaluation studies. The majority of the studies (16, 55%) examine interventions to improve adherence \(^{122-136}\), followed by prescription errors (8, 28%) \(^{22, 126, 137-142}\) and inappropriate prescribing (4, 14%) \(^{117, 119, 131, 139}\).

Six studies (21%) address more than one aspect of suboptimal use of medicines:

- Compliance with guidelines and adherence \(^{125}\)
- Prescription errors and adherence \(^{126}\)
- Prescription and dispensing errors \(^{138}\)
- Prescription, dispensing and administration errors \(^{137}\)
- Inappropriate prescribing and adherence \(^{131}\)
- Inappropriate prescribing and prescription errors \(^{139}\).

More than half of the studies (17, 59%) examine interventions targeted at a specific diseases or therapies, such as cardiovascular disease (7, 24%) \(^{125, 143}\), human immunodeficiency virus (3, 10%) \(^{132, 134, 144}\), antibiotics (2, 7%) \(^{117, 119}\), cancer \(^{139}\), paediatric use of injectable medication \(^{137}\), anaesthesia \(^{118}\), psychoactive medication \(^{145}\), eradication of Helicobacter pylori \(^{122}\) and anticoagulant monitoring \(^{146}\). Various types of interventions are evaluated: pharmacist-led interventions (17, 59%) \(^{122-131, 53-54, 57-58, 60, 145, 146}\), support tools or devices (5, 17%) \(^{122, 137-139, 62}\), software support (4, 14%) \(^{137, 138, 140, 143}\), nurse-led support (4, 14%) \(^{132, 133, 144, 137}\), multidisciplinary medicines management (2, 7%) \(^{136, 117}\), financial incentives (2, 7%) \(^{134, 135}\), dose simplifications \(^{136}\) and quality improvement initiatives \(^{142}\). Three studies (10%) compare different types of interventions \(^{136-138}\) and in another the intervention consists of pharmacist-led counselling in association with leaflets and compliance diary charts \(^{122}\).

Table 7 summarises the type of analysis and the sources of effectiveness data. Most studies (19, 66%) conduct a within-trial economic evaluation using data from a single randomised controlled trial (RCT) \(^{122, 124, 125, 129, 130, 133, 134, 143, 145}\) or a non-randomised study, such as before and after, \(^{118, 119, 123, 128, 142, 146}\) or cohort studies \(^{117, 127, 131, 139, 141}\). Eleven studies (38%) use a model, either based on a single study \(^{22, 129}\), a review of the literature \(^{126, 135, 136, 144, 140, 144}\) or from expert elicitation \(^{138}\). De Giorgi et al. estimates cost-effectiveness using effectiveness estimates derived by a consensus panel \(^{137}\).
Table 5  Aspect of suboptimal use of medicines and interventions in cost-effectiveness studies (references in superscript numbers)

<table>
<thead>
<tr>
<th>Aspect of suboptimal medicines use</th>
<th>Number (%)</th>
<th>Disease area</th>
<th>Software</th>
<th>Pharmacist-led intervention</th>
<th>Nurse-led support</th>
<th>Multidisciplinary medicines management</th>
<th>Financial incentives</th>
<th>Tools or devices</th>
<th>Dose simplification initiative</th>
<th>Quality improvement initiative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of compliance with guidelines</td>
<td>2 (7%)</td>
<td>Cardiovascular 125, 143</td>
<td>143</td>
<td>125</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufficient generic prescribing</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inappropriate prescribing (including antibiotics)</td>
<td>4 (14%)</td>
<td>Antibiotic prescribing 117, 119</td>
<td>119, 117</td>
<td>110, 131</td>
<td>117</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cancer 159</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescription errors</td>
<td>8 (28%)</td>
<td>Injectables in paediatrics 137</td>
<td>137, 138, 140</td>
<td>137, 138, 139, 141</td>
<td>137</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cancer 139</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicines reconciliation and discharge</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dispensing errors</td>
<td>2 (7%)</td>
<td>Injectables in paediatrics 137</td>
<td>137, 138</td>
<td>137, 138</td>
<td>137</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administration errors</td>
<td>2 (7%)</td>
<td>Injectables in paediatrics 137</td>
<td>137</td>
<td>137, 137</td>
<td>137</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analgesia 114</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicines management in care homes</td>
<td>1 (3%)</td>
<td>Psychoactive medication 145</td>
<td>145</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence</td>
<td>16 (55%)</td>
<td>Eradication of Helicobacter pylori 122</td>
<td>122, 132, 133</td>
<td>132, 131, 132</td>
<td>134, 135, 136</td>
<td>136, 134, 135, 132</td>
<td>136</td>
<td>132</td>
<td>136</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Human immunodeficiency virus 122, 130, 144</td>
<td>122, 133, 144</td>
<td>132, 133, 144</td>
<td>136, 134, 135, 132</td>
<td>136, 134, 135, 132</td>
<td>136</td>
<td>132</td>
<td>136</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiovascular 125, 127, 128, 129, 131</td>
<td>122, 133, 144</td>
<td>132, 133, 144</td>
<td>136, 134, 135, 132</td>
<td>136, 134, 135, 132</td>
<td>136</td>
<td>132</td>
<td>136</td>
<td>134</td>
</tr>
<tr>
<td>Monitoring</td>
<td>1 (3%)</td>
<td>Anticoagulant monitoring 146</td>
<td>146</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (%)</td>
<td>-</td>
<td>12 (41%)</td>
<td>17 (59%)</td>
<td>4</td>
<td>17</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(14%)</td>
<td>(59%)</td>
<td>(14%)</td>
<td>(14%)</td>
<td>(7%)</td>
<td>(7%)</td>
<td>(17%)</td>
<td>(3%)</td>
<td>(3%)</td>
</tr>
</tbody>
</table>
Table 6  Methods used in the economic evaluation studies included in the review (references in superscript numbers)

<table>
<thead>
<tr>
<th>Source of effectiveness data</th>
<th>N (%)</th>
<th>Single RCT</th>
<th>Single study (non-RCT)</th>
<th>Review of the literature</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple extrapolation</td>
<td>1 (3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within-trial</td>
<td>19 (62%)</td>
<td>122, 124, 125, 130, 133, 134, 143, 145</td>
<td>117-119, 123, 127, 128, 131, 135, 141, 142, 146</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model based – Decision tree</td>
<td>4 (14%)</td>
<td>22, 129</td>
<td></td>
<td></td>
<td>126</td>
</tr>
<tr>
<td>Model based – Markov cohort</td>
<td>2 (7%)</td>
<td></td>
<td></td>
<td></td>
<td>135</td>
</tr>
<tr>
<td>Model based- other</td>
<td>3 (14%)</td>
<td></td>
<td></td>
<td></td>
<td>140, 144, 132</td>
</tr>
<tr>
<td>Total (%)</td>
<td>29 (100%)</td>
<td>10 (34%)</td>
<td>11 (38%)</td>
<td>6 (21%)</td>
<td>2 (7%)</td>
</tr>
</tbody>
</table>

RCT: Randomised controlled trial.

Figure 3 presents the effectiveness measures used in the economic evaluation studies. Clinical outcome measures are the most frequently used (8, 28%), namely blood pressure 125, 127, 133, cholesterol levels 143, proportion of treatment success 117, 122, and rate of thrombotic or haemorrhagic events 131, 146. Measures of adherence are used in six studies (21%) 128-131, 133, 134. Measures of appropriateness of the medication are used in five studies (17%), such as proportion of patients on first line anti-hypertensive 125, point reduction in the criticality index 137, proportion of patients on inappropriate psychoactive medication 145, and proportion of patients on the appropriate drug 117, 119. Quality-adjusted life years (QALYs) are used in five studies (17%) 132, 135, 136, 138, 144.
Figure 4  Types of effectiveness measures used in the economic evaluation studies (n=29)

Other types of outcome refer to patient’s willingness to pay for the service, drug preparation time, safety and usability scores and proportion of patients with allergy status documented.

4. DISCUSSION

The medicines pathway is a complex process that involves multiple stakeholders across different stages, namely prescribing, dispensing, record keeping, monitoring and administration. Research on suboptimal use of medicines has typically evaluated interventions on one particular stage of the medicines pathway in terms of their effect on intermediate outcomes. There is a large body of evidence on the effectiveness of interventions to improve adherence to medication; however, most are specific to a particular disease area. Interventions to improve the different aspects of suboptimal prescribing form the second largest body of literature, particularly those aimed at reducing prescription errors and inappropriate prescribing. Interventions to address other aspects of suboptimal use of medicines have been evaluated to a lesser extent. The literature on cost-effectiveness is much smaller than on effectiveness. Nonetheless, a similar picture emerges: interventions to improve adherence are the focus of the majority of cost-effectiveness studies, particularly in specific clinical areas such as cardiovascular disease, followed by interventions to improve prescribing. A small number of studies evaluate interventions in terms of cost per QALY gained and only one study includes the full medicines pathway.

The evidence base, although large, is insufficient to draw conclusions on (i) which aspect of suboptimal use of medicines is a key driver of costs or health losses, (ii) which stage of the medicines pathway is more likely to benefit from intervention and (iii) the effective and cost-effective interventions to achieve medicines
optimisation. In addition, it is unclear whether interventions evaluated in a particular disease are generalisable to people with co-morbidities using multiple medications. Another issue is related to the outcome measures used in the literature. Since most of the studies used intermediate outcome measures, such as adherence or error rates, it remains unclear whether interventions have an impact on final health outcomes. However, using outcomes such as mortality or QALYs in primary research may require large sample sizes to detect any effect.

This review provides an indication of the scale, costs and health lost as a result of suboptimal use of medicines in the NHS. It has also scoped the evidence on effectiveness and cost-effectiveness of interventions to address this problem. The scoping review is systematic, in terms of the searches, data extraction and presentation of results. Only systematic reviews are included in the review of effectiveness for pragmatic reasons; a review of the primary literature or of the grey literature would have been impractical within the time available. The same motive guided the decision to use NHS EED and DARE abstracts as the main source of data. Using these abstracts facilitated the completion of this review within the short time frame available. However, it created difficulties in extracting details on the setting of the studies included and types of interventions evaluated. Therefore, the classification of interventions may not reflect their full spectrum.

Despite the limitations of this review, there are some implications for research given the gaps identified in the evidence. First, more research is needed on the effects of interventions to improve suboptimal use of medicines in terms of final outcomes such as costs and quality adjusted survival. Second, interventions should be investigated for their generalisability across different patient populations and contexts. Third, research should consider the full medicines pathway and establish which aspect of suboptimal medicines use fits in the wider optimisation context.

Decision analytic modelling has the potential to address some of these issues. A decision analytic model is able to simulate the medicines pathway by relating different pieces of data obtained from a variety of sources. This model could indicate the aspects of suboptimal use of medicines that have the greatest impact in terms of costs and health lost and where interventions could provide the greatest benefits. In addition, the model could predict the costs and consequences of alternative interventions to address the different aspects of suboptimal use of medicines. This information could help inform decisions on which interventions should be prioritised for implementation in the NHS. Finally, the model could indicate the key areas of uncertainty with the greatest impact to costs and health which further research should investigate. The decision analytic model would need to focus on specific disease areas given that the risks and the consequences from suboptimal use of medicines differ depending on the disease and the medication concerned. For example, warfarin and lithium need close monitoring to avoid dangerous adverse effects, whereas most drugs do not require regular monitoring; elderly patients, patients with severe debilitating conditions and care home residents may find it more difficult to detect and act on a medication error than younger patients; poor adherence to medicines with strict dosing schedules, such as anti-retrovirals, has greater consequences than in medicines with longer half-lives or that are taken on a ‘when required’ basis. Therefore, the definition of our populations of interest would be taken in
collaboration with clinical advisors and commissioners in light of the costs and health loss that each disease represents for the NHS.

The decision analytic model has the advantage over further primary data collection alone for a number of reasons. It can synthesise all the relevant evidence from a variety of sources, including both observational and experimental data. The model can compare the full range of alternative interventions where further data collection is limited to a feasible number of comparators. The model can simulate the costs and consequences over a longer time horizon, such as the patients’ lifetime, which would be unfeasible in an RCT. Finally, the model can evaluate how the uncertainty in the available evidence translates into uncertainty in the decision, i.e. the probability that a given decision is correct and the costs and health loss associated with that uncertainty. For these reasons, a decision analytic model, although an ambitious and challenging undertaking, has the potential to address the key issues impeding medicines optimisation.
5. REFERENCES


2. Institute of Medicine, Best Care at Lower Cost: The Path to Continuously Learning Health Care in America. 2012, Institute of Medicine.


5. IMS Institute for Healthcare Informatics, Advancing the responsible use of medicines. Applying levers for change. 2012.


17. Care Quality Commission, Managing patients’ medicines after discharge from hospital. 2009.


47. Dean, A.J., J. Walters, and A. Hall *A systematic review of interventions to enhance medication adherence in children and adolescents with chronic illness (Structured abstract)*. Archives of Disease in Childhood, 2010. 717-723.


64. Al-Jumah, K.A. and N.A. Qureshi *Impact of pharmacist interventions on patients' adherence to antidepressants and patient-reported outcomes: a systematic review (Structured abstract).* Patient Preference and Adherence, 2012. 87-100.


78. Wal, M.H., T. Jaarsma, and D.J. Veldhuisen *Non-compliance in patients with heart failure: how can we manage it? (Structured abstract).* European Journal of Heart Failure, 2005. 5-17.


6. APPENDICES

6.1. APPENDIX 1  FULL SEARCH STRATEGIES

Cochrane Database of Systematic Reviews (The Cochrane Library –
http://www.thecochranelibrary.com/)
Issue 1 of 12 Jan 2013
Search on 22/02/2013
Retrieved 63 hits

Key:
MeSH descriptor = indexing term (MeSH heading)
* = truncation
“ “ = phrase search
:ti,ab = terms in either title or abstract fields
near/1 = terms within one word of each other (any order)
near/2 = terms within two words of each other (any order)
next = terms are next to each other

Search Strategy:
ID  Search
#1  MeSH descriptor: [Medication Reconciliation] this term only
#2  (Medication* near/3 (concordance or compliance or comply or adherence or adhere or
optimal or optimisation)):ti,ab
#3  (Medicine* near/3 (concordance or compliance or comply or adherence or adhere or
optimal or optimisation)):ti,ab
#4  (drug* near/3 (concordance or compliance or comply or adherence or adhere or optimal or
optimisation)):ti,ab
#5  (Prescription* near/3 (concordance or compliance or comply or adherence or adhere or
optimal or optimisation)):ti,ab
#6  (prescrib* near/3 (concordance or compliance or comply or adherence or adhere or optimal
or optimisation)):ti,ab
#7  MeSH descriptor: [Medication Errors] this term only
#8  MeSH descriptor: [Inappropriate Prescribing] this term only
#9  (Medication* near/3 (nonconcordance or noncompliance or nonadherence or non-
concordance or non-compliance or non-adherence or suboptimal or error* or mistake* or
mismanage* or misuse or over-use or overuse or inappropriate or irrational or waste or
wastage)):ti,ab
#10  (Medicine* near/3 (nonconcordance or noncompliance or nonadherence or non-
concordance or non-compliance or non-adherence or suboptimal or error* or mistake* or
mismanage* or misuse or over-use or overuse or inappropriate or irrational or waste or
wastage)):ti,ab
#11 (drug* near/3 (nonconcordance or noncompliance or nonadherence or non-concordance or non-compliance or non-adherence or suboptimal or error* or mistake* or mismanage* or over-use or overuse or inappropriate or waste or wastage)):ti,ab

#12 (Prescription* near/3 (nonconcordance or noncompliance or nonadherence or non-concordance or non-compliance or non-adherence or suboptimal or error* or mistake* or mismanage* or misuse or over-use or overuse or inappropriate or waste or wastage)):ti,ab

#13 (prescrib* near/3 (nonconcordance or noncompliance or nonadherence or non-concordance or non-compliance or non-adherence or suboptimal or error* or mistake* or mismanage* or misuse or over-use or overuse or inappropriate or waste or wastage)):ti,ab

#14 (underprescrib* or overprescrib* or misprescrib* or under-prescrib* or over-prescrib* or mis-prescrib*):ti,ab

#15 (or #1-#14) from 2000 to 2013, in Cochrane Reviews (Reviews and Protocols)

DARE – Database of Abstracts of Reviews of Effects, and NHS EED - NHS Economic Evaluation Database
(The Cochrane Library – http://www.thecochranelibrary.com/)
Issue 1 of 4 Jan 2013
Searched on 22/02/2013
Retrieved 393 hits

Key:
MeSH descriptor = indexing term (MeSH heading)
* = truncation
“ “ = phrase search
:ti,ab = terms in either title or abstract fields
near/1 = terms within one word of each other (any order)
near/2 = terms within two words of each other (any order)
next = terms are next to each other

Search Strategy:
#1 MeSH descriptor: [Medication Reconciliation] this term only
#2 (Medication* near/3 (concordance or compliance or comply or adherence or adhere or optimal or optimisation))
#3 (Medicine* near/3 (concordance or compliance or comply or adherence or adhere or optimal or optimisation))
#4 (drug* near/3 (concordance or compliance or comply or adherence or adhere or optimal or optimisation))
#5 (Prescription* near/3 (concordance or compliance or comply or adherence or adhere or optimal or optimisation))
#6 (prescrib* near/3 (concordance or compliance or comply or adherence or adhere or optimal or optimisation))
#7 MeSH descriptor: [Medication Errors] this term only
#8 MeSH descriptor: [Inappropriate Prescribing] this term only
#9 (Medication* near/3 (nonconcordance or noncompliance or nonadherence or non-concordance or non-compliance or non-adherence or suboptimal or error* or mistake* or mismanage* or misuse or over-use or overuse or inappropriate or irrational or waste or wastage))
#10  (Medicine* near/3 (nonconcordance or noncompliance or non-adherence or suboptimal or error* or mistake* or mismanage* or misuse or over-use or overuse or inappropriate or irrational or waste or wastage))
#11  (drug* near/3 (nonconcordance or noncompliance or non-adherence or suboptimal or error* or mistake* or mismanage* or over-use or overuse or inappropriate or waste or wastage))
#12  (Prescription* near/3 (nonconcordance or noncompliance or non-adherence or suboptimal or error* or mistake* or mismanage* or misuse or over-use or overuse or inappropriate or waste or wastage))
#13  (prescrib* near/3 (nonconcordance or noncompliance or non-adherence or suboptimal or error* or mistake* or mismanage* or misuse or over-use or overuse or inappropriate or waste or wastage))
#14  (underprescrib* or overprescrib* or misprescrib* or under-prescrib* or over-prescrib* or mis-prescrib*)
#15  (or #1–#14) from 2000 to 2013, in Other Reviews and Economic Evaluations

DARE – Database of Abstracts of Reviews of Effects, and NHS EED - NHS Economic Evaluation Database
(CRD website – http://www.crd.york.ac.uk/crdweb/)

Searched on 26/02/2013
Retrieved 187 hits

Key:
* = truncation
Each line was limited to “all fields”

Search strategy:
1  (Medication* OR Medicine OR drug* OR prescription OR prescrib*) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  1005
2  (concordance or compliance or comply or adherence or adhere or optimal or optimisation) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  93
3  (nonconcordance or noncompliance or non-adherence or non-concordance or non-compliance) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  2
4  (nonconcordance or noncompliance or non-adherence) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  1
5  (non-adherence) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  2
6  (suboptimal or error* or mistake* or mismanage*) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  213
7  (over-use) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  0
8  (overuse*) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  0
9  (overuse or inappropriate or irrational or waste or wastage) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  7
10  #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9  277
11  (underprescrib* or overprescrib* or misprescrib* or under-prescrib* or over-prescrib* or mis-prescrib*) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013  0
(underprescrib* or overprescrib* or misprescrib*) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013 0
(under-prescrib* or over-prescrib* or mis-prescrib*) IN DARE, NHSEED WHERE PD FROM 17/12/2012 TO 28/02/2013 0
MeSH DESCRIPTOR medication errors EXPLODE ALL TREES IN DARE,NHSEED 37
#1 AND #10 150
#14 OR #15 187