

# Concordance, adherence and compliance in medicine taking

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***Report for the National Co-ordinating  
Centre for NHS Service Delivery and  
Organisation R & D (NCCSDO)***

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## **Executive Summary**

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This report is a product of a scoping exercise commissioned by the NHS National Coordinating Centre for Service Delivery and Organisation (NCCSDO) with the following aims:

- 1 Summarise current knowledge about the determinants of medication-taking.
- 2 Construct a conceptual map of the area of compliance, adherence and concordance.
- 3 Identify priorities for future research of relevance to the NHS, with particular emphasis on identifying what new knowledge is needed to be able to develop effective, realisable, efficient and equitable interventions to promote the appropriate use of medicines for the benefit of patients and the NHS.

The scoping exercise involved analysis of the literature, a listening exercise involving consultation with both a user group and with a group of academics, health care professionals and managers, plus feedback from an Expert Panel.

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## **Main findings and take home messages**

Nonadherence to appropriately prescribed medicines is a global health problem of major relevance to the National Health Service (NHS).

Nonadherence prevents patients from gaining access to the best treatment, and this may be particularly problematic in chronic medical conditions, including current NHS priorities such as mental health, cancer, diabetes and respiratory illness. We agree that: 'Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments'.<sup>1</sup> The NHS should take action but requires quality research to guide and evaluate this.

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<sup>1</sup> Haynes, R., McDonald, H., Garg, A., & Montague, P. (2002). Interventions for helping patients to follow prescriptions for medications. *The Cochrane Database of Systematic Reviews*, 2, CD000011.

## ***Concordance, adherence and compliance in medicine taking***

The challenges for research in medication adherence are similar to those for other health-related behaviours, such as smoking cessation, exercise and diet: how to influence and change behaviour.

Our review offers clear insights into not only why previous interventions have failed, but also how we can improve the content, development and testing of new approaches.

We recommend that the NCCSDO commissions a coherent programme of research to inform the development of effective, patient-centred interventions to facilitate informed choice and optimal adherence to appropriate prescriptions where adherence matters most.

The time is right to address this agenda as there is a strong coherence with the concept of a patient-led NHS and related policy developments, such as the expert patient programme and medicines usage review.

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### **Why this scoping exercise is necessary**

The prescription of a medicine is one of the most common interventions in healthcare. In England there were 686 million NHS prescriptions dispensed in 2004, costing £8 billion. The optimal use of appropriately prescribed medicines is vital to the self-management of most chronic illnesses including those designated as NHS priorities.

Reviews conducted across disease states and countries are consistent in estimating that between 30 and 50 per cent of prescribed medication is not taken as recommended.

This represents a failure to translate the technological benefits of new medicines into health gain for individuals. There are potential losses for patients, the NHS and pharmaceutical industries.

Nonadherence is often a hidden problem: undisclosed by patients and unrecognised by prescribers.

There is no evidence that the problem of nonadherence has been solved by recent advances in the design and presentation of medicines or by the evolution of healthcare services that have tended to become more 'patient-centred.'

There is a pressing need to develop effective strategies to make the delivery of healthcare more efficient and responsive to patients' needs by addressing the problem of nonadherence.

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### **A conceptual map and research agenda**

The size and scope of the literature on medication-taking can make it difficult for practitioners to find their way around. The complexity of the topic is illustrated by the fact

## ***Concordance, adherence and compliance in medicine taking***

that there are at least three terms in common usage: compliance, adherence and concordance.

This document does not involve an exhaustive review of the primary literature – this has already been researched to good effect and is beyond the scope and timescale of the project. Rather it provides a conceptual map to guide policy-makers, clinicians and health services researchers through this complex field. The conceptual map has two elements:

An explanation of the concepts of compliance, adherence and concordance and recommendations for use of terminology.

A summary of current knowledge about the factors influencing medication-taking and how these might be influenced.

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### **Terminology – compliance, adherence and concordance**

Compliance is defined as: 'The extent to which the patient's behaviour matches the prescriber's recommendations.' However, its use is declining as it implies lack of patient involvement.

Adherence is defined as: 'The extent to which the patient's behaviour matches agreed recommendations from the prescriber.' It has been adopted by many as an alternative to compliance, in an attempt to emphasise that the patient is free to decide whether to adhere to the doctor's recommendations and that failure to do so should not be a reason to blame the patient. Adherence develops the definition of compliance by emphasising the need for agreement.

Concordance is a relatively recent term, predominantly used in the United Kingdom (UK). Its definition has changed over time from one which focused on the consultation process, in which doctor and patient agree therapeutic decisions that incorporate their respective views, to a wider concept which stretches from prescribing communication to patient support in medicine taking. Concordance is sometimes used, incorrectly, as a synonym for adherence.

It can be seen that these terms are related but different. Two issues underpin this. First, whether patients should take their medicines or not depends on whether the prescribing was appropriate – we do not want to promote patients taking inappropriate medicines. Hence all terms refer back in varying degrees to the act of prescribing. Second, all these terms involve varying normative agendas – understandings of what is good and right about prescribing and medicine taking; we explore these concepts in Chapter 5.

### ***Terminology recommendations***

We recognised that these three terms are now used interchangeably and that this has generated some confusion. After discussion within the Project team and with our Expert Panel and Consultation Groups, we recommend 'adherence' as the term of choice to describe patients' medicine taking behaviour.

We recognise that adherence is not always a 'good thing' as a prescription may be inappropriate or not reflect the patients' changing needs. We assume that adherence is appropriate and beneficial if it follows a process that allows patients to influence the decision making if they wish, and an appropriate choice of medicine is made by the prescriber.

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## **Determinants of medication-taking behaviour**

We grouped the literature on adherence into four core themes: explaining patient behaviour; patient-provider interactions; societal policy and practice; and interventions. These are underpinned by complex notions of the various, and sometimes conflicting, things we consider to be 'good' about prescribing and medicine taking. We pause to explore these issues in between the policy and intervention themes. Medicine-taking needs to be understood as a variable behaviour, which occurs within, and is influenced by, external, environmental factors including interactions with healthcare providers and by the wider context of societal-policies and practice. Theme four spans these domains as interventions to facilitate optimum medicine-taking can be targeted at one or more of these domains. Below we present a résumé of current knowledge and key outstanding research questions for each them. The research agenda as it relates to SDO research priorities is presented at the end of this Executive Summary.

### ***Theme 1: Explaining medication-taking behaviour***

The research evidence shows that variation in adherence cannot be explained by a range of fixed factors, such as the type or severity of disease; sociodemographic variables or personality traits. Adherence is positively correlated with income when the patient is paying for treatment but not with general socio-economic status. Furthermore, providing clear information, although essential, is not enough to guarantee adherence. Nonadherence is often lower for more complex regimens, but significant nonadherence remains when the frequency of dosing is reduced. Depression, but not anxiety, is related to nonadherence to medication prescribed for conditions other than depression.

## ***Concordance, adherence and compliance in medicine taking***

The main development in adherence-related research over the past decade has been an increasing recognition of the importance of patients 'common-sense' beliefs about their illness and treatment as determinants of adherence. This work shows that, although nonadherence may be puzzling or frustrating from the prescribers' perspective, viewed from the patient's perspective, it often represents a logical response to the illness and treatment in terms of their own perceptions, experiences and priorities, including concerns about side effects and other unwelcome effects of medicines. Patients therefore seek to balance perceived necessity and concerns and to minimise their use of prescribed medicines.

We endorse an approach to nonadherence that acknowledges patients' own beliefs and active decision-making but also recognises the constraints and practical barriers that reduce people's ability to take medicines as prescribed. Nonadherence is therefore best seen as variable behaviour with intentional and unintentional causes.

Unintentional nonadherence arises from capacity and resource limitations that prevent patients from implementing their decisions to follow treatment recommendations and involves individual constraints (eg, memory, dexterity, etc) and aspects of their environment (eg, problems of accessing prescriptions, cost of medicines, competing demands, etc). Intentional nonadherence arises from the beliefs, attitudes and expectations that influence patients' motivation to begin and persist with the treatment regimen.

Research to date gives a good indication of the factors influencing intentions and constraints but we know little about the extent of intentional versus unintentional nonadherence or their interrelationships. Internal factors such as motivation and capacity may be moderated by external factors, such as the quality of communication between the patient and healthcare provider, as discussed in Theme two (Chapter 3), and by the wider societal contexts, such as access to resources and societal policy and practice, as outlined in Theme three (Chapter 4).

Most research has been cross-sectional whereas adherence is a dynamic process that may change over time and needs to be followed-up. We now need longitudinal studies to investigate how patients' choices and adherence behaviours change over time and how they might be influenced by interventions. There is a particular need to examine intentional and unintentional influences in vulnerable groups, such as children, adolescents and the elderly, as well as vulnerable groups defined by social exclusion or other factors, such as ethnicity. We also need to include how patients judge their personal need for medication in different situations and stages of illness.

## ***Theme 2: Patient-provider interactions and communication in healthcare***

Our review of the empirical evidence identified surprisingly few studies that systematically evaluate the direct effects of the prescribing consultation on medication adherence behaviour. Further basic research is needed to clarify the effects of the consultation on medication adherence, the extent to which consultation skills training can improve adherence, and how different messages from different sources influence patients' medication-taking behaviour.

We know little about how physicians' beliefs influence the process and content of prescribing and this is a priority for further research. We also need to know more about how we can equip prescribers (and their patients) to deal with the cognitive and emotional challenges of working in partnership to achieve appropriate prescribing, and optimal adherence. This is a key challenge for NHS workforce development, especially as new prescribers (such as nurses and pharmacists) come 'on-line'. We need concomitant research on how prescribers can most efficiently support patient informed choice and optimal adherence both individually and as part of a multidisciplinary team.

## ***Theme 3: Societal policies and practice***

The impact of nonadherence at a societal level is probably substantial, but existing data in the UK are too poor to fully characterise this, possibly because, until recently, the management of adherence has not featured strongly in NHS policy. However, several core policy initiatives such as the Expert Patient programme, National Service Frameworks and Medicines Use Reviews (MURs) now place patient self-management and involvement in decisions at the forefront of healthcare delivery. These offer strong incentives and provide an excellent context for the development of interventions to help patients with long term illnesses to get the best from medicines. However, research is needed to inform their development and assess their impact on the medication needs and practices of patients and their carers.

Key policies that are predicted to affect medicines-taking behaviour are the prescription tax system, deregulation of prescription only medicines and expansion of prescribing rights. The accelerated rate of deregulation of medicines in the UK needs to be assessed: does use of medicines change and is this change in use appropriate or inappropriate? Does deregulation lead to financial barriers that reduce use in some groups? The recent introduction of supplementary and independent prescribing rights for non-medical prescribers has generally been welcomed by health professional groups. However, it is not clear whether patients will perceive this development as a welcome or confusing plurality of service provision, or whether or not it will improve medicines-taking behaviour.

### **Doing the right thing: the normative theme**

Underpinning this whole report are two questions – what is good prescribing and what is good medicine taking? These questions, in contrast to questions of effectiveness, have had little in depth exploration in the literature, yet they must be addressed to inform policies and practices. We found these questions to be relevant across each of our four themes and devoted a separate chapter of the report (Chapter 5) to explore this normative agenda (questions of what is right and good). These questions are complex. For example, in Chapter 5 we identify a dozen values around these areas which can be legitimately held, yet there is little exploration of how patients and prescribers should deal with situations in which the values conflict. There is a need for more work in this area to support patients and prescribers in their practice.

Questions about 'good' and 'right' are normative questions; they need to be addressed partly by philosophical argument and partly by empirical research. In particular, work is needed on joint decision making. What is the ideal nature of communication? What sort(s) of reasoning should be used so that the decision is truly 'joint'? Which forms of joint decision making are possible and what are their strengths and weaknesses? Linked to this is the important research question of the effect of different forms of accountability on patient and prescriber. Currently decision making may be joint but accountability is with the prescriber; this limits the potential for patients to influence a decision. Research is needed into the practical and psychological implications of increasing patient accountability in line with their responsibility for the prescribing decision.

### ***Theme 4: Interventions to facilitate adherence***

The literature on adherence interventions has been the subject of three major systematic reviews over the past five years, culminating in a Cochrane systematic review in 2002. As part of our scoping exercise we extended the scope of the Cochrane review by including studies that met the stringent quality criteria, but were not eligible for inclusion in the Cochrane review because they had measured adherence but not clinical outcome. We do not dispute the Cochrane reviewers' rationale that improving adherence is only valuable if it brings clinical benefits to the patient. However, we wanted to examine whether including studies that had measured adherence (but not clinical outcome) might provide valuable information about how to change



## ***Concordance, adherence and compliance in medicine taking***

adherence behaviours.<sup>2</sup> Our analysis of the findings of previous systematic reviews, including our extension of the Haynes review, can be summarised as:

- 1 Interventions to promote adherence are broadly efficacious. However, the effects were generally modest. We know that adherence can be increased, but there is considerable room for improvement.
- 2 Few interventions have been systematically developed, using appropriate theoretical models, nor have they been modelled and piloted with assessment of process variables as well as outcomes (as recommended in the MRC framework for complex interventions to effect behaviour change). Consequently, it is difficult to tell why some interventions work and others do not.
- 3 Comprehensive interventions that combined approaches were typically more effective than interventions focusing on single causes of nonadherence. However, few interventions could be described as 'patient-centred' as they did not individualise the approach to match patients' needs and preferences.

### ***Research priorities***

Because medicines carry the potential for harm as well as benefit we have identified a *normative* agenda to address questions of what is good-prescribing and good medicine-taking and an *empirical* research agenda to address how adherence might be improved. In an ideal world the normative agenda would come first and inform the empirical agenda, however, realistically both need to be pursued in parallel.

There is an imperative to move ahead with the empirical agenda in conditions where there is strong supporting evidence for the benefits of medication and importance of adherence. This is particularly relevant for the NHS SDO programme as the prescription of a medicine is one of the most common and, therefore, costly medical interventions. Optimising use of prescription medicines is a key priority for the delivery and organisation of healthcare.

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<sup>2</sup> There have been no large scale systematic reviews of the intervention literature since 2003. It is possible that more effective interventions may have emerged since then. However, neither the Project Team nor our Consultation Groups and Expert Panel were aware of a significant body of studies to contradict our analysis of the interventions literature, based on published systematic reviews.

## ***Concordance, adherence and compliance in medicine taking***

### ***The empirical research agenda***

The main research priority is the development of effective, efficient, realisable and equitable interventions to facilitate adherence to appropriate prescriptions<sup>3</sup> where adherence matters most. These can be defined as:

- 1 Conditions where there is strong evidence supporting the benefits of medication, above other treatment options and over doing nothing.
- 2 Treatments where there is strong evidence that high levels of adherence are essential to ensure efficacy or prevent problems such as the emergence of treatment-resistance.

Although more work is needed to develop a framework for adherence priorities, we can immediately identify examples that seem to fit the criteria. These might include: highly active anti-retroviral therapy for HIV, pharmacological treatment of diabetes, immunosuppressant medication following transplantation, preventer medication in asthma, medicines for severe mental illness, preventative medicine for cardiovascular disease, anti-tuberculosis treatment and anti-cancer agents.

In this scoping exercise we grouped the literature on adherence into core themes: explaining patient behaviour, patient-provider interactions and societal policy and practice, all of which are relevant to our forth theme, the development of interventions. Our review of the literature identified existing knowledge and outstanding research questions within each of the themes that can inform the development of innovative interventions to facilitate optimal adherence to appropriate medicines.

Our analysis of the literature on the causes of nonadherence and our assessment of the reasons for the limited success of interventions provide clear pointers to improving content, development and testing of interventions. The main lessons are:

**Content** Interventions should be tailored to meet the needs of patients taking account of the particular perceptual (eg, beliefs and preferences) and practical (eg, capacity and resources) factors influencing intentional and unintentional nonadherence for that individual.

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<sup>3</sup> How we define an 'appropriate' prescription may vary according to individual circumstances, and this needs to be addressed within a normative research agenda. However, the essence of appropriate prescribing is the application of the scientific evidence base to the unique needs and preferences of the individual, taking account of their desires and capacity for involvement in the decision.

## ***Concordance, adherence and compliance in medicine taking***

***Development and testing*** Interventions should be developed using an appropriate theoretical framework with a phased approach to testing that includes assessment of the process (ie, the things that are targeted for change), as well as outcomes. The MRC framework for complex interventions to effect behaviour change may be useful in this respect.<sup>4</sup>

The fundamental questions that need to be addressed in order to develop such interventions are:

- 1 What are the most effective methods for addressing the cognitive (eg, beliefs; attitudes), emotional and capacity (eg, memory limitations; changes in routines/habits, etc) factors, which result in reduced adherence to appropriate medication?
- 2 How can we enable prescribers and other members of the NHS workforce to support patients by facilitating informed choice and optimal adherence to appropriate prescriptions?
- 3 How can we incorporate an awareness of patient needs in relation to medicines and adherence support into the organisation and delivery of everyday healthcare to meet the requirements of NSFs, a patient-led NHS and the drive for greater efficiency in healthcare delivery?

This research agenda is highly relevant to the NHS SDO research priorities of patient choice, access and continuity of care, workforce, e-health, methodological research and governance.<sup>5</sup> We have mapped the key research questions relating to facilitating informed choice and optimal adherence to appropriate prescription onto the NHS SDO priorities in Chapter 7 and at the end of this Executive Summary.

### ***The normative research agenda***

Work is needed on what types of prescribing can be considered 'good,' and what should be considered good medicine taking. These questions need to be answered in ways that are deliverable by patients and prescribers, and underpin the successful implementation of policy in areas such as the Expert Patient and NSFs. The normative questions are linked to empirical questions in Chapter 5 to ensure that realistic, acceptable, achievable answers will result. While the SDO may wish to fund some of this work they may also wish to draw the attention of humanities and social science Research Councils or other funding agencies to the need for fine grained philosophical work in this area.

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<sup>4</sup>Campbell, M., Fitzpatrick, R., Haines, A., Kinmonth, A. L., Sandercock, P., Spiegelhalter, D., et al. (2000). Framework for design and evaluation of complex interventions to improve health. *BMJ*, 321 694-696.

<sup>5</sup> <http://www.sdo.lshtm.ac.uk/commissioninggroups.htm>

### ***Conclusions and Recommendation***

- 1 The evidence from this and previous reviews is that nonadherence to appropriately prescribed medicines is a global health problem of major relevance to the NHS.
- 2 Current levels of nonadherence imply a failure to address patients' needs and preferences and represent a fundamental inefficiency in the delivery and organisation of the NHS. Nonadherence prevents patients from gaining access to the best treatment, and this may be particularly problematic in chronic medical conditions, including current NHS priorities.
- 3 We agree with the authors of a recent Cochrane systematic review that: 'Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.'<sup>6</sup> The NHS should take action but we require quality research to guide and evaluate this and the development of novel patient-centred interventions to facilitate informed choice and optimal adherence to appropriate prescriptions which is the overarching priority.
- 4 The challenges for a research agenda in medication adherence are similar to those for other health-related behaviours such as smoking cessation, exercise and diet: how to influence and change behaviour.
- 5 Although previous interventions to facilitate adherence have met with only limited success, it would be a mistake to interpret this as an indication that intervention is likely to be futile. On the contrary, our review offers clear insights into, not only *why* previous interventions have failed, but also *how* we can improve the content, development and testing of new approaches. This includes work on the ideal types of patient-prescriber relationship and roles of the patient and prescriber during medicine taking.
- 6 This report sets out the key research questions that need to be addressed to enable us to do this and these map onto the NHS SDO research priorities.
- 7 We recommend that the NCCSDO commissions a coherent programme of research to inform the development of effective, patient-centred interventions to facilitate informed choice and optimal adherence to appropriate prescriptions where adherence matters most. This programme is essential to guide the delivery of recommendations for medicines use within NHS NSFs

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<sup>6</sup> Haynes, R, McDonald, H, Garg, A, and Montague, P. 2002. 'Interventions for helping patients to follow prescriptions for medications', *The Cochrane Database of Systematic Reviews*, 2, CD000011.

## ***Concordance, adherence and compliance in medicine taking***

and address a fundamental inefficiency in healthcare delivery. The potential benefits are likely to include: better care tailored to patient needs, higher rates of adherence to appropriate medication, fewer unwanted and unused prescriptions, more effective management of chronic illness, increased patient safety and satisfaction and fewer emergency admissions. The time is right to address this agenda as there is a strong coherence with the concept of a patient-led NHS and related policy developments, such as the expert patient programme and medicines usage review.

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## Mapping research questions onto the SDO research priorities

Key research questions mapped onto SDO research priority areas

### ***Patient choice***<sup>7</sup>

- 1 In what ways can and should patients' initial choices and preferences be modified?
- 2 In what ways and under what circumstances should patient choice form the basis for decision making in prescribing and medicine-taking?
- 3 What are most effective ways of representing evidence for the likely benefits and risks of medication?
- 4 How can we tailor medicines information to match the requirements of individual patients and their carers?
- 5 Where patients' decisions are based on misplaced beliefs or misconceptions about the illness and treatment, how and when should this be addressed?
- 6 How can we help people make 'informed choices' about adherence to prescribed medication?
- 7 How should we communicate and deal with uncertainty within prescribing-relating consultations?
- 8 How can professional and lay accountability be best aligned to support patient choice?
- 9 How do patient preferences for involvement in medication-related decisions vary and how should prescribers responds to this?
- 10 How do patients' perceptions, preferences, choices and medication-taking behaviour change over time in

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<sup>7</sup> CARERS – Many of the questions that are relevant to patient choice and support will also apply to patients' carers and there is scope for synergy and continuity with the SDO Programme on carers.

## ***Concordance, adherence and compliance in medicine taking***

conditions where adherence to medication matters most?

### ***Access and continuity of care***

- 11 How can we help patients to overcome the capacity and resource limitations preventing access to effective healthcare?
- 12 How can we address and identify misconceptions about illness and treatment that prevent access to appropriate medication

### ***Workforce***

- 13 How can we equip prescribers (and their patients) to deal with the cognitive and emotional challenges of working in partnership to achieve informed choice and optimal adherence to appropriately prescribed medicines, where adherence matters most?
- 14 How can adherence review and adherence support be incorporated into medication-usage review in a way that promotes informed choice and supports adherence to agreed, appropriate prescriptions?
- 15 What are patients' perceptions and behavioural reactions to new prescribers (eg, nurses and pharmacists)?
- 16 What are the barriers to effective and efficient multi disciplinary approaches to appropriate prescribing and adherence support? How can these be overcome?
- 17 How can we enable new and existing prescribers to identify patients who are priority for medication-review and adherence support?
- 18 How can we support prescribers to meet the challenges of quality frameworks relating to medication-usage as a component of self-management?
- 19 In what ways is it possible to supplement the activities of the NHS workforce in facilitating optimal medication usage through other, complimentary approaches (eg, the use of 'expert patients', family support, etc).

### ***e-Health***

- 20 How can technological developments (eg, computers, mobile telephones, etc) be utilised to provide ongoing support for informed choice and adherence to agreed prescriptions?
- 21 How can we develop and apply effective 'technologies' to facilitate behaviour-change to achieve optimal adherence to appropriate and agreed prescriptions? Here technologies may be 'talk treatments,' such as cognitive behaviour approaches.

### ***Methodologies***

- 22 How can we facilitate the honest disclosure of medication-taking behaviours within prescribing-related consultations and medication use reviews? How can we equip health practitioners to respond appropriately and effectively?
- 23 What are the alternatives to full-scale Randomised Controlled Trials (RCTs) that can be used to conduct preliminary evaluations of the components of interventions to support informed choice and adherence? (corresponding to MRC Phases 1 and 2)
- 24 How can existing validated methods for assessing adherence-related perceptions and adherence behaviours be adapted for routine use in the NHS?
- 25 How can we enable new and existing prescribers to identify patients at risk of nonadherence or who are a priority for medication-review and adherence support and how can we provide it – new methods, new practitioners (eg. health trainers)?
- 26 How should we operationalise ‘informed choice’ in relation to medications taking?

### ***Governance***

- 27 How do differences in the arrangements existing in England, Wales and Scotland, such as the role of prescription charges, affect prescription filling for essential and non-essential medicines, subsequent patient health, present and future health service and societal cost?

### ***Adherence in vulnerable groups***

Consideration of vulnerable groups cuts across the explanatory themes and is relevant for most research questions, regardless of whether research is targeted at explaining individual behaviour, investigating communication in healthcare, societal policy and practice or evaluating interventions. Work in this area requires systematic reviews of the available literature followed by empirical studies.

Specific questions are:

- 1 What are the effects of social disadvantage and ethnicity on accessing prescriptions and adherence to prescribed medication?
- 2 How do the perceptions and life circumstances of different age groups (children, young adults, elderly people) influence adherence and what are the implications for interventions?
- 3 What are the particular barriers to medicines use for people with multiple pathologies (and their informal carers) and what interventions are required?

**Disclaimer**

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**Addendum**

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The management of the Service Delivery and Organisation (SDO) programme has now transferred to the National Institute for Health Research Evaluations, Trials and Studies Coordinating Centre (NETSCC) based at the University of Southampton. Prior to April 2009, NETSCC had no involvement in the commissioning or production of this document and therefore we may not be able to comment on the background or technical detail of this document. Should you have any queries please contact [sdo@southampton.ac.uk](mailto:sdo@southampton.ac.uk)