Invitation to Tender

Policy Research Programme: Evaluation of the New Medicines Service

1. The New Medicines Service (NMS) is being developed to improve the adherence to newly prescribed medicines by people with long-term conditions. The service will be implemented during 2011/12, with a target implementation date of 1st October. At present, the NMS is time-limited until March 2013. It may continue beyond this time if all parties agree that the service has provided demonstrable value to the NHS. The Department of Health is now inviting tenders for a research project to evaluate the benefits and costs of the NMS and to produce learning to inform decisions about continuation of the service and changes to implementation.

POLICY BACKGROUND

2. In England, around 15 million people have a long-term condition (LTC), most of which are treated with prescribed medicines. In 2009-10 there were 813.3 million NHS prescriptions dispensed by community pharmacies in England. International evidence suggests that between 30% and 50% of prescribed medicines are not taken as recommended (Clifford et al 2006) and that around 5% of all hospital admissions are due to the adverse effects of medicines, many a which are avoidable (Pirmohamed et al 2004), resulting in a reduction in the potential health benefits of prescribed medications and significant costs to the health service.

3. The New Medicines Service (NMS) is being developed to improve the adherence to newly prescribed medicines by people with long-term conditions. Initially the NMS will focus on particular patient groups and conditions (see below), and consists of a structured programme of patient-centred engagement, advice-giving and support. This will be supported by a maximum investment of £55 million per annum in both 2011/12 and 2012/13.

4. The Department of Health, NHS Employers and the Pharmaceutical Services Negotiating Committee (PSNC) are currently finalising the details of the changes to the contract[1] (including the implementation of the NMS), and are working collaboratively with NHS, community pharmacy and other stakeholders to develop a comprehensive implementation programme. Pharmacies can choose whether to provide the service, but will need to fulfil certain criteria that are also being

[1] Contract is used to describe the community pharmacy contractual framework, which is laid down in secondary legislation (Regulations and Directions).

finalised. The NMS payment mechanism will include target payments based on the level of activity that pharmacies undertake, together with a one-off implementation payment (payable between 1 October 2011 and 31 March 2012).

5. The New Medicines Service will be the fourth Advanced Service to be introduced into the NHS community pharmacy contract[2]. The service will be implemented during 2011/12, with a target implementation date of 1st October. The NMS is time-limited until March 2013, and it may continue beyond this time if all parties agree that the service has provided demonstrable value to the NHS.

THE NEW MEDICINES SERVICE

6. The NMS will be provided to individual patients and will consist of three stages, which are described in outline below:

- Patient engagement
- Intervention
- Follow up

PATIENT ENGAGEMENT

7. Following the prescribing of a new medicine for the management of a LTC, patients will be recruited to the service by prescriber referral, or opportunistically by the community pharmacy. The patient may not have visited the pharmacy on a previous occasion. The service does not cover patients whose prescription is a change of dose or formulation of a currently prescribed medicine.

The conditions/therapies included in the initial roll out of service are:

- Asthma and COPD
- Diabetes (Type 2)
- Antiplatelet / Anticoagulant therapy
- Hypertension

However, patients will be identified as eligible for receiving the service if they have been prescribed one or more medicines (as specified in a nationally defined list) that are prescribed for these conditions.

The new medicine will be dispensed in accordance with the Terms of Service of Pharmacists.

Initial advice will be given to the patient about the medicine and its use in

[2] Advanced services are those services pharmacies choose to provide if they meet certain requirements as set out nationally. Details of the other Advanced Services can be found at: http://www.psnc.org.uk/pages/advanced_services.htm.

accordance with the Terms of Service. At this stage the pharmacist may also offer the patient opportunistic advice on healthy living/public health topics in line with the promotion of healthy lifestyles essential service. The intervention and follow up stages of the service will also be opportunities to offer the patient healthy lifestyle advice.

The pharmacy and patient will agree a method and time for the intervention (typically between seven and 14 days after patient engagement).

The patient will be given information on the service - for example, in the form of a leaflet - which will include an explanation that information may be shared with their GP as necessary and with the PCT or successor organisation as part of clinical audit, and with the PCT or successor organisation and the NHS Business Services Authority as part of post payment verification.

INTERVENTION

8. The pharmacist and patient will have a discussion at the agreed time and via the agreed method. It is expected that this will normally be a face to face conversation, but alternatively it could take place as a telephone conversation if the patient prefers this. If the discussion does not happen at the agreed time, the pharmacist will make at least one attempt to follow up the patient.

At the start of the discussion, the pharmacist will confirm that the patient understands the information they were given during patient engagement and that they consent to information being shared with their GP as necessary, and with the PCT or successor organisation as part of clinical audit, and with the PCT or successor organisation and the NHS Business Services Authority as part of post payment verification. If the patient does not consent to share information then the intervention is not provided.

Face-to-face discussions with patients will take place in a consultation area. In order to deliver the service a pharmacy must have a consultation area which is at least at the level required for the provision of the Medicines Use Review (MUR) service. Telephone discussions with patients should be conducted on the pharmacy premises and take place in circumstances where the telephone conversation cannot be overheard.

The pharmacist may use a common semi-structured interview to assess adherence, identify problems and the patient's need for further information and support.

The pharmacist will provide advice and further support and will agree one of the following next steps with the patient:

a. Patient adhering to regimen – agree method and time of follow up (typically between 14 and 21 days after the initial intervention)

b. Problem identified – pharmacist and patient agree solution and agree method and time of future contact (typically between 14 and 21 days after the initial intervention). For the current cohort of patients, solutions could include items such as reminder charts but these solutions should not create an extra cost pressure on the NHS

c. Problem identified – exit from service with explanation to the patient of any potential clinical risk and referral to the GP. At this point the service will have been completed

At this stage the pharmacist may also offer the patient opportunistic advice on healthy living / public health topics in line with the promotion of healthy lifestyles essential service.

FOLLOW UP

9. The pharmacist and patient will have a discussion at the agreed time and via the agreed method (again it is expected that this will normally be a face to face conversation but alternatively it could take place as a telephone conversation). If the discussion does not happen at the agreed time, the pharmacist will make at least one additional attempt to follow up with the patient (i.e. the pharmacist will try to arrange another face-to-face meeting with the patient or will try to have another telephone conversation with the patient). If the pharmacist is unable to contact the patient then the service will have been completed.

The pharmacist will provide advice and further support and agrees one of the following next steps with the patient:

a. Patient adhering to regimen – exit from service. At this point the service will have been completed

b. Problem identified – referral to the prescriber for review. At this point the service will have been completed

At this stage the pharmacist may also offer the patient opportunistic advice on healthy living / public health topics in line with the promotion of healthy lifestyles essential service.

The patient will not normally be eligible for a MUR within six months of completing the service, unless in the reasonable opinion of the pharmacist the patient would benefit from an MUR during that period. For example a patient with multiple long-term conditions may be prescribed a new medicine for one condition and be supported in using this medicine by the NMS, but may benefit from the wider advice and support provided

in an MUR in relation to medicines they use for another condition. Patients on high risk drugs, or patients who experience a "trigger event" which would highlight the need for an MUR, may also benefit.

AIMS OF THE RESEARCH

10. The aim of the research is to determine the effects of the New Medicines Service (for patients newly prescribed a medicine for certain LTCs) on:

    - Patients' adherence to their newly prescribed medications and pharmaceutical regimes;
    - Patients' understanding of their medicines and the extent to which they are informed and supported in their medicines-related behaviour and engaged in shared-decision-making;
    - Patients' health status and health outcomes;
    - Patient (and/or carer) and professional experience;
    - Inter-professional relationships;
    - The cost-effectiveness and cost-utility of community pharmaceutical services for the four conditions currently included

ANTICIPATED OUTCOMES OF THE NMS

11. The principal outcomes for determining the effectiveness of the NMS are:

    - Patients' adherence to their prescribed medications and pharmaceutical regimes;
    - The resource use and the cost-effectiveness/cost-utility of the management of people with LTCs.

12. The Department of Health is also interested in a range of other outputs and outcomes, some of which (to be subsequently confirmed) will be collected by pharmacy contractors as a requirement of service provision, including:

    - Patients' health status and health outcomes;
    - Patient and professional experience;
    - Reduced medicines wastage;
    - Rate of hospital admissions (and service utilisation more generally) due to adverse events from medicines;
    - Yellow Card reporting of adverse reactions to medicines by pharmacists and patients, thereby supporting improved pharmacovigilance;
    - Total number of patients that have exited the service;
    - Number of adherent patients that exit the service;
    - Number of non-adherent patients that are referred to the prescriber;
    - Number of patients that exit the service following the prescriber stopping the treatment;
    - Details of interventions / solutions to problems agreed with the

patient at the intervention stage (using a standardised set of descriptions of solutions);
- Number of people lost at the patient engagement, intervention and follow up stages;
- Number of patients offered opportunistic advice on healthy living / public health topics at the patient engagement, intervention or follow up stages.

13. To the extent that it is possible without compromising key aims and without excessive resource implications, the research should identify any particular differential impacts relating to gender, age, ethnicity, sexual orientation, disability and socio-economic inequalities.

14. It is anticipated that research proposals will lay out a framework for prioritising and addressing the range of outcomes identified above. The Department is also interested in whether the evaluation can generate insights relevant to developing better routine outcome measures of community pharmacists' services.

RESEARCH DESIGN ISSUES

(i) Impact evaluation

15. A counterfactual design is required to determine the relative impact of the NMS. Given the way in which the NMS will be implemented across England (based on voluntary self-selection by pharmacies) a straightforward randomised controlled trial may not be possible and other quasi-experimental or comparative designs may be more practicable. Applicants, however, should feel free to propose how a randomised controlled trial might be undertaken.

16. Applicants should indicate what methods they would use to establish a counterfactual (with or without an RCT), and offer a detailed evaluation design. Applicants are advised that the NMS will not be rolled out in Wales, which might provide opportunities for establishing a comparison or control group in that jurisdiction.

17. The Department of Health requires that the impact of the NMS needs to be established for *each* of the four conditions (asthma and COPD; diabetes (Type 2); antiplatelet/anticoagulant therapy; hypertension) separately. Consequently, applicants should give careful consideration to, and details of, how they would select samples of appropriate size to ensure sufficient statistical power.

18. Applicants should be aware of a previous randomised controlled trial of patient-centred advice for improving adherence to medicines (Clifford et al 2006) and cost effectiveness assessment (Elliott et al 2008). Whilst this provided some positive 'proof of concept' for "a new, patient-centred way for pharmacists to support patients who are newly started on a

medicine for a chronic condition" (Clifford et al, 2006:170), the authors acknowledged the need for a substantially larger trial to confirm that the effect is real and sustained. The same authors also reported a higher than expected drop-out rate in their samples (particularly in the intervention group), largely attributable to patients having their prescriptions changed by general practitioners. Clifford et al advised that "more thought needs to be given about how these cases should be handled in future studies" (*op cit*: 169). Applicants are therefore advised to offer their proposals for handling sample attrition.

19. Applicants are also advised to take note of the methodological issues raised in a Cochrane systematic review of '*Interventions for Enhancing Medication Adherence'* (Haynes, et al 2008)[3].

(ii) Process evaluation

20. This evaluation also seeks evidence on the effects of the NMS on patients' understanding of their medicines, and the extent to which they are informed and supported in their medicines-related behaviour. Furthermore, the Outline Service Specification[4] indicates an interest in how and under what conditions a successful service can be achieved. This should include whether and why (i) some clinical areas are more successful than others and implications affecting potential roll-out to other clinical areas, and (ii) the relative effectiveness of different approaches adopted by pharmacists and pharmacies in implementing the NMS.

21. Consequently, the evaluation must include a quantitative and qualitative analysis of patients', pharmacists' and general practitioners' experiences (including integrated working between health care professions) and perceptions of the NMS's processes and procedures. Applicants must therefore provide detailed proposals on how they would undertake an evaluation of these processes, procedures, perceptions and experiences. The process evaluation design should attempt to identify effective (and less effective) implementation mechanisms, as well as ways of improving the NMS.

22. The financial arrangements underpinning the NMS involve assumptions regarding the proportion of patients presenting with a first prescription and eligible for the service. Evidence on this aspect and also implications of distribution of first prescriptions across pharmacies and how the payment mechanism influences service delivery will be valuable.
Additional questions/issues that are of interest include:

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[3] Available at: http://www2.cochrane.org/reviews/en/ab000011.html

[4] Available at: http://www.psnc.org.uk/data/files/PharmacyContract/Contract_changes_2011/outline_nms_service_spec.pdf

- Have GP's embraced the service?
- Has the NMS been integrated into care pathways?
- How the NMS influences hospital and community pharmacy relationships.
- What is the inter-relationship between the NMS and MURs?
- What are the qualitative aspects of the pharmacist-patient interaction and impact of consultations?

23. Whilst not of primary importance, this research may usefully provide insights into how routine outcome/quality/performance measures might be generated for such services delivered in community pharmacy settings and potentially performance measures for the generality of pharmaceutical services.

(iii) Economic appraisal

24. Establishing the cost-effectiveness, cost-utility and effective use of health care resources is a key aim of the NMS evaluation. Applicants must therefore provide detailed proposals for how they would undertake such an economic appraisal of the NMS. Their proposals should also indicate how modelling techniques might be used to extrapolate from the data and information gathered on the four LTCs under consideration to other long term conditions.

(iv) Data availability and requirements

25. The Outline Service Specification indicates that pharmacy records for the NMS will be defined nationally and will include:

- Method of entry to service (i.e. referral or pharmacy recruitment)
- Patient demographic details
- Registered GP practice
- Details of new medicine(s)
- Method of intervention and follow up (e.g. face-to-face in pharmacy or via telephone)
- Outcome of intervention, follow up and reasons for referrals

26. These data should be available to the evaluation team, although there is likely to be a time lag and details of information provision are still being finalised. Applicants should indicate what additional quantitative and qualitative data they will use from existing health services data, and what they will need to collect using survey methods, qualitative data collection methods, and economic data. This should include detailed proposals of samples and sample sizes, methods of gathering qualitative data, and the use of existing standardised generic health related quality of life measures (such as EQ-5D, SF36, HU13).

EVALUATION TEAM REQUIREMENTS

27. The evaluation team must be able to demonstrate a good track record in undertaking impact, process and economic evaluations (in particular how to elicit appropriate health outcomes in this setting, and information on service utilisation). Applicants should also demonstrate a previous track record in designing, undertaking, and reporting evaluations of this nature within the time frame of this specification.

28. Given the range of disciplinary knowledge and expertise required by this evaluation, applicants may seek to form a consortium, or other collaborative arrangements, for undertaking this evaluation. Clear leadership arrangements for the work should be evident.

GOVERNANCE ISSUES

29. Day-to-day management of this research will be provided by the principal investigator. They and their employers should ensure that they identify, and are able to discharge effectively, their respective responsibilities under the Department of Health (DH) Research Governance Framework for Health and Social Care[i], which sets out the broad principles of good research governance.

30. All successful research involving National Health Service (NHS) and social care users, carers, staff, data and/or premises must be approved by the appropriate research ethics committee (REC) or social care research ethics committee (SCREC). For further information on RECs, please visit the National Research Ethics Service website: www.nres.npsa.nhs.uk

31. The successful research team must adhere to the Data Protection Act (1998) and the Freedom of Information Act (2000). Effective security management, and ensuring personal information and assessment data are kept secure, will be essential. In particular:

    - The research team shall, at all times, be responsible for ensuring that data (including data in any electronic format) are stored securely. The research team shall take appropriate measures to ensure the security of such data, and guard against unauthorised access thereto, disclosure thereof, or loss or destruction while in its custody.

    - Personal data shall not be made available to anyone other than those employed directly on the project by the research team, to the extent that they need access to such information for the performance of their duties.

32. For any research involving clinical trials, the successful team will be expected to be familiar with the Medical Research Council (MRC) Framework for Evaluating Complex Interventions[ii], and to follow the

principles of the MRC Guidelines for Good Clinical Practice in Clinical Trials[iii] in proposing structures for oversight of such trials.

RISK MANAGEMENT

33. Applicants should submit, as part of their proposal, a summary explaining what they believe will be the key risks to delivering their research, and what contingencies they will put in place to deal with them. Please ensure this is detailed in the Management and Governance section of the online application form.

34. A risk is defined as any factor which may delay, disrupt or prevent the full achievement of a project objective. All risks should be identified. The summary should include an assessment of each risk, together with a rating of the risks likelihood and its impact on a project objective (using a high, medium or low classification for both). The risk assessment should also identify appropriate actions that would reduce or eliminate each risk, or its impact.

35. Typical areas of risk for an evaluation study might include ethical approval, site variation in data gathering, staffing, resource constraints, technical constraints, data access and quality, timing, management and operational issues; however, please note this is not an exhaustive list.

PATIENT AND PUBLIC INVOLVEMENT (PPI)

36. The Policy Research Programme (PRP) expects the active involvement of patients and the public (e.g. service users and carers) in the research that it supports. However, the nature and extent of Patient and Public Involvement (PPI) is likely to vary depending on the context of the study. Applicants should describe how the issue of PPI will be addressed throughout the research process. For example, this could include Patient and Public Involvement in refining research questions, designing research instruments, advising on approaches to recruitment, assisting in the collection and analysis of data, participation or chairing advisory and steering groups, and in the dissemination of research findings.

37. Applicants are required to detail what active involvement is planned, how it will benefit the research and the rationale for their approach. PPI needs to be undertaken in a manner that acknowledges that some people may need additional support, or to acquire new knowledge or skills to enable them to become involved effectively (see INVOLVE publications for guides for researchers) http://www.invo.org.uk/. Applicants should therefore provide information on arrangements for training and support. In addition, applicants should note that a budget line for the costs of PPI is included in the finance form.

38. Where no PPI is proposed, a rationale for this decision must be given.

39. For further information and guidance about PPI, please visit the INVOLVE website: http://www.invo.org.uk/

OUTPUTS AND REPORTING ARRANGEMENTS

40. The research team will be expected to provide regular progress reports over the lifetime of the research and will be provided with an Interim Report template to complete at regular intervals. In addition to describing progress, these reports will allow researchers to indicate any significant changes to the agreed protocol, as well as setting down milestones for the next reporting period, giving an update on PPI and also any publications or other outputs. Information on emergent findings that can feed more immediately into policy development will be encouraged and should be made available as appropriate.

41. A final report on the research, with an accessible executive summary, will be required within one month following completion of the research. The report will be peer reviewed and circulated to policy makers in the Department of Health. Once your study is complete, a summary of your final report will be placed in the public domain, on the DH PRP Central Commissioning Facility website. This is where the outputs resulting from expenditure of public funds are made available for public scrutiny so it is important that the summary of your final report is easily accessible to the lay reader.

42. Research contractors are obliged to give at least 28 days notice before submission of any publication arising from research funded by the Department of Health Policy Research Programme. In this instance, 'publication' concerns any presentation, paper, press release, report or other output for public dissemination arising from a research project funded by the PRP. There is no time limit to this provision and research contractors remain under an obligation to provide notice even after the contract has ended. Publication of PRP-commissioned research is subject to prior consent of the Secretary of State, which will not be withheld unreasonably and cannot be withheld for more than three months from the time the publication is submitted.

DISSEMINATION

43. Applicants should describe how the research findings could be disseminated most effectively, ensuring that results of this research impact on policy and practice in the NHS, DH and in social care.

44. Publication of scientifically robust research results is encouraged. This could include plans to submit papers to peer reviewed journals, national and regional conferences aimed at service providers, professional bodies and professional leaders. It might also include distribution of executive summaries and newsletters. Less traditional dissemination routes are also welcomed for consideration.

BUDGET AND TIMESCALE

45. The Department of Health is seeking to commission new research on the implementation and impact, including an economic appraisal, of the NMS with a view to the successful team - whether in a single institution or consortium - being in place before the end of 2011. The final report is required in June 2013. However, the contractor must plan the research so that robust evidence will be available to report in September 2012 to help determine whether continuing the service beyond 2012/13 can be justified. Further interim reports may be required between September 2012 and June 2013.

46. Costings can include **up to 100% full economic costing** (FEC) but should **exclude output VAT**. Applicants are advised that value for money is one of the key criteria that peer reviewers and commissioning panel members will assess applications against.

47. The DH expects that the research outlined in this call will be delivered within a cost of **£450,000**.

48. A selection decision for this call is expected to be given by late **October 2011**. All applications are expected to start within 6 months of funding being agreed.

TRANSPARENCY

49. In line with the government's transparency agenda, any contract resulting from this tender may be published in its entirety to the general public. Further information on the transparency agenda is at:

    http://transparency.number10.gov.uk/

50. If you wish to view the standard terms and conditions of the Policy Research Programme contract, please go to:

    http://www.dh.gov.uk/en/Aboutus/Researchanddevelopment/Policyresearchprogramme/DH_4002138

APPLICATION PROCESS

51. To access the research specification and application form, please visit the Policy Research Programme Central Commissioning Facility (PRP CCF) website at www.dh.gov.uk/prp-ccf and follow the instructions under "Current PRP calls for research proposals".

52. The Central Commissioning Facility runs an online application process and all applications must be submitted electronically. No applications will be accepted that are submitted by any means other than the online process. **Deadlines for the submission of research applications occur at 5pm on the day indicated and no applications can be**

accepted after this deadline. We strongly recommend that you submit your application the day before.

53. Once the 5.00pm deadline passes, the system shuts down automatically and CCF Programme Managers are unable to re-open it. If you are experiencing any technical difficulties submitting your application, please contact the CCF on 020 8843 8027 in good time, before 5.00pm on a closing date.

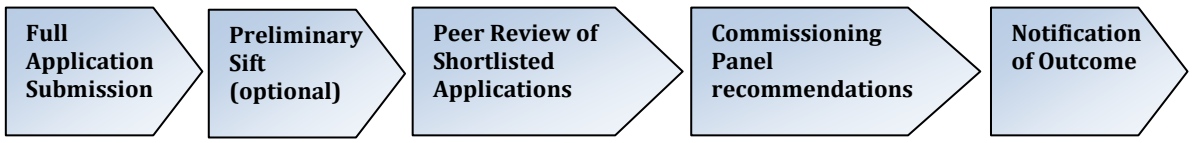
54. This is a single-stage tender and a **full application** is required to be submitted online by **5.00pm on 05/09/2011**.

55. Applicants are expected, before submitting applications, to have discussed their applications with their own and any other body whose co-operation will be required in conducting the research. The **declarations and signatures form** must be printed off and signed by an administrative or finance officer for the host (contracting) institution to confirm that the financial details of the application are correct and that the host institution will agree to administer the award if made. This is the only part of the form required in hard copy.

The hard copy of the declaration and signatures page should be submitted within one week of the closing date to:

New Medicines Service
PRP CCF
Grange House
15 Church Street
Twickenham, TW1 3NL

The PRP application process for this call:



56. Applications may be short-listed by a Sifting Panel (a sub-group of the Commissioning Panel). Incomplete applications and those too remote from the issues set out in the research specification or those that have clearly inadequate presentation or methods may be rejected at this stage.

57. Applications that are successfully short-listed by the Sifting Panel will be peer-reviewed by both stakeholder and independent academic referees. Wherever time permits, applicants will be given one week to respond to the peer reviewers' comments.

58. The short-listed applications, peer reviewers' comments and any responses to those comments will then be considered by the Commissioning Panel, which is comprised of independent experts (possibly with observers from other government departments and executive agencies) who will advise the DH on which applications are most suited to receive funding. The Panel will be informed by the reviewers' comments and any responses made to these comments by the researchers. However, it is ultimately the responsibility of the Panel to make any funding recommendations to the Department of Health.

SELECTION CRITERIA

Criteria used by peer reviewers and members of the commissioning group to assess applications for funding from the PRP include:

- **RELEVANCE** of the proposed research to the research specification
- **QUALITY** of the research design
- **QUALITY** of the work plan and proposed management arrangements
- **STRENGTH** of the research team
- **IMPACT** of the proposed work
- **VALUE** for money (justification of the proposed costs)
- **INVOLVEMENT** of patients and the public

TIMETABLE

It is anticipated that commissioning of this research will occur to the following approximate timetable:

- Issue of invitation to tender: 12/07/2011
- Deadline for receipt of full applications: 05/09/2011
- Peer review to be completed: 30/09/2011
- Notification of outcome: 14/11/2011
- Award of contract: 12/12/2011

In order to maximise the benefit from the findings, the research will need to commence as soon as possible following selection of the successful bid and placing of a contract. Capability to start promptly will be an advantage and should definitely be within 6 months of award of a contract.

CONTACTS

General enquiries regarding the application and commissioning process can be directed to the following PRP CCF Programme Manager:

Dr Gil Shalom
Phone: 020 8843 8030
E-mail: gil.shalom@prp-ccf.org.uk

REFERENCES AND KEY DOCUMENTS

Sarah Clifford et al, 2006. Patient-centered advice is effective in improving adherence to medicines
Pharm World and Science, **28**, 165-170.

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Pirmohamed et al, 2004. Adverse drug reactions as cause of admission to hospital: Prospective analysis of 18 820 patients BMJ July 3: 329 (7456): 15-19

[i] Department of Health. Research governance framework for health and social care [Online]. 2nd Ed. London: HMSO; 2005 [cited 2008 March 26]; Available from URL: www.dh.gov.uk/en/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962

[ii] Medical Research Council. A framework for development and evaluation of RCTs for complex interventions to improve health [Online]. 2000 [cited 2008 March 26]; Available from URL: http://www.mrc.ac.uk/

[iii] Medical Research Council. Guidelines for good clinical practice in clinical trials[Online]. 1998 [cited 2008 March 26]; Available from URL: http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002416