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J Raftery, J Bryant, J Powell, C Kerr and S Hawker

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Payment to healthcare professionals for patient recruitment to trials: systematic review and qualitative study

J Raftery,[1*] J Bryant,[1] J Powell,[2] C Kerr[1] and S Hawker[1]

[1] Wessex Institute for Health Research and Development (WIHRD), University of Southampton, UK

[2] Health Sciences Research Institute, University of Warwick, Coventry, UK

* Corresponding author

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The research reported in this issue of the journal was commissioned by the HTA Programme as project number 03/66/01. The contractual start date was in July 2005. The draft report began editorial review in January 2007 and was accepted for publication in October 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

Payment to healthcare professionals for patient recruitment to trials: systematic review and qualitative study

J Raftery,[1*] J Bryant,[1] J Powell,[2] C Kerr[1] and S Hawker[1]

[1] Wessex Institute for Health Research and Development (WIHRD), University of Southampton, UK

[2] Health Sciences Research Institute, University of Warwick, Coventry, UK

* Corresponding author

Objectives: To review UK guidelines regarding the use of financial incentives for healthcare professionals to become involved in clinical trials, and to survey perceptions and current practice.

Data sources: Electronic databases were searched from inception to June 2006. Interviews were held with NHS healthcare professionals, research managers from the pharmaceutical industry and members of the public.

Review methods: From the searches, 634 identified studies were assessed for inclusion in the systematic review, but only three met the criteria for data extraction. Fifty-eight individuals were interviewed: 38 chief investigators, six non-research active clinicians, eight public and six pharmaceutical managers. Investigators were selected from those funded by the HTA Programme, the other by 'snowballing' and personal contact.

Results: The evidence from the literature was limited and inconclusive. In UK guidelines, the issues around payments to clinicians or patients were implied rather than stated, usually linked to discussion of conflict of interest and disclosure of any such conflicts. Developments in NHS research governance had led to increased transparency in all payments for research participation and for payments to be made to NHS Trusts rather than individual clinicians. While reimbursement of costs incurred by research was strongly supported by the interviewees, payments to incentivise recruitment were not. A code of practice was suggested for payments in publicly funded trials, which was closely linked to the principles of Good Clinical Practice in research. Factors such as interest in the topic, scope for patient benefit and good communication were considered more important than payment. Interviews with the general public indicated low levels of awareness of the existence of payments to clinicians linked to patient recruitment in trials, and unanimous support for full disclosure. Interviews with managers in the pharmaceutical industry showed greater familiarity with payments for research involvement. GPs were seen as the only group for whom scope existed for individual payments. Concerns were expressed by the pharmaceutical company interviewees at the rising cost of research and unnecessary bureaucracy.

Conclusions: The ethical stances outlined in Good Clinical Practice in research were widely endorsed by the three groups interviewed. These allow reasonable payments to clinicians, subject to disclosure of any possible conflicts of interest. The potential for incentivising clinicians to recruit was limited as any payments should be based on the cost of inputs and should not be made to individuals but to their host organisation. NHS professionals were concerned that payments could damage the quality of research and also considered full disclosure to patients as challenging. Patients and members of the public favoured full disclosure and payment of expenses to patients involved in research. Pharmaceutical company interviewees viewed payment to the NHS for all research activities as normal and highly regulated. They complained that the prices charged were high and so variable that they required benchmarking. Considerable scope exists for compiling data on the factors that help and hinder the progress of clinical trials and also for experimenting with different incentives to encourage involvement in clinical research. Further research should focus on improved reporting of those organisational aspects of trials that are known to affect recruitment; retrospective analysis of the factors associated with different levels of recruitment to RCTs; prospective comparative research on trial recruitment; qualitative research on participants' experiences of being involved in different kinds of trials, and proposals to include within trials experiments with payments methods.

Contents

Glossary and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Glossary

Chief investigator Means: (a) in relation to a clinical trial conducted at a single trial site, the investigator for that site; (b) in relation to a clinical trial conducted at more than one trial site, the authorised healthcare professional, whether or not he or she is an investigator at any particular site, who takes primary responsibility for the conduct of the trial. That is: (a) a doctor, (b) a dentist, (c) a nurse, (d) a pharmacist.

Collaborative group A group of clinicians collaborating in a clinical trial.

Collaborator Clinician collaborating in a clinical trial.

Investigator Clinician or nurse involved in a clinical trial.

Participant Person participating in a clinical trial.

Phase I Phase I or healthy volunteer studies are non-placebo-controlled studies, and the first test of a drug in humans:
- to establish safe/tolerable levels
- to establish initial pharmacology in humans
- usually carried out on volunteers who may be paid.

Phase II Phase II studies are non-placebo-controlled or randomised studies:
- to provide evidence of activity and better evidence of safety
- to define dosage and regimen
- includes participants with the disease.

Phase III Phase III studies are usually larger scale comparative, controlled trials:
- to assess the risks and benefits
- to compare benefits/side-effects with those of other drugs or a placebo
- includes participants with the disease.

Randomised controlled trial (RCT) Most clinical trials should be designed so that the results are applicable to clinical practice in the general population, e.g. pragmatic:
- assesses risks and benefits
- addresses practical questions, under 'real-life' conditions
- should X or Y be recommended overall?
- broader range of issues including cost, side-effects, compliance.

Sponsor Individual/organisation responsible for the initiation, management/financing of a clinical trial.

List of abbreviations

ABPI	Association of the British Pharmaceutical Industry
BHF	British Heart Foundation
BMA	British Medical Association
BNP	brain natriuretic peptide
CCT	Current Clinical Trials
CI	confidence interval
COREC	Central Office for Research Ethics Committees
CPD	continuing professional development
CRO	contract research organisation
CTD	Clinical Trial Directive
EU	European Union
FDA	Food and Drug Administration
FP	family physician
GCP	Good Clinical Practice
GMC	General Medical Council
GMP	Good Manufacturing Practice
HD	hospital doctor
HR	healthcare researcher
MHRA	Medicines and Healthcare Products Regulatory Agency
MOPS	Maintenance of Professional Standards
MRC	Medical Research Council
MREC	Multi-centre Research Ethics Committee
NCCHTA	National Coordinating Centre for Health Technology Assessment
NIHR	National Institute for Health Research
NRR	National Research Register
OR	odds ratio
PCT	Primary Care Trust
PI	principal investigator
PICTF	Pharmaceutical Industry Competitiveness Taskforce
PPI	Public and Patient Involvement
QOF	Quality and Outcomes Framework
RAE	Research Assessment Exercise
RCT	randomised controlled trial
SD	standard deviation

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

Payment of healthcare professionals is one way to encourage recruitment to clinical trials. However, little is known about the effects of financial incentives for clinicians to become involved in these trials, whether as lead investigators or as collaborators.

Objectives

The objectives of the systematic review were:

- to synthesise the evidence on the effectiveness of monetary incentives to healthcare professionals to recruit patients to clinical trials
- to provide an overview of the ethical issues from the published literature
- to identify current UK guidelines on financial incentives to healthcare professionals to recruit patients to trials.

The objectives of the primary research were:

- to identify the attitudes, beliefs and behaviour of healthcare professionals and the public in relation to financial incentives for recruitment to trials
- to explore how financial incentives were viewed in relation to other barriers and facilitators to healthcare professionals recruiting patients to clinical trials
- to provide an overview of the current UK practice regarding the payment of financial incentives to healthcare professionals for recruitment of patients to trials.

Methods

A systematic review of the evidence was undertaken using *a priori* methods, purposive review and summary of relevant literature.

Primary research in the form of qualitative interviews of three groups of people: NHS healthcare professionals, research managers from the pharmaceutical industry and members of the public.

Data sources

Electronic databases were searched from inception to June 2006 to identify studies for the systematic review.

The qualitative investigation involved semi-structured interviews with purposive samples of healthcare professionals, research managers from the pharmaceutical industry and the public.

Study selection

English language studies were included in the systematic review if they fulfilled the standard criteria to interventions (payments), participants (healthcare professionals) and outcome (patient recruitment). Randomised controlled trials (RCTs), cohort, cross-sectional and before/after designs were included.

From the searches, 634 identified studies were assessed for inclusion through two stages with titles and abstracts. Only three were then selected to be assessed independently by two reviewers.

Fifty-eight individuals were interviewed: 38 chief investigators, six non-research active clinicians, eight public and six pharmaceutical managers. Investigators were selected from those funded by the HTA Programme, the other by 'snowballing' and personal contact.

Data extraction and quality assessment

For the systematic review, data extraction and methodological quality assessment of the included studies were performed independently by two reviewers. Studies meeting the systematic review criteria were synthesised using a narrative approach with full tabulation of results from all included studies.

For the primary research, interviews were transcribed verbatim and entered into NVivo software for analysis and management. A hierarchical coding system was centralised around themes of 'motivation' and 'incentives' for healthcare professionals, and 'patient experiences' and 'incentives' for the public. Data are presented as representative quotations. Results were 'triangulated' between the included groups.

Results

The evidence from the literature was limited and inconclusive. Three cross-sectional surveys examined the association of demographic characteristics and perceived motivating factors of clinicians with recruitment. One primary care study reported no relation between incentive-driven motivation and number of patients recruited; the other primary care study did not report a correlation between financial reimbursement and recruitment rates. A hospital-based study reported that payment to participating clinics was considered of minor importance for recruiting patients.

In UK guidelines, the issues around payments to clinicians or patients were implied rather than stated, usually linked to discussion of conflict of interest and disclosure of any such conflicts. Developments in NHS research governance had led to increased transparency in all payments for research participation and for payments to be to NHS Trusts rather than to individual clinicians.

Interviews with NHS health professionals, mainly clinical chief investigators, indicated concerns over the likely effects of payment. While reimbursement of costs incurred to do with research was strongly supported, payments to incentivise recruitment were not. Direct payment to clinicians was rare in publicly funded trials. A code of practice for any such payments was suggested by interviewees, closely linked to the principles of Good Clinical Practice in research. Factors such as interest in the topic, scope for patient benefit and good communication were considered more important motivations for research involvement.

Interviews with the public indicated low levels of awareness of the existence of payments to clinicians linked to patient recruitment in trials, and unanimous support for full disclosure of any such payments. Interviews with research managers in the pharmaceutical industry showed greater familiarity with payments for research involvement, which had in recent years shifted to payment to institutions rather than to individual clinicians. GPs were the only group to whom scope existed for individual payments. Concerns were expressed by the pharmaceutical company interviewees at the rising cost of research and unnecessary bureaucracy.

Conclusions

The ethical stances outlined in Good Clinical Practice in research were widely endorsed by the three groups. These allow reasonable payments to clinicians, subject to disclosure of any possible conflicts of interest. The potential for incentivising clinicians to recruit was limited by two main factors: first that any payments should be based on the cost of their inputs, and second that payments should not be to individuals but to their host organisation.

NHS professionals were concerned that payments could damage the quality of research. They considered full disclosure to patients as challenging. Patients and members of the public favoured full disclosure and payment of expenses to patients involved in research. Pharmaceutical company interviews showed that payment to the NHS for all research activities was normal and highly regulated. They complained that the prices charged were high and so variable that they required benchmarking. Considerable scope exists for compiling data on the factors that help and hinder the progress of clinical trials and also for experimenting with different incentives to encourage involvement in clinical research.

Research recommendations

Further research is recommended in the following areas.

- Improved reporting of those organisational aspects of trials that are known to affect recruitment, including the type and extent of payments.
- Retrospective analysis of the factors associated with different levels of recruitment to RCTs, including payment of expenses to patients.
- Prospective comparative research on trial recruitment including between commercial and publicly funded trials within the NHS research networks and also between the roles of investigators and collaborators.
- Qualitative research on participants' experiences of being involved in different kinds of trials, and also to do with the appropriateness of the guidelines on payment for participation.
- Consideration by funders of clinical trials of proposals to include within trials experiments with payments methods, comparing different levels of disclosure and of payment.

Chapter 1

Objectives of the project

This project on financial incentives for healthcare professionals to recruit patients to trials had two main elements, a systematic review and qualitative primary research involving interviews with healthcare professionals and healthcare consumers.

The objectives of the systematic review were:

- to synthesise the evidence on the effectiveness of monetary incentives to healthcare professionals to recruit patients to clinical trials
- to provide an overview of the ethical issues from the published literature
- to identify current UK guidelines on financial incentives to healthcare professionals to recruit patients to trials.

The objectives of the primary research were:

- to identify the attitudes, beliefs and behaviour of healthcare professionals and the public in relation to financial incentives for recruitment to trials
- to explore how financial incentives were viewed in relation to other barriers and facilitators to healthcare professionals recruiting patients to clinical trials
- to provide an overview of the current UK practice regarding the payment of financial incentives to healthcare professionals for recruitment of patients to trials.

Chapter 2
Background

Description of the problem

Establishing the effectiveness and cost-effectiveness of interventions in healthcare largely depends on good-quality randomised controlled clinical trials (RCTs). One element of quality is the recruitment of sufficient participants in order to test *a priori* hypotheses with statistical confidence. Many RCTs fail to meet recruitment targets.[1] Given that these targets are based on statistical power calculations, this has implications for the validity of the findings of these projects.

Data held by the National Coordinating Centre for Health Technology Assessment (NCCHTA) shows that two-thirds of funded trials fail to pass 80% of their recruitment target (personal communication; anonymised confidential data available on request). Other work has shown that many clinical research trials are unable to recruit the target number of participants.[2] One UK study suggested that only 10% of eligible patients were recruited.[3] This presents a major problem for research funders such as the NHS Health Technology Assessment (HTA) Programme, which spends £10 million per year mainly in clinical trials. Studies that recruit too few patients might not only miss clinically important effects, but also raise ethical questions about exposing volunteers to new treatments in inconclusive research. There are also questions about the use of resources on inconclusive trials or on funding extensions for trials that have failed to meet their recruitment targets. Failure to recruit can have adverse effects on clinical practice and academic development.[4]

There are two main stages of recruitment, first contracting with clinicians to recruit patients and second recruiting patients. Less than half of participating clinicians recruit any patients in trials.[5,6] One difficulty is the need to keep a balance between active research participation and efficient clinical practice. Barriers to clinicians participating in randomised trials in two systematic reviews included time constraints, lack of staff and training, worry about the impact on the doctor-patient relationship, concern for their patients, loss of professional autonomy, difficulty with consent procedures and lack of reward and recognition.[1,7] However, a review of cancer trials suggested that the methodological limitations did not allow a clear interpretation of the barriers, moderators and benefits involved in trial participation.[7] More trials are taking place in primary care with increased pressure for GPs to participate in research. As many GPs may not be interested in research,[8] trials in primary care are difficult.[9,10] Strategies that facilitate the involvement of clinicians, particularly GPs, in trials are essential.

Financial incentives

Payment of healthcare professionals is one method to encourage recruitment to clinical trials. Some UK research funders, particularly the pharmaceutical industry, are thought to pay healthcare professionals to recruit patients, but this is uncommon in publicly funded trials. A publicly funded research programme such as the NHS HTA programme would need to have confidence in the value of paying incentives in order to consider this option. Much clinical research in the NHS relies on the goodwill and academic interest of clinicians alongside non-financial incentives such as recognition. A recent American study estimated that in a 12-month Phase III clinical trial of a new cancer drug the average extra cost to the clinic per enrolled patient was US$6000 including US$2000 for non-clinical costs.[11]

Financial incentives include paying individual recruiters in cash, such as per recruit enrolled, or reimbursing to the practice or trust to cover additional costs associated with participation in a trial.[12] Gifts can be seen as equivalent to cash payments.

Financial incentives are widely used but the exact extent is not known. The HTA Programme pays a nominal amount, if requested by the study, of £20 administration fee per patient recruited (NCCHTA has indicated that although it does not routinely collect data on how often these payments are made, they are rarely used). Payments in publicly funded research may be in the region of £100–200 per patient recruited from which costs such as laboratory tests may be paid. Commercial

trials funded by pharmaceutical companies may pay large sums per patient. In the USA, some pay investigators several thousand dollars per patient recruited to ensure rapid recruitment of sufficient numbers.[13]

Financial incentives raise ethical issues. Payment may encourage inappropriate recruitment procedures, for example, flawed consent procedures, enrolment of ineligible participants or coercion. Payment could undermine trust in the doctor–patient relationship. There are also issues of whether payments for recruitment should be disclosed to (potential) trial participants, and whether the person obtaining consent from participants should be free from any link with payment whether to individuals or organisations.

Incentives, motivations and behaviour

Complex interactions exist between incentives, motivations and behaviour and can impact on the design of public policy. It has been argued that people respond to a spectrum of motivations from extreme altruism ('knights') to pure self-interest or egoism ('knaves').[14] Knaves might respond to self-interested incentive structures and knights to altruism.

Individuals motivated to help others with no private reward are thought to be prevalent in the public sector. Altruistic behaviour can interact in complex ways with more self-centred motivations. Self-interest may take various forms, including material wealth, security, autonomy, status, fame and reputation. Some of these, for example power, could be desired for the purpose of being in a position to help others in which case they become a knightly rather than a knavish motivation.[14]

Different kinds of knight can be distinguished.[14] Act-irrelevant knights are motivated by compassion or feelings of injustice but do not need to perform knightly acts themselves. Act-relevant knights are motivated by the need to perform the helping act themselves. This in turn may lead to 'warm-glow' feelings, alleviation of guilt or feelings of duty. Evidence suggests that much altruistic behaviour is of the act-relevant kind.[14]

Incentives can influence the balance of knightly and knavish behaviour in the individuals affected. Individual motivation may have incentive thresholds above and below which behaviour is different. Payments below a threshold may reinforce altruism by acknowledging the sacrifice being made, but payments above that threshold may erode the sacrifice and the motivation for the act. It has been suggested that the best strategy in healthcare policies is likely to be the adoption of robust incentive structures that appeal to both knightly and knavish motivation.[14]

The above discussion has been at the general level of healthcare policy; we know of no application to healthcare research.

Research need

Research is needed to summarise what is known about the effects of financial incentives to healthcare professionals to recruit patients to clinical trials, which explores the associated ethical issues of incentives, and which assesses whether incentives lead to unacceptable methods of recruitment.[15] Research could lead to a better understanding of the factors which influence clinician participation in trials and help develop methods to improve recruitment.

This systematic review synthesises the evidence concerning the effectiveness of monetary incentives in improving participation in research studies. Two previous systematic reviews in this area did not focus on the issue of financial incentives to clinicians. A systematic review published in 1999 considered the factors that have been identified as limiting the quality, number and progress of RCTs reported in the literature up to 1996;[1,16] a Cochrane review considered strategies to improve recruitment to research studies aimed at participants (after this report was drafted, the Cochrane Collaboration published a systematic review[17] of incentives and disincentives to participation by clinicians in RCTs, which concluded that further research was needed).[18] The present review also considers ethical issues relating to offering financial incentives and, finally, reports findings on current UK guidelines on financial incentives.

To explore the factors motivating healthcare professionals participating in research, primary research on the views of researchers on the likely effects of payments and other motivations was seen as necessary. Ideally this should include not only active researchers but also those who might become involved. The extent and types of payment made in publicly funded and commercial trials might be explored. The views of the public and patients on payments for participation in trials should also be included. Given the lack of data on these issues, qualitative exploration in the form of interviews was deemed appropriate.

Chapter 3

Research methods for the systematic review

The methods for systematically reviewing the evidence of the effectiveness of payment to healthcare professionals for recruitment of patients to trials, and to review ethical issues and guidelines, were described in the research protocol (Appendix 1). Some changes, additions or points of clarification were made to the methods discussed in the original protocol and these are outlined below:

- The interpretation of study design inclusion criteria was kept broad in order to report the limited existing evidence. Studies that used financial incentives were included even if their primary aim was not to investigate the effectiveness of financial incentives to healthcare professional for increasing recruitment of patients to trials. Although surveys were not explicitly mentioned in the protocol as study designs to be included in the systematic review, they were included in the systematic review if they met other inclusion criteria, given the absence of any other evidence to highlight the clinician-related issues thought important in recruiting patients to trials.
- The types of payment to healthcare professionals for recruitment of patients to trials considered in this review included all financial incentives and financial reimbursements to cover research costs paid to the individual healthcare professional or clinic/practice.
- Quality assessment of the included studies was performed by using a modified tool by DuRant,[19] incorporating the most appropriate elements for use with the included studies.

The methods outlined in the protocol are summarised below.

Research questions

The questions addressed were as follows: to assess the effectiveness of payment to healthcare professionals for patient recruitment to trials through a systematic review of the evidence; to provide a critical overview of the ethical issues as debated in the published literature; and to identify current UK guidelines on financial incentives.

Search strategy

The sources of information, search terms and a flow chart outlining the identification of studies for the systematic review, for overview of ethical issues and for UK guidelines, are described in Appendix 2.

The electronic search strategy, developed in consultation with an information scientist, aimed to generate a comprehensive list of studies meeting the inclusion criteria for the systematic review. This was then refined to provide information for identifying papers on ethical issues and guidelines. Only English language studies were included as the aim was to provide sufficient systematic evidence from relevant effectiveness literature, current guidelines and ethical discussions, to inform future practice in the UK. Reference lists from all publications retrieved were checked for additional publications not identified by the electronic searches. Experts in the field and key organisations were contacted to check that relevant studies had been identified and to obtain any studies that remain unpublished and to identify guidelines. It was hoped that these efforts would reduce the effects of publication bias and inaccurate indexing in databases. Searches were updated periodically; the last update was undertaken in June 2006.

Inclusion and exclusion criteria for systematic review

Studies identified in the search strategy were assessed for inclusion in the systematic review of effectiveness depending upon the interventions used, the participants, the outcomes assessed and the study design.

Interventions

Studies that included financial incentive strategies to healthcare professionals involved with the recruitment of patients to clinical trials were included in the systematic review. Incentives included payments to an individual or to a health service organisation such a hospital, primary care practice or clinic. Studies were excluded if they

used financial incentives in conjunction with other incentives where it was impossible to separate out the effects of the different interventions on outcomes or if the study did not clearly define the payment used. However, such studies were considered for inclusion in the overview of ethical issues if they contributed information to the debate on ethics.

Participants

Any healthcare professionals involved in recruiting patients into clinical trials were included in the systematic review.

Study designs

Systematic reviews, RCTs, quasi-RCTs, controlled clinical trials, cohort studies, before-and-after studies, interrupted time series, cross-sectional studies and qualitative studies were searched for, with the emphasis on studies including an appropriate comparator group, such as people/institution receiving some financial reward with those that do not.

Outcome measures

The level of patient recruitment was the primary outcome measure considered within the systematic review. Secondary outcomes included other measures of recruitment such as achievement of sample size, proportion of patients with full follow-up and qualitative measures of professional attitudes and of effects on participants. The primary outcome measure was used for judgements regarding the inclusion or exclusion of studies. However, both primary and secondary outcomes were extracted from the included studies and analysed in the systematic review.

Inclusion criteria for ethical issues

Peer-reviewed papers addressing ethical issues of payment to healthcare professionals for patient recruitment to trials and commentaries and discussion papers were included in this scoping, narrative review.

Inclusion criteria for guidelines

Guidelines produced by UK research funding institutions, both public and private sector, that addressed the issue of payment to healthcare professionals for patient recruitment to trials were included in the guideline scoping exercise.

Application of methods for systematic review

Studies identified by the search strategy were assessed for inclusion through two stages, using criteria described above. For the systematic review of effectiveness, the titles and abstracts of all studies identified by the search strategy were screened independently by two reviewers with any differences in decisions to include or exclude resolved through discussion or through recourse to a third independent reviewer. Studies included in the systematic review at this stage were obtained to allow examination of the full text of the study. Any studies on which a decision to include or exclude could not be made at the title and abstract stage due to a lack of information were also obtained. The full text of the retrieved studies was examined by two independent reviewers to check the decision made. Any disagreements were resolved by discussion or recourse to independent assessment by a third reviewer. These procedures were used to reduce the effects of bias in study selection, which can occur due to the effects of pre-existing opinions of the researcher and to minimise the risk of errors of judgement. Studies excluded from the review of effectiveness are listed in Appendix 3.

In order to obtain the information needed for the systematic review of effectiveness from the included studies, data were extracted independently by two reviewers using a data extraction form developed *a priori*. The data extraction form noted all of the data items to be extracted in order to minimise bias. As with other decisions in the systematic review of effectiveness, any disagreements were resolved through discussion or through recourse to independent assessment by a third reviewer.

The methodological quality of the studies included in the systematic review of effectiveness was assessed using a modified quality assessment tool developed by DuRant[19] (Appendix 4). The assessment of the methodological quality of studies is an essential element of the systematic review of evidence as it allows a judgement to be made as to the rigour of the study and the potential for bias and, as a consequence, the validity of the results.

The most appropriate elements of the DuRant quality assessment tool which consider the clarity of the objectives and hypothesis, clarity of the study design, sampling, attrition and generalisability were applied. The quality criteria

used in the assessment of the studies of effectiveness were applied independently by two reviewers, with any disagreements resolved through discussion or through recourse to an independent third reviewer.

Synthesis of evidence

Studies included in the systematic review of effectiveness were synthesised using a narrative approach. Tables that summarised the results of the included studies were generated, and these results were discussed fully in the text. Statistical synthesis by meta-analysis of the data was not appropriate due to the differences between the studies in terms of study design, financial incentive, healthcare professional setting and outcome measures reported.

Papers exploring ethical issues underwent critical narrative synthesis and identified guidelines were synthesised as an overview of current policy in the UK.

Chapter 4

Effectiveness of payments to healthcare professionals to recruit patients to trials

Quantity of research

No systematic reviews, experimental, quasi-experimental, cohort or before-and-after studies assessing the effectiveness of financial incentives to healthcare professionals to recruit patients to clinical trials that met the inclusion criteria of the review were identified.

Three cross-sectional surveys, two within the context of RCTs and one in a combined RCT–cohort study, which examined the association of clinician characteristics, including financial incentives, with recruitment rates, were identified. (*Table 1* and Appendix 4)

Methodological quality of research

The studies show several methodological limitations. The main issue is that all three of the included studies relied on surveys to identify practice and clinician characteristics or motivating factors associated with patient recruitment. All three set out to find correlations and associations rather than to prove a hypothesis by looking at the effects on recruitment rates of the absence or presence of a financial incentive. None of the studies included a comparator, in the form of a control group which did not receive any financial incentive, in order to compare the characteristics of those physicians receiving incentives with those

TABLE 1 *Summary of study details*

Study name	Study design	Payment	Participants	Outcome measures
de Wit *et al.*, 2001[20] The Netherlands	Survey within RCT and cohort study of dyspepsia treatment in primary care	US$25 per patient recruited to cohort study US$70 per patient recruited to RCT Paid to family physician as financial reimbursement for time spent on research	165 Family physicians in academic network of Utrecht University	Number of patients recruited to study; demographic and practice data; initial motivation to participate; evaluation of project logistics; motivation to participate in future projects
Hjorth *et al.*, 1996[21] Sweden, Norway, Denmark	Survey within RCT of melphalan–prednisone vs melphalan–prednisone + interferon for myeloma in hospital-based clinics	SEK1000 (US$150) per patient recruited to RCT, with stepwise increase to maximum of SEK3000 for patients with follow-up time >18 months Reimbursement paid to clinic	93 principal investigators at participating clinics	Patient inclusion rate; characteristics of main investigators; attitudes of investigators to patient accrual
Pearl *et al.*, 2003[22] New Zealand	Survey within RCT to determine usefulness of brain natriuretic peptide in diagnosis of heart failure in the community	NZ$150 per patient recruited to RCT Financial reimbursement paid to GPs	186 Auckland GPs	Number of patients recruited to study; socio-demographic characteristics of GPs; process evaluation (study communication, study organisation, patient involvement, GP participation)

who did not. Additionally, there were no comparisons between non-participating clinicians and participating clinicians to allow an examination of the factors that may have played a part in the clinician's decision to initially participate in the research project in the two studies which reported most demographic factors.[20,21]

Also, there are the inherent problems of questionnaire surveys where a limited range of responses are prespecified, and where respondents may be biased to give socially acceptable answers.

Another methodological issue is of response bias. Whereas the initial healthcare professionals targeted to participate may have been appropriate, the actual included sample who responded was self-selected.

The generalisability of the studies is also uncertain. In one study,[20] generalisability may be limited by either the subject area (dyspepsia physicians), the fact that half of the physicians had research experience or the fact that participants were generally very active in numerous professional activities. The study involving GPs in New Zealand[22] did not report the extent of GP involvement in research or professional activity. In the Nordic study,[21] most participating clinicians were specialists in internal medicine, one-third of whom also had a subspecialty in haematology, and a fifth had research experience. Clinicians in Nordic countries are familiar with the practice of reporting newly diagnosed cases, being obliged to report all new cases of malignant disease to national cancer registries.

Two studies used multivariate analyses.[20,22] One study did not use statistical testing for perceived factors of importance for patient recruitment on the basis that the study aim was to indicate relationships rather than proving hypotheses.[21] Statistical tests were used for associations between investigators' attitudes and their clinic inclusion rates, which were not a simple recruitment rate but a calculation based on diagnosis of cases. Multiplicity (multiple comparisons) was not corrected for. Dichotomisation of data was used in two studies,[20,21] which may not have been appropriate, particularly where response data for 'adequate' and 'low' categories were grouped together[21] and where 'no patients recruited per family physician' were grouped together with 'up to four patients recruited'.[20]

Description of included studies

Two studies were in primary care, one in The Netherlands[20] and the other in New Zealand,[22] and the third was a hospital clinic-based study in Sweden, Norway and Denmark.[21]

The study conducted in The Netherlands[20] took data from a primary care study of dyspepsia, the CIRANO study (CIsapride or Ranitidine in NonOrganic dyspepsia).[23] The CIRANO project consisted of two parts: a cohort study, in which dyspeptic patients were included and followed up for 1 year, and an RCT in which patients selected from the cohort study were treated with either an H2 blocker or a prokinetic drug. In the cohort study, the workload for the participating physicians included identification and inclusion of patients, who then had to complete a validated dyspepsia symptom score, a quality of life questionnaire and a mental health state check list. The practice assistant performed the *Helicobacter pylori* whole-blood test. Follow-up of the patient was done by the research group. For the clinical trial the family physician (FP) workload included patient inclusion, then after randomisation to one of the treatment arms, to see patients at 1-month treatment and at follow-up after 3 months. Monitoring and data recording, verification and analysis were performed by the research group. Univariate associations were calculated (odds ratios) and relevant factors entered into a logistic regression model that predicted patient recruitment.

The New Zealand primary care study[22] examined GP and recruitment issues in a randomised clinical trial, the Natriuretic Peptides in the Community Study in Auckland, developed to investigate the usefulness of brain natriuretic peptide (BNP) measurement in the diagnosis of heart failure in the community setting.[24] Each eligible, interested GP was visited by a study investigator and given a study pack. Then each participating GP was asked to identify patients suitable for study at normal consultations. The GP gave each eligible patient a brief explanation of the study and provided a patient information sheet, and completed a simple study documentation sheet that was faxed to the study centre. Two weeks later the GP reviewed the patient with or without a BNP result and the final study documentation was complete. Following completion of the study, all GPs who agreed to participate were sent an evaluation questionnaire to complete. Questionnaires were analysed by multivariate analysis.

The Nordic Myeloma Study Group[21] undertook a multicentre RCT of melphalan–prednisone therapy compared with melphalan–prednisone combined with low-dose interferon as induction therapy.[25] Participating investigators were asked to report all patients with newly diagnosed myeloma to the study secretariat, who were then randomised between the treatment groups. Principal investigators (PIs) at each local centre were responsible for completing a registration form covering 30 items for each newly diagnosed patient and a follow-up form for the included patients covering 25 items for each return visit at 6-week intervals over a minimum of 1 year follow-up. The patient inclusion rate for each hospital in the study was calculated by dividing the number of entered patients by the expected number of newly diagnosed cases of myeloma (estimated from the crude incidence for the time period and catchment population). Comparisons of inclusion rate between groups of centres were done using Student's *t*-test.

Financial incentive used

In the primary care study in The Netherlands,[20] the financial incentive comprised a reimbursement for the extra practice time spent completing the research protocol. The estimated overall time investment was 2 hours, with an additional 5 minutes per patient included in the cohort study and an additional 1 hour per patient included in the RCT. Reimbursement reflected the workload and was US$25 per patient in the cohort study and US$70 per patient in the RCT.

In the New Zealand study,[22] GPs received a payment of NZ$150 for each patient they enrolled in the study, which was reimbursement for time spent on study matters and the cost of the final consultation as this was to be free to the patient.

In the Nordic study,[21] a monetary reimbursement was offered to the participating clinics for research and educational purposes, amounting to SEK1000 (approximately US$150) for each randomised patient with a stepwise increase to a maximum of SEK3000 for patients with a follow-up time exceeding 18 months. No reimbursement was paid directly to participating clinicians. In addition, the collaborating pharmaceutical company paid costs for the study administration and offered free drug to the patients randomised to interferon therapy.

Questionnaire

All participating physicians in The Netherlands study[20] were sent an anonymous questionnaire 5 months after the project was completed which considered demographic and practice data, initial motivation to participate, evaluation of the logistics of the project and motivation to participate in future research. The evaluation questions were Likert type (a scale of four answer categories); motivation was analysed by asking respondents to indicate the most important reasons. Questionnaires that were not fully completed were excluded.

Two questionnaires were used in the New Zealand study,[22] one for GPs who had been referred and the other for those who had not been referred patients. Both questionnaires consisted of rating scales to determine GP attitudes to aspects of the study and research in general, with some items common to both questionnaires. The questionnaire was designed to facilitate multivariate analysis with a trunk statement – 'Overall this has been a good study to be involved in' – and branches addressing study communication, study organisation, patient involvement, GP participation and the importance of reimbursing GPs for involvement in trials. Within each branch, a number of specific points were tested by presenting a statement and then asking the respondent to answer with a rating from 1 to 5 (1 = strongly disagree, 5 = strongly agree).

Participating physicians in the Nordic study[21] were surveyed by means of a mailed questionnaire with respect to their attitudes towards clinical trials. A reminder was mailed out to non-responding investigators at 1 and 6 months after the original questionnaire was sent out. The questionnaire consisted of 66 questions, of which 32 were designed to explore the attitudes of investigators that could have an important influence on patient accrual. Individual responders' perceptions of the most important factors for their decision to participate in the trial were explored by ranking prespecified alternatives; their subjective opinions concerning the most important factors for trialists' readiness to enter patients into clinical trials were explored through nine questions; responders' conceptions of the most important factors for their own readiness to enter patients in this particular trial were explored by a ranking list of eight prespecified alternatives. The remaining 21 questions were force-choice questions with 2–5 response options concerning attitudes about the scientific aims of the trial, ethical considerations, information and communication, workload, study participation and patient recruitment. For these questions, the response options were dichotomised into options reflecting a positive attitude and

options reflecting a negative attitude. In order to explore any association between the answers to these questions and the inclusion rate, the dichotomised groups of responders were compared with respect to inclusion rate for the corresponding centres.

Outcome measures

The main outcome measures for each of the included studies were socio-demographic characteristics of participants, motivation for taking part in the study and/or evaluation of the project, and the number of patients recruited to the study.

Assessment of effectiveness

The demographic results of the studies are shown in *Table 2* and the association of motivating factors and recruitment rate in *Table 3*. Further details are presented in Appendix 4.

Demographic factors

The response rate for the questionnaire in The Netherlands study[20] was 80%. Most responders were male and half had been in practice for more than 5 years. Most were involved in other professional activities. Half of the responders worked in a group practice and over half had previous research experience.

Most of the participating clinicians in the Nordic hospital-based study[21] were male, specialists in internal medicine, 39% also had a subspecialty in haematology and 20% had research experience.

In the New Zealand primary care study,[22] the socio-demographic characteristics of the GPs who referred patients were very similar to those of non-referring GPs for the variables measured with no significant differences between the two groups. Most GPs were male, with about 9% in solo practice and a median of about 19 years since graduation. The response rate for the questionnaire sent to referring GPs was 64% and for the questionnaire sent to GPs who agreed to participate but did not refer it was 27%.

Motivation and project evaluation

The initial motivation for participation in the project conducted in The Netherlands[20] varied as shown in *Table 3*. For most participants, the research topic and the participation of the academic research group were the most important factors. One-third of the respondents who regarded participation a professional obligation were attracted by the personal appeal of the research group or were intrigued by the presentation of the project. The involvement of the sponsor and the financial incentive were important for only a minority in their decision to participate. Only 15% of the participants stated

TABLE 2 *Demographic characteristics of study participants*

Study	Demographic characteristic	Study results
de Wit, 2001[20]	Male responders	87%
	In practice more than 5 years	50%
	Semi-urban areas of The Netherlands	68%
	Involved in other professional activities (e.g. CME/CFP[a])	77%
	In group practice	50%
	Practices 'specialised'	>60%
	Participants with previous research experience	57%
Hjorth, 1996[21]	University hospital	13
	County hospital	80
	Specialty – internal medicine + haematology	36
	Specialty – internal medicine	54
	Specialty – oncology	3
	Academic degree beyond MD	16
	Not PhD but spending 25% of working hours on research	3
	Male	80
	Female	13
	Age (median)	46 years
Pearl, 2003[22]	Male responders	61% (113/186)
	In solo practice	9% (17/186)

[a] CFP, College of Family Physicians; CME, continuing medical education.

TABLE 3 *Associations of motivating factors and inclusion rate/patient accrual*

Study	Motivating factors	Number (proportion) motivated by this factor	Cohort OR for patient recruitment (95% CI)	RCT OR for patient recruitment (95% CI)
de Wit, 2001[20]	Participation of the academic research group	63% FPs	2.8 (1.2 to 6.6)	2.2 (1.0 to 4.8)
	Research topic	59% FPs	0.9 (0.4 to 2.0)	1.0 (0.5 to 2.2)
	Professional obligation	39%	1.9 (0.8 to 4.5)	1.7 (0.7 to 3.7)
	Personal appeal by the research group	37%	0.3 (0.1 to 0.7)	0.4 (0.2 to 0.9)
	Presentation of the project	28%	0.9 (0.4 to 2.3)	1.3 (0.6 to 3.1)
	Financial incentive	15%	1.2 (0.4 to 4.1)	2.0 (0.6 to 6.4)
	Participation of the sponsor	11%	2.0 (0.4 to 9.7)	3.1 (0.7 to 14.7)
	Participation of a clinical research organisation	10%	4.2 (0.5 to 33.8)	2.8 (0.6 to 13.4)
	Patients recruited by 128 FPs		**Cohort study**	**RCT**
	Total number		793	527
	Mean (SD) per FP		6.3 (6.6)	4.2 (4.9)
	% FP recruited 0 patients		15%	21%
	% FP recruited 4+ patients		59%	Not reported
	% FP recruited 2+ patients		Not reported	65%
	Multivariate analysis		**Adjusted OR (95% CI)**	**Adjusted OR (95% CI)**
	Motivation by the participation of academic research group		3.5 (1.4 to 9.0)	2.9 (1.2 to 6.9)

Study	Motivating factors	Number (proportion) of responders	Mean percentage of patients recruited (80% CI)	*p* (t-test)
Hjorth, 1996[21]	Importance of quality of life analysis in main study:			
	Very	65	44 (41 to 48)	$p < 0.01$
	Somewhat/not important	28	31 (28 to 34)	
	Any preference as to treatment arm patient would be randomised:			
	Several times, once	49	47 (43 to 51)	$p < 0.01$
	Never	42	35 (31 to 38)	
	Complying with study protocol:			
	Very or fairly easy	62	44 (40 to 47)	$p < 0.05$
	Neither or difficult	31	34 (29 to 39)	
	Extra work generated by study			
	Very much, onerous, some, acceptable	53	45 (41 to 49)	$p < 0.05$
	Fairly little, very little extra	40	33 (28 to 37)	
	Participation in investigator meetings			
	All of them, >50% but not all	60	45 (41 to 49)	$p < 0.01$
	About 50%, <50%, none	33	33 (28 to 37)	
	Benefit to clinic in terms of care given to myeloma patients:			
	Very or fairly great benefit	61	43 (40 to 47)	$p < 0.05$
	Little or almost no benefit	31	34 (29 to 39)	
	Did you hesitate to participate in the study due to anticipated increase in healthcare expenses?			
	Yes	17	51 (43 to 58)	$p < 0.01$
	No	75	38 (35 to 42)	
	Patient accrual			
	Patients recruited	1014		
	% expected newly diagnosed case	72		

continued

TABLE 3 *Associations of motivating factors and inclusion rate/patient accrual (cont'd)*

	Inclusion rate		
	Mean (80% CI)	40 (38% to 43)	
Pearl, 2003[22]	**Evaluation questionnaire**	**Non–referring GPs**	**Referring GPs**
	Agreed or strongly agreed GPs should participate in research	92% (23/25)	97% (57/59)
	Agreed or strongly agreed Dept of GP should be involved in research based in GP	Not reported	93% (55/59)
	Agreed or strongly agreed that GPs should be reimbursed for involvement in trials	76% (19/25)	85% (50/59)
	Agreed or strongly agreed that could not participate in research without reimbursement	36% (9/25)	46% (27/59)
	Agreed or strongly agreed that bimonthly newsletter helpful	Not reported	80% (47/59)
	Agreed or strongly agreed that MOPS points important	Not reported	39% (23/59)
	Agreed or strongly agreed good study to be involved in	Not reported	97% (57/59)
	Multivariate analysis – overall satisfaction independently related to:		
	(i) involvement of Dept of GP	partial r^2 = 25%	
	(ii) patient benefit	partial r^2 = 17%	
	Patients referred		
	Total patients	–	307
	Median per GP (range)	–	1 (1–14)
	0 patients referred	50.5%	–
	1 patient referred	–	18.8%
	2–5 patients referred	–	20.4%
	6–10 patients referred	–	7.6%
	>10 patients referred	–	2.7%

that the financial incentive was an initial motivation to participate. This project was well evaluated, with 80% respondents stating that the project had fully (56%) or partially (24%) met their expectations and 60% noted that they would consider participation in a similar research project in the future. Overall time investment in the project was considered too burdensome by 47% of participating physicians and one-third mentioned a negative impact of application of guidelines on the workload of the project.

In the New Zealand primary care study,[22] of the referring GPs 97% agreed or strongly agreed that GPs should participate in research and 93% agreed or strongly agreed that the Department of General Practice (at the University of Auckland) should be involved in research based in primary care. About 85% of referring GPs agreed or strongly agreed that GPs should be reimbursed for involvement in trials and 46% agreed or strongly agreed that they could not participate without reimbursement. The provision of Maintenance of Professional Standards (MOPS) points was not an important factor for referring GPs when deciding to participate in the study, and the bimonthly news letter was helpful for 80% of referring GPs. Of the referring GPs, 97% found it a good study to be involved in, with multivariate analysis showing that overall satisfaction was independently related to the involvement of the Department of General Practice (partial r^2 = 25%) and patient benefit (partial r^2 = 17%). Similar responses were seen for non-referring GPs, although the response rate was low; 92% agreed that it was important that GPs participated in research, 76% agreed that GPs should be paid for involvement in trials and 36% stated that they could not participate without reimbursement.

The most important factor in determining the investigators' decisions to participate in the Nordic study[21] was the contribution to the progress of medical science, followed closely by

educational and medical care benefits. Monetary benefits were not considered important. The scientific purpose of a trial and simplicity of the study protocol were considered to be the most important factors in enhancing recruitment. Ethical concerns, rapport with the study organisation and participation in investigators' meetings were also considered important, whereas workload and participation in decision-making were considered less important. Monetary reimbursement was considered least important. The scientific aim of the study was ranked the most important factor by the majority of investigators for their own incentive for entering patients in the trial. Ethical considerations were also considered important, as were participation in decision-making and investigators' meetings. Workload, academic qualification and reimbursement were not considered important.

Recruitment

During the primary care study in The Netherlands,[20] 128 physicians recruited 793 patients in the cohort phase of the study {mean 6.3 [standard deviation (SD) 6.6] per physician} and 527 in the clinical trial [mean 4.2 (SD 4.9)]. A total of 15% recruited no patients in the cohort study whereas 59% recruited four or more patients, and a total of 21% did not recruit any patients in the clinical trial with 65% recruiting two or more. Univariate analysis showed that two factors, 'active in continuing medical training/college of FP activities' and 'motivation by the academic research group', were associated with the number of recruited patients in both the cohort study and clinical trial. These two factors were entered into a logistic model together with seven factors identified from the literature (sex, list size, number of years in practice, practice location, research experience, high specialisation and financial incentive-driven motivation). Multivariate analysis indicated that the factor 'motivation by the participation of the academic research group' predicted the number of patients recruited in the cohort study [adjusted odds ratio (OR) 3.5, 95% confidence interval (CI) 1.4 to 9.0] and clinical trial (adjusted OR 2.9, 95% CI 1.2 to 6.9). Multivariate analysis showed that incentive-driven motivation was not related to the number of patients recruited for both the cohort study and clinical trial.

Of the GPs who agreed to participate, 51% did not refer any patients to the New Zealand primary care study.[22] The remaining 92 GPs referred 307 patients with a median of one patient per GP (range 1–14). Two female GPs referred the largest number of participants (14 each), but overall male GPs referred more patients to the study. The main reason for not referring was having no patients who met the study criteria. Referring GPs were very supportive of GP participation in research and strongly agreed that GPs should be reimbursed for involvement in trials.[22] The results suggest that patient recruitment may be aided by the use of a range of strategies, including financial reimbursement, early consultation with GPs at the time of study design and effective communication between primary care professionals and researchers.

In the Nordic hospital-based study,[21] 1014 patients were included from the 93 participating centres, or 72% of the expected total number of newly diagnosed cases.

The individual patient inclusion rate varied between the participating clinics. The mean inclusion rate was 40% (80% CI 38 to 43). Danish hospitals had a lower inclusion rate with a mean of 24% versus 43% for Swedish and 41% for Norwegian hospitals. No statistically significant differences in inclusion rate were found between groups of centres when considering hospital category, specialisation, research experience or academic qualifications of the PI. A statistically significant association was found between eight questions exploring attitude toward the trials and their association to inclusion rate. Positive correlations were found for questions relating to the scientific aim of the study, particularly the importance of the quality of life analysis, which received a higher score of positive responses than did the main study; their preference as to which treatment arm their patient would be randomised; their conception of the simplicity of the study protocol; their perception of workload, with physicians who reported that the study caused excessive work having a higher recruitment rate than those who reported little extra work; their frequency of participation in investigators' meetings; their belief that participation would greatly benefit myeloma patients in terms of their medical care; and their awareness of cost and reimbursement, with investigators who regarded the reimbursement level as adequate or low having a higher inclusion rate than those who thought that no reimbursement should be paid or those who were unaware of the level of reimbursement. Scientific aim was the most important factor both in determining the investigators' decision to participate in the trial and for their readiness to enter patients in the trial. Also important for patient accrual was communication between the

study group and the participating clinicians. Reimbursement was considered to be of only minor importance both for participation in trials and for patient accrual.

Summary of effectiveness of payment to healthcare professionals to recruit patients to trials

Quantity of evidence

The literature assessing the effects of financial incentives to healthcare professionals for recruiting patients to clinical trials is very limited. No evidence from controlled or comparative studies of incentives was identified. Three surveys within the context of experimental studies were identified which considered recruitment rates and reimbursement; two in the primary care setting and one hospital based. None took place in the UK. These cross-sectional studies examined the association of demographic characteristics and perceived motivating factors of clinicians with recruitment. They are summarised here due to the lack of any other empirical evidence.

Methodological quality

Methodological problems with the literature include lack of hypothesis testing, lack of control group without incentives, inherent problems with survey design with prespecified questions, self-selected respondents, analysis limitations and uncertain generalisability.

Results

In all three studies, the financial incentive consisted of a small payment, to cover expenses, which was paid per patient recruited to the study. In the two primary care studies the payment was paid to GPs whereas in the hospital based study the reimbursement was paid to the clinic. One primary care study reported that successful patient recruitment is determined more by motivation driven by the research group than by financial incentives, the research topic or research experience. The other primary care study concluded that patient recruitment by GPs may be aided by the use of a range of strategies, including financial reimbursement, which might be enhanced by closer collaboration between GPs and researchers.

The hospital-based study found that reimbursement to the participating clinics was of only minor importance for both participation in trials and for recruiting patients. The scientific aims of the study were considered to be the most important factor with ethical considerations and communication between participants and researchers also of importance.

Discussion

The systematic review reported here summarises what is known about the effectiveness of financial incentives to healthcare professionals to recruit patients to trials. It shows that the evidence is very limited in quantity and quality and is inconclusive. Although more information is needed on whether and when financial incentives work, the studies included in the systematic review do identify some key issues relating to the factors which may motivate clinicians to take part in research and those that may be barriers to research participation (see the section 'Motivation and project evaluation', p. 12).

Two related factors which appear to be important in influencing clinicians' decision to participate in research in both primary and secondary care settings are the research topic and scientific aim of the study.[20,21] FPs were mainly motivated to participate by the research subject and by the fact that the project was affiliated with an academic primary care research group.[20] The scientific aim of the study and its contribution to the progress of medical science were the most important factors determining the investigator's decision to take part in the trial and as an incentive to recruit patients in one study.[21] These factors were followed closely by medical care benefits associated with research participation.[21] It has been shown that early consultation in the research project, effective communication and close collaboration between researchers and primary healthcare professionals were important factors for GP recruitment of patients,[22] as were participation in decision-making and investigators' meetings.[21] These findings suggest that the level of personal interest and ownership are key factors in motivating research participation by healthcare professionals.

Another factor found to be important in motivating research participation was the belief that health practitioners should participate in research and that it is a professional obligation to do so.[20,22] A substantial number of the participating FPs felt this in one study which may have stemmed from the emphasis during the introduction to the project on the evidence missing from the national guidelines on a condition and on the need for primary care-based research to fill this gap.[20]

Ethical considerations were also considered important to the question of research participation, but ethical concerns about informed consent and randomisation did not have any important negative impact on patient accrual.[21] The majority of clinicians in one study stated that they sometimes had conflicting feelings regarding their responsibilities towards their patients and the study and yet they still recruited patients. This indicates that a commitment to the scientific purpose and future patients can sometimes override ethical concerns. If the scientific question is sound and generally accepted, the participating clinicians will more easily cope with the ethical considerations.[21]

Financial incentives and monetary benefits were not considered a major reason to participate in research,[20,21] although proper reimbursement for the time invested was thought important.[20] GPs recruiting patients in one study strongly agreed that GPs should be financially reimbursed for involvement in trials.[22]

Other factors not considered important as motivations to take part in research include personal acquaintance with the researchers, as shown in one study where most of the participants were not known to the members of the research group,[20] and any academic qualifications[21] and professional point system resulting from taking part in research.[22]

A factor which hindered participation in research was the time investment in the research project being too burdensome,[20,22] which was perceived as disruptive to clinical practice, although workload was not considered an important barrier to take part in research in one study.[21]

Conclusion

The poor level of evidence available from the literature is inconclusive as to whether financial incentives to healthcare professionals for recruiting patients to trials are likely to prove effective in increasing either their involvement in trials or recruitment of patients. Rigorous evidence from well-conducted studies is needed to inform recruitment strategies.

Chapter 5

Ethical issues relating to financial incentives to healthcare professionals for recruitment of patients to trials

History of Good Clinical Practice

Good Clinical Practice (GCP) has its origins in World War II, specifically the callous abuses of medical research carried out in German concentration camps.[26] The Nuremberg code (1947) arose from the war crimes tribunal, which laid down 10 codes to which physicians must conform when carrying out experiments on human subjects:

1. Voluntary consent.
2. Experiment likely to yield useful results.
3. Well-designed experiment.
4. Conducted to avoid all unnecessary suffering.
5. No experiment with *a priori* likelihood of death or disabling injury.
6. Risk should not exceed the humanitarian importance of the problem to be solved by the experiment.
7. Adequate preparations should be made to protect participants from even remote possibilities of injury, disability or death.
8. The experiment should be conducted by scientifically qualified persons.
9. During the course of the experiment the subject should be at liberty to terminate the experiment.
10. During the course of the experiment the scientist should be prepared to terminate if continuation may lead to injury, disability or death of the subject.

This code was adopted by the World Medical Assembly in 1964 and amended in 1975, 1983, 1989 and 1996 with 17 principles, essentially as those in the Nuremberg code but with additional detail (*Box 1*).

This code has been adopted widely by pharmaceutical licensing authorities, notably Food and Drug Administration (FDA) in the USA and the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK and become the norm in research funded by pharmaceutical companies.

Non-commercial medical research remained outside these guidelines until the European Union (EU) Clinical Trial Directive (CTD) of 1999. The UK implemented the EU CTD[27] in 2004 with the Medicines for Human Use (Clinical Trials) Act (2004).[28] This applied largely the same standards to both commercial and non-commercial research for the first time. Results included policy development on research ethics committees and research governance by the Department of Health and Medical Research Council (MRC) and also the General Medical Council (GMC) and MHRA. The MHRA became responsible for the enforcement of these regulations including regular checks to NHS organisations.

Ethical issues identified in the literature

A scoping literature review was conducted. A systematic search identified 458 papers exploring various ethical issues. Two reviewers independently reviewed titles, abstracts and papers. Most papers considered the ethics of funding medical research in general. Fifteen papers[28–42] made some mention of the ethical issues relating specifically to financial incentives to healthcare professionals for recruitment of patients to trials. Two reviewers independently abstracted the themes discussed in these papers. In this section of the report, these issues are summarised from the UK perspective.

The literature reflected the themes in the World Medical Assembly codes. Tensions were recognised between the need for medical progress and the care of the individual, especially when the financial support comes from industry.[29] One study suggested that as more clinical research was funded by industry, with an increasing proportion of investigators receiving direct payment for both the recruitment of patients, ethical issues became more important.[30]

These key ethical issues involved potential conflicts of interest, the disclosure of financial

BOX 1 *Ethical principles for medical research involving human subjects, 1996*

It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

1. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.
2. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
3. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.
4. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.
5. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
6. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
7. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
8. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.
9. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
10. The subjects must be volunteers and informed participants in the research project.
11. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimise the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
12. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
13. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
14. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorised representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
15. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorised representative.
16. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorised surrogate.
17. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

incentives to potential trial participants and the impact on the informed consent procedure and the doctor–patient relationship. Each of these issues is discussed below.

Conflicts of interest

Conflict of interest can be defined as a set of conditions in which professional judgement about a primary interest tends to be unduly influenced by a secondary interest.[31] In the healthcare context, primary interest includes both the health of subjects and the integrity of research, and secondary interest includes financial gain or personal prestige. While there is nothing inherently unethical about a potential conflict of interest, what matters is whether the conflict of interest is recognised and how it is dealt with.[32] It has been argued that a potential conflict of interest may not be a real conflict of interest for a person of integrity. As long as one maintains one's objectivity there is no conflict of interest. A conflict of interest only occurs if that objectivity has been compromised. Perceived and real conflict of interest should be distinguished. Even if a person maintains objectivity it may be difficult to convince the others that moral responsibilities have not been compromised.[33] This should in no way detract from the basic conflict between the primary ethic of the doctor to promote the patient's best interests and the primary ethic of industry to promote profitability.[34]

Conflict of interest first began to receive serious attention in the medical literature in the 1980s.[35] When the roles of clinician and investigator overlap, the subjects' welfare and a scientific integrity of the data may be compromised by these dual roles. Financial conflict of interest could lead clinicians to refer patients to trials inappropriately. There is the concern about the competency of physicians to conduct clinical trials, and care for patients outside their specialty, although this is more of an issue for community-based physicians in the USA.[35]

Countering conflicts of interest

Few mechanisms exist to ensure that the primary interests of patient welfare and scientific objectivity are not unduly influenced by the secondary interest of financial gain. The primary assurance of integrity and the golden rule for dealing with conflict of interest is disclosure.[32,33]

Disclosure of potential conflicts of interest is required by research ethics committees in the UK. However, disclosure statements may apply to just the PIs and not to all the investigators in multicentre studies. Disclosure is discussed further below. Other safeguards could include limiting the area of research to the clinician's field of expertise, ensuring fully informed consent is obtained and ensuring that the treating clinician is a different person to the clinician obtaining the patient's consent to participate, ensuring that financial compensation is commensurate with the efforts of performing research and is at a fair market rate, ensuring that compensation is the same for the first and last enrolee and is not volume related and ensuring full disclosure to the patient at the time of consent. The medical profession can promote ethical research by ensuring investigators are trained in research ethics but individual clinicians must remain personally accountable for any recommendations they make to patients regarding enrolment to trials. Clinicians should be aware of the potential conflicts in their roles of clinician and investigator, including financial conflicts.[35] Fiduciary principles, which require physicians to refrain from placing their own interest above those of the patients, should guide ethical behaviour whenever clinicians engage in clinical trials.

As more research is undertaken by clinicians being involved with industry-funded trials, it is essential to guard against conflicts of interest to ensure the integrity of research and to protect the welfare of subjects.[35]

Disclosure of financial payments

The amount and basis for payments for research are disclosed to research ethics committees but not necessarily to potential trial participants. Failure to disclose such potential conflicts is potentially unethical, a poor basis for involving patients in research and could damage efforts to involve patients more fully in clinical trials, it has been suggested.[36]

The ideal that patients give voluntary consent based on full disclosure of relevant information could be corrupted by not disclosing pecuniary interest. One American study found that over half of patients questioned found payments to clinicians unacceptable. Over 80% believed that they had a right to know that their doctor would be paid for enrolling them. Doctors and patients agree that information about financial ties to a research sponsor should be part of informed consent, although proportionally fewer doctors than patients thought the physician should inform a patient of any fees paid for enrolling patients.[37] Disclosure to patients including how finances are allocated might help to alleviate some of the concern felt by patients.[38]

The impact of disclosure has been debated in the literature. It has been suggested disclosing financial payments may call unnecessary attention to a problem that may not exist.[39] On the other hand, disclosure of conflicts of interest might alert the public to potential bias. Disclosure may reduce the public's confidence in the validity of medical advice and research, with far-reaching consequences. However, consent obtained on the basis of withholding information on an issue that patients consider important can hardly be termed fully informed consent.

Informed consent

Whereas the importance of informed consent is generally acknowledged, debate continues about whether financial incentives invalidate the informed consent process. For the informed consent process to be meaningful and valid, it should include information about doctors' remuneration[40] and an explanation of the distinction between research activity in general and specific subject recruitment.[41] Large payments by drug companies to doctors within hospital departments are often put into research funds, but in general practice the doctor is often personally remunerated. This has been sufficiently lucrative for GPs in the UK to set up companies to administer trials and proceeds, which has been described as 'the doctors' status is effectively bought by the company to legitimise the trial'.[40]

The ethical norms of human subject research demand that people should not be coerced to become research subjects. Pressure to recruit and retain subjects is evolving in ways that increase the prospect for coercion with more aggressive strategies[29] which could lead to the consent process being compromised. Subtle pressure on patients to participate may undermine the patient's autonomy and even their right to withdraw. The clinician may consciously or unconsciously 'shade' the discussion of alternative treatments to make it more likely that an eligible patient will choose to become a research subject.[30]

Financial incentives, particularly inappropriately generous remuneration, may improperly promote the recruitment of patients on the margins of a particular protocol's eligibility criteria and introduce financial bias into the research process.[29,30,41] Bias could also be introduced by promoting more intensive case finding, from computer records or opportunistic detection of eligible patients during consultation for unrelated reasons, and skew the representativeness of cases drawn from the study population.[42] Pragmatic trials, where patient eligibility depends on clinicians' opinions, might be more vulnerable to misrepresentation than explanatory trials with tighter entry criteria. Deviation from inclusion/exclusion criteria could put research subjects at unacceptable risk.[30]

It may only be possible to know retrospectively if judgment has been tainted such as if harm results from a trial treatment for which a patient was ineligible.[35] It has been suggested that safeguards are necessary to avoid doctors pressurising patients to take part in trials and to deter fraudulent case finding and entry.[42]

Doctor–patient relationship

Financial incentives can also impact on the doctor–patient relationship. When consenting to participate in a trial, patients usually believe their doctor is involved in scientific inquiry for the common good, but this is not always the case.[40] Patients believe the doctor is their advocate and will act in their interest. But there may be no potential benefit to the patient from participating and sometimes there may be considerable risk. Their normal treatment may be changed, and treatment withdrawn at the end of the trial even if a benefit was evident. That patients do consent has been seen as testimony to the strength of the relationship and trust they have in their doctor and their desire to enhance that relationship.[40] Patients may feel under duress to take part in research as they would be helping their doctor by attracting funds into the practice or department.[38,40]

Even if payment involved no conflict of interest, its perception could still damage the relationship. Research that seems to be done for individual profit has the potential to erode the trust that patients and members of the public place in the profession.[30]

Other issues

Some have expressed the view that paying doctors to recruit patients under their care to take part in clinical trials corrupts the ideal that clinicians should participate in the trial because they are in equipoise about the treatments being tested.[36] Cash payments can potentially influence equipoise. In commercially driven trials, doctors may have little control over the research question, design, methods, safety monitoring, analysis, reporting or publication. It has been suggested that it may not be the 'buzz of research' that motivates doctors to join such trials.[36] However, personal ethics may deter some doctors from taking part in research where payment is based on fees per patient recruited.[42]

Commercial and non-commercial trials may be in competition to recruit clinicians. Phase IV trials or post-marketing uncontrolled observational cohort studies may be used to familiarise doctors and patients with new drugs. A system that allows commercially driven and clinically dubious research to crowd out much-needed clinical trials, and denies patients the opportunity to put their altruism to the best possible use, is considered unethical.[36] Doctors and patients disagree about whether remuneration of doctors in Phase IV trials is acceptable. One study found that most doctors (64%) found it acceptable to be paid a fee whereas most patients (56%) found a fee unacceptable.[37]

Another concern is that paying clinicians to recruit patients to trials might lead to research activity taking priority over standard patient care and that patients may bias clinicians' judgement as to what is in their best medical interests.[43] Clinicians may be more lenient with respect to informed consent procedures; they may convince themselves that research participation is in the best interests of the patient and be overly flexible with regard to inclusion/exclusion.[43]

Financial incentives to clinicians to recruit patients may be unfair to other practice or clinic staff. Research activity could increase the burden on non-research-active staff. Some staff central to research, such as specialist and practice nurses, may not be paid for their contributions.[42] Payments may compensate doctors, especially GPs, for lack of recognition from collaborating in other people's trials.[42]

Other factors which derive from financial incentives include the opportunity costs of participating in research, and whether their impact may compromise other patients' quality of care,[42] and whether speedier access to care results via research participation.[43]

Counter to these arguments, it has been suggested that payment may actually improve the generalisability of results if it encourages a higher proportion of less research-active practices to take part in trials than has been the case. Practices funded by regional or national initiatives to support or lead research activities over-represent atypical GPs (such as those with research degrees) serving atypical populations (such as rural populations).[42] Also, if payments increase the response rate, the time required to complete the trial will be reduced and save money and deliver quicker results. However, there are debates about the sums involved and whether they are for compensation of time and effort devoted to study, and whether they are appropriate for the level of effort.[41]

Critique of GCP

The implementation of GCP has been subject to some criticism, notably a *Lancet* review which pointed to the lack of evidence base for these guidelines.[44] The following deficiencies of GCP were noted:

- The title is a misnomer referring not to good clinical practice but rather to the conduct of clinical research. The unofficial jargon refers to the FDA regulations and guidelines
- GCP is based on the weakest approach to guideline development: informal consensus. More formal approaches would include consensus and evidence-based guideline development.
- Important missing information included methods for avoiding selection bias in RCTs, lack of authors or references, not updated since 1996, no updates planned and no evidence of benefit.
- Important constituencies were omitted, such as academic researchers, the medical profession and public health advocacy organisations,
- Methods for ensuring detection of fraud and accurate transcription of data are the focus of GCP but the effectiveness of GCP in achieving these was not clear.

More generally, GCP imposes considerable costs, the value of which was neither considered nor known (except that they may be considerable). Whereas the burden may have a role in relation to licensing trials, its usefulness in non-commercial trials was unclear.

Solutions suggested by the review included either dropping GCP for research not destined for a regulatory agency or revising GCP, perhaps by some neutral organisation, making the guideline up to date, scientific, flexible and simple.

Summary and conclusions

The guidelines for GCP in research, which were developed from the Nuremberg code, became statutory in the UK in 2004. The literature review indicated discussion around the key themes of potential conflicts of interest and disclosure, including financial interests. The literature reviewed explored some of these themes but provided no empirical examples. Full disclosure to

patients of all trials financial arrangements, although supported in principle, was generally seen as unpracticable. Financial incentives, it was suggested, could introduce bias and damage the doctor–patient relationship. A recent critique of GCP suggested that it failed most of the criteria for good guideline development and should be reformed.

Chapter 6

Guidelines on financial incentives to healthcare professionals

Introduction

One of the aims of this research was to identify current UK guidelines on financial incentives to healthcare professionals to recruit patients to trials. A small exploratory email survey of the major UK research funders and other relevant organisations attempted to identify their guidelines. Seven organisations were contacted: the MRC, the Wellcome Trust, the British Heart Foundation (BHF), the Clinical Trials Directive, the Central Office for Research Ethics Committees (COREC), the British Medical Association (BMA) and the Association of the British Pharmaceutical Industry (ABPI). Six of the seven responded, all indicating that none of these organisations had any guideline relating specifically to financial incentives. A review of guidelines to do with the conduct of clinical trials showed (discussed below) that the specific issues concerning financial payments were included in these more general guidelines.

Good Clinical Practice

The EU Directive 2001/20/EC on GCP in research[27] prompted major changes in UK law concerning the governance of research and codes for payment of research, both commercial and non-commercial. Although the specific issues of payment of clinicians for recruitment of patients to clinical trials or of payment of patients are not dealt with, they were implied. In brief, payment to clinicians in commercial research was required to be transparent and to be made to their employing NHS body. Payment to patients other than travel expenses was not allowed (payment to healthy volunteers for Phase I studies was dealt with differently).

The extent to which these regulations changed practice whereby individual clinicians had previously been paid individually for recruitment to clinical trials is unclear. Some interviewees quoted in later chapters suggested payment of individual clinicians had been common. Although this may be of interest, it has little relevance for the present study.

The Medicines for Human Use (Clinical Trials) Regulations 2004[28] implemented the EU Directive into UK law. Guidance followed from the Department of Health, GMC, BMA and ABPI, each of which is briefly reviewed below.[45–58]

UK law

Although most of the provisions were in line with then current practice in UK, some changes were required:

- Phase I trials were required to have MHRA authorisation.
- Investigational products had to be manufactured to Good Manufacturing Practice (GMP) standards by licensed manufacturers.
- Each trial had to have a sponsor.

Other new requirements included:

- The establishment of ethics committees on a statutory basis.
- All clinical trials had to follow GCP.
- Sponsors had to provide trial medicines free of charge.
- Inspection by MHRA would ensure that GCP and GMP standards are maintained.
- Additional protection was introduced for minors and physically or mentally incapacitated subjects.

In relation to payment, documentation to the ethics committee had to include details of any financial arrangements between the sponsor and the investigator and the extent of any payments to patients. This requirement guaranteed disclosure to the ethics committee and meant that any payments considered unduly high could be questioned on ethical grounds.

Department of Health guidance relating to research payments and incentives

Research governance framework for health and social care[51] (2001, 2nd edition, 2005) laid down standards for research as well as responsibilities and accountability following the Medicines for Human Use (Clinical Trials) Regulations 2004.[28]

Of relevance to the present project, the ethics to do with clinical trials emphasised key elements of GCP, notably the aims of research, informed consent and ethics review. It went further to emphasise that relevant service users and carers should be involved wherever possible in design, conduct, analysis and reporting of research. No mention was made of payments to clinicians for involvement or recruitment of patients into clinical trials.

Commercial sponsorship – ethical standards for the NHS[50] provided guidance on these matters in 2000, emphasising the necessity for any collaborative partnerships with a pharmaceutical company to comply fully with the Medicines Advertising Regulations (1994) relating to inducements and hospitality. These regulations put tight limits on personal gifts. The guidance required full transparency from NHS staff of any financial interests (such as company shares held by researchers) in any organisation with which they have to deal. Specifically referring to R&D, 'any funding for research purposes should be transparent'.

ABPI

The ABPI *Code of practice for the pharmaceutical industry* (2006),[46] updated annually, provides guidance under 22 headings of which two are relevant here: '18. Gifts, inducements, promotional aids and the provision of medical and educational goods and services' and '19. Meetings and hospitality'. Although not specific to research, they lay down tight limits on spending under these headings.

Arising from the recommendations of the Pharmaceutical Industry Competitiveness Taskforce (PICTF),[49] the ABPI with the Department of Health drew up a model Clinical Trial Agreement for use in commercially sponsored clinical trials involving NHS patients.[56] In response to the PICTF concern that the NHS lacked consistent methods for costing clinical research, the financial arrangements were specified in some detail, requiring disaggregation of costs by staff time and visits. The NHS was to be the recipient of all payments connected with a clinical trial. In addition, feasibility studies would establish the likely number of patients to be recruited in order to set targets. Any bonuses payable for meeting recruitment targets had to be specified in the financial schedule.

MRC

The MRC Guidelines for Good Clinical Practice in Clinical Trials (1998)[57] outlined standards for its trials but applicable to all non-commercial trials. This largely repeated elements of GCP (informed consent, protocol, host institution, independent scrutiny, etc.) but with less attention to issues of payment.

GMC

The GMC, which is responsible for the registration of doctors, issued guidelines, *Research: the role and responsibilities of doctors* (2002),[45] which, besides reiterating elements of GCP, had sections on conflicts of interest and funding and payments. On conflicts of interest, it stressed that doctors must always act in the patients' best interests when carrying out research, that doctors' judgements should not be influenced by financial, personal, political or other external interests and that any conflicts of interest should be declared. It stated that doctors must be open and honest in all financial and commercial matters relating to research, including declaring to research ethics committees all financial interests and sums of money to be paid for the research, providing information to participants on how the research was funded, including any benefits which would accrue to researchers or their departments, responding honestly and fully to participants' questions about direct payments and not offering payments at a level that could induce research participants to take risks they would otherwise not take.

Summary and discussion

These guidelines govern payments to investigators and to patients in trials using NHS patients:

- For commercial trials in NHS organisations, full cost must be charged, with disaggregation by input. Payments should be based on the model Clinical Trial Agreement unless good reason exists to the contrary. Payment must be to the relevant NHS body, not to the individual researchers.
- Ethics committee approval is mandatory and requires submission of full information on all payments to researchers and patients,
- GMC guidelines require doctors engaged in research to disclose to patients entering trials how the research is funded and any benefits to them or their departments,
- Payments should not be offered at a level that could induce participants to take risks they would not otherwise take.

Taken together, these principles leave little room for payments over and above costs to incentivise doctors to recruit patients. However, these

principles are stated within broader guidelines, many of which make no specific mention of payments to individuals. The ABPI and Department of Health guidelines in particular do not mention payments. The GMC guidelines are the clearest and together with the requirement of financial disclosure to ethics committees, provide the core guidance on these matters.

Chapter 7

Primary research – rationale and methods

Rationale for primary research

The results of the studies included in the systematic review (Chapter 3) related to specific settings, specialties and countries and thus might not be generalisable. A recent study on governance and incentives in healthcare concluded that a programme of study on incentives and their application to the NHS would be valuable.[59]

This chapter outlines the methods used in the primary research, with the results presented in later chapters.

Research methods for primary research

The qualitative research was based on semi-structured interviews with purposive samples of healthcare professionals and healthcare consumers. The aim was to interview individuals with a range of experience of clinical research and payment methods to answer the following questions:

- What are the attitudes, beliefs and behaviour of healthcare professionals and consumers in relation to financial incentives for recruitment to trials?
- How are financial incentives viewed in relation to other barriers and facilitators to healthcare professionals recruiting patients to clinical trials?
- What is current UK practice regarding the payment of financial incentives to healthcare professionals for recruitment of patients to trials?

For each group interviewed, the aim was to continue interviews until 'saturation' or diminishing returns were reached. Three groups were interviewed: NHS healthcare professionals, members of the public and pharmaceutical company research managers.

The sample

We used maximum variation sampling to ensure that all perspectives were considered. In addition to those with research experience, we aimed to include some health professionals and health consumers who had chosen not to participate in clinical trials.

Semi-structured interviews were developed for health professionals and for the public to elicit views on incentives. Eight pilot interviews with health professionals took place. Questions were structured around two main themes: what motivated them to take part in clinical trials; and their experience of, and attitudes to, the payment of incentives for recruitment.

Health professionals

Health professionals were defined as members of the various healthcare professions, mainly medically qualified doctors but including some non-medical health service researchers. The former are generally key players in the recruitment of patients to clinical trials, both as lead investigators and as collaborators.

Several tasks were undertaken to identify the scope of characteristics of health professionals to be included in the sample. Examination of clinical trials published in the *BMJ* and *The Lancet* between September 2004 and September 2005 confirmed that both primary and secondary care settings were important. Searches of the databases of ongoing and completed research trials in the National Research Register (NRR) and the Clinical Trials Register showed that PIs were principally clinicians, but a sizeable minority were other health professionals. Trial centres were spread throughout the UK, including major centres in London, Oxford and other large cities across England, Scotland and Wales. Trials covered the range of medical specialties.

As a result of this scoping work, the sample aimed for maximum variation over four variables:

- geographical location
- primary and secondary settings
- clinicians (GPs and hospital doctors) and non-clinicians
- medical specialties.

After unsuccessful attempts to identify active researchers from the NRR, the register of ongoing trials funded by the National Coordinating Centre

for Health Technology Assessment was used to identify leading investigators of ongoing clinical trials. Since these data are publicly accessible via the Internet, we decided that it was reasonable to write to a sample, stratified as above, inviting them to take part in this study. To enable us to check the representativeness of the sample, we asked those who agreed to be interviewed about their support from other funders, including the MRC, charities and commercially funded trials.

Since it was not possible to identify healthcare professionals who were not performing research using the above methods, we attempted to identify these by 'snowballing' from those who were research active. This method of snowballing led to more active than inactive researchers. Whereas hardly any active researchers refused to be interviewed, a high proportion (around 70%) of inactive researchers identified refused to be interviewed, mainly on the grounds of being too busy or having nothing to contribute. Eventually, six non-research-active health professionals were interviewed.

Thirty-eight interviewees were lead investigators of a least one clinical trial and actively engaged in health research. The six non-active researchers increased the total to 44.

A balance was also sought geographically with interviewees from 11 centres, including London, Birmingham, Newcastle, Edinburgh, Bristol and Southampton. These were mixed between teaching and non-teaching hospitals and districts.

The characteristics of those interviewed are summarised in *Tables 4–7*.

All interviews took place at the respondents' place of work and were audio-tape recorded. Signed consent was obtained prior to all interviews.

Early interviews indicated the importance of commercially funded clinical research. Interviewees spontaneously mentioned that payment for research involvement was common in trials funded by pharmaceutical companies, and that guidelines were more relevant to such studies. Although we had not initially defined pharmaceutical company research managers as healthcare professionals, we decided that it would be valuable to include their views. To do this, we contacted six pharmaceutical companies using personal contacts, asking if they were prepared to be involved and if so to suggest who we should interview. All six companies agreed to be involved and identified appropriate people to interview. Interviews were carried out by the same researcher (CK) in each of the companies, using the same format. The interviewees held fairly senior research management posts: a director of clinical research, a medical director, a managing director, a clinical projects lead, a study management director and a head of outsourcing. Their companies were split between those that did their own clinical research and those that contracted it out to contract research organisations. Their clinical trials covered primary and secondary care, with the bulk in the latter. Although the number of interviewees was relatively small, the similarity of their views led us to conclude that little would be gained from increasing the number of interviews. Their views are reported in Chapter 11, which also contains a summary of the views of the NHS professionals of the pharmaceutical industry.

Regular ongoing discussions between the interviewer (CK) and the project director (JR) led to decisions on how many people it was necessary to interview to achieve 'saturation'. Since this had to be done before the interviews were transcribed (let alone analysed), judgement was required. As noted above, it was on the basis of the findings from the interviews with the healthcare professionals that the group from the pharmaceutical companies was added.

Members of the public and patients

The protocol for the study was amended at a late stage by the funder, the HTA Programme, to

TABLE 4 *NHS professionals by group and sex*

Background	GP	Hospital doctor	Health researcher	Nurse	Total
Total	14	13	9	2	38
Of which:					
Male	13	9	6	0	28
Female	1	4	3	2	10
Age 45–59 years	14	13	9	2	38

include qualitative work with the public and/or patients. Personal contacts of the lead interviewer (CK) and the project director (JR) were used to snowball a list of potential interviewees. The aim was to include members of the public who had experience as participants in clinical research trials, and if possible some who had declined to participate. Eight people were interviewed in their homes by the lead qualitative researcher (CK), using broadly the same format as for the interviews with the healthcare professionals. As with the pharmaceutical company interviews, although the number of interviewees was relatively small, the similarity of their views on payment of clinicians led us to conclude that little would be gained from increasing the number of interviews. This may not necessarily apply, however, to other issues such as payment of patients for involvement in clinical trials, something which is returned to in Chapter 12.

Characteristics of total interviewed

The breakdown of the total 58 persons interviewed was as shown in *Table 8*.

TABLE 5 *Pharmaceutical company interviewees by sex and age*

By sex:	
Male	5
Female	1
By age:	
45–59 years	6
Total	6

TABLE 6 *Members of the public interviewees by sex and age*

By sex	
Male	2
Female	6
By age	
45–59 years	8
Total	8

TABLE 8 *Number of people interviewed by type of profession*

Type	Number	Total
Healthcare professions		
Primary care clinicians	13	
Secondary care clinicians	14	
Other healthcare professionals	2	
Non-clinical researchers	9	
Non-research-active clinicians	6	
Total		44
Members of the public	8	
Pharmaceutical company research managers	6	
Total		58

Data analysis methods

All interviews were transcribed verbatim. Transcriptions were checked for accuracy and respondents were given code numbers; any identifying information was removed to anonymise the data. Five members of the research team (JR, JP, JB, SH and CK) read a sample of the transcripts. The researchers CK and SH read all transcripts and individually undertook line-by-line preliminary open coding. Transcripts and field notes were entered into the NVivo software package,[60] which was used to assist data management and analysis. The aim at this stage was to identify empirically grounded descriptive labels (categories) for phenomena related to the research aims. In NVivo, these were applied as 'free nodes'. After comparison and discussion, a system of coding was devised by CK and SH, approved by the wider research team and applied to the transcripts. For health professionals, the hierarchical coding structure was centred on the themes 'motivation' and 'incentives'. For consumers, the coding was concerned with 'patient experiences' and 'incentives'. During coding, the researchers were attentive to the possibility of further categories arising from the data. In the presentation of data in this report, identifiers at the end of each quotation relate to individual respondents. Quotations have been selected on

TABLE 7 *NHS professionals by geographical location*

Location	GP	Hospital doctor	Health researcher	Nurse
London	2	4	1	–
North East	–	–	2	–
Wales	–	1	–	–
Scotland	1	3	2	–
South	9	3	2	2
Midlands	2	2	2	–
Total	14	13	9	2

the basis of being indicative of the views expressed and are attributed to three professional groups: GPs, hospital doctors (HDs) and other healthcare researchers (HRs).

Chapter 8 reviews the findings on the views of healthcare professionals' financial incentives and Chapter 9 their views on what motivated involvement in research. Chapter 10 considers the views of members of the public on paying doctors to recruit patients. Chapter 11 discusses the pharmaceutical industry, both how it was received by healthcare professionals and how it viewed financial incentives.

Chapter 8

The views of NHS health professionals on financial incentives

The effects of financial incentives

This chapter reports on the qualitative interviews by theme. Quotes are attributed to the professional groups GPs, HDs and HRs.

A strong distinction was made by interviewees between financial incentives and expenses. Many claimed little experience of financial incentives but in discussion all had paid or received expenses for research activities. Expenses were not considered as 'incentives' but as fair and necessary. However, respondents did not always have considered views on these matters and sometimes changed their views in the course of the interview. Negative and positive effects of incentives were identified along with their likely effect on altruism. Finally, some principles were suggested for payments related to research.

Expenses versus financial incentives

> "In the trials in which I've been principal investigator we have not used incentives or anything that I would term an incentive. We have made absolutely sure in our calculations that we have covered the costs, so a lot of the work I do is with practices. I think if you ask a GP or a practice nurse to do something, it's going to cost money, and I think we've been very careful to look at what those costs might be and then to ensure that within our funding envelope that we could reimburse those costs, at least on an average basis across all our practices. I don't know whether you would term that an incentive, but I mean I think I probably wouldn't, I think it would be a disincentive not to pay it."
>
> (GP1)

Many respondents felt that GPs in particular would not participate in trials without recompense. This was often explained by the fact that GP practices were 'small businesses', something which the new GP contracts encouraged.

> "I think the key thing if you're doing a trial in primary care now, if you don't offer any money then it's not going to happen."
>
> (HR6)

> "Most of our work is obviously with primary care researchers and primary care clinicians and, you know, to be fair they are pretty much resource driven, so they won't do anything … terribly altruistic … . It isn't to say they are out to make a lot of money out of it but they certainly don't want to be out of pocket for getting involved in things. … it's been proven time and again if you put financial incentives into primary care then they will work because GPs are very good at meeting financial targets."
>
> (GP2)

> "… because the GPs' contracts are so performance based… it would be reasonable to pay for the GPs' time, or else for them to get some reward for it in terms managerial assistance … I think it is perfectly reasonable to pay the GPs for their time … ."
>
> (HD5)

> "I suppose we do actually have incentives, it's just that they are not badged as incentives … where we find we really need to use monetary incentives and where we get the most amount of difficulty is in primary care. Primary care is used to being paid for work that they do. And it's almost the first question when you go into a practice – will we be paid and how much will we be paid to do this work? And it can be a very small amount of work. So we don't do a 'pay-per-patient' but what we kind-of end up doing is making a token payment which covers a range of different tasks which may or may not be undertaken by the practice at the end of the day. So for example we pay to have Practice Managers assist with record searches and we give a generous payment for that and it's not always undertaken by the Practice Manager but unless we make this offer we can't get through the front door."
>
> (HR9)

> "My standard policy for any trial is that I would not expect people to do this for nothing because if you ask them to do it for nothing, nothing is going to happen, and I can tell you that trying to do this stuff in General Practice you will get nobody if you don't pay the GPs for their time – just don't even THINK about doing it."
>
> (GP10)

Although respondents were anxious to point out that reimbursement should be based on actual costs to the investigator, these payments were sometimes worked out on a per-patient basis. This respondent describes how this worked in his centre:

> "All the trials I design at the moment … have moved to a pharmaceutical model of paying per patient rather then paying for research nurses … I mean it's

> difficult to say whether they're incentives, they're incentives to recruit in a sense that the more patients you recruit the more money you get. It is intended to be much more closely than is the case in pharmaceutical funded trials, a payment to represent the work that goes in, in recruiting and administrating that patient. … We work out what their likely recruitment rate should be and then we set the payment per patient based upon the number of patients we would like them to recruit. So that they can feel that if they recruit a reasonable number of patients, which within their capacity, they would be able to appoint a half-time research nurse from the income they get in for it … It does make it more risky for the participating centres because if they don't recruit and they make that commitment to hire somebody to, then they obviously, they're picking up the salary not us. But it's sort of a risk sharing thing … ."
>
> (HR2)

Another health researcher used a similar system, but based on a number of patients identified by the centre they were recruiting:

> "… usually it would be saying if you're a centre that's going to recruit and you estimate you're going to recruit *x* number of patients, we've worked out roughly what that would cost in terms of your time, we'll give you some money up front that means you can either employ somebody or give something to one of the secretaries or whatever. And if they're not recruiting well then it might be taken away, it might be time limited. We tend to think of it in terms of if they're not really fulfilling their part of the bargain, then they shouldn't go on getting the money."
>
> (HR3)

The risk of supplying trial nurses was mentioned by another PI (HD10) who had employed several on different hospital sites in a recent trial. Not all of them had produced results: "one never recruited anybody". Other models described included paying GPs on a sessional basis, supplying clerical or administrative support and research nurses (both to hospitals and GP practices), or asking investigators to invoice the PI for the actual costs incurred. One respondent (HR9) argued that reimbursing on this basis was too risky as costs could "run away with you". Another explained that the practices were very diverse, with only some having the infrastructure in place to carry out trials efficiently. This principal investigator worked out a "flat rate payment of a reasonable rate across a series of practices".

The process of paying reasonable and fair reimbursement was described by most respondents as complex and time-consuming but essential for patient recruitment to trials.

Positive effects of financial incentives

Respondents identified positive effects of offering incentives, including: improving external validity by encouraging the recruitment of a "wider generality of people" (HD10) and valuing the researcher's time: "if people feel respected and their time valued, they will do a lot more for it" (GP3). "Incentives could give the research legitimacy within the investigator's organisation" (HR7). Paying financial compensation to investigators was seen as acknowledging the commitment of the participating doctors, and made it easier to enforce quality control as this example shows:

> "I think if you are paying at the going rate for their time, and after all, if you see general practice as a business and this is time that people are having to invest over and above what they would invest in standard patient care, I don't have any problem. I think it makes – if it's a legitimate activity – it makes it easier to quality control. If you are asking people to do things for free and then you think they may be doing something strange with the randomisation process or something – it isn't quite so easy to go in and negotiate … ."
>
> (GP7)

Most respondents believed that paying higher amounts would increase recruitment to trials:

> "The money falling where the patient is is important to ensure recruitment. There's no doubt if we had, for example, offered an incentive of a certain number of pounds to a service we're delivering *x* number of patients that would have improved recruitment without a doubt. With the ability to penalise the people if they don't."
>
> (HD2)

Negative effects of financial incentives

Although it was acknowledged that increased incentives could boost recruitment, almost all respondents felt that this would be at a cost:

> "I do think it's a two-edged sword, you know with my hat on as an investigator and a director of a trials unit, I'm clearly keen to meet recruitment targets in the studies, and feel somehow maybe incentives are the way to do that. But yet I kind of think of the ethical and the financial implications and have some reluctance to start getting onto that slippery slope."
>
> (HR4)

Some thought that incentives would encourage "*unsuitable*" researchers making it harder to get

valid answers from studies. Commenting that some commercial funders paid large sums of money to investigators one GP (GP12) remarked "whether they're the sort of GPs we necessarily want is another matter".

Respondents believed that 'vigilance' and attention to detail could be compromised by high incentives, with pressure to cut corners to meet patient targets, causing bias and encouraging researchers to recruit patients that turn out to be ineligible:

> "I think if your incentive is only financial, then I don't think you're going to be a particularly vigilant researcher, personally. I think the size of the incentive is unlikely to be in proportion for a genuine recompense for alternative ways of earning a lot of money. I think if you are … doing it for money you've already built a bias into the design."
>
> (HD4)

> "… if they are being paid by … their unit to do research and to bring in patients, they may work harder at bringing in patients which is what we want, but they may work harder at bringing in patients who aren't necessarily the most appropriate and they may coerce their patients … ."
>
> (HR3)

Respondents believed that paying incentives raised ethical issues, particularly conflicts of interest, and thought incentives were potentially coercive:

> "Because just paying people to do something doesn't necessarily mean they'll do it well or be committed to it very successfully or will follow up on it. And I mean I have a very strong view that people shouldn't be recruiting to trials unless they're properly informing people, and I think there's a real problem with paying people to get recruitment numbers that, you know, the opportunity then to coerce people is, you know, it's there. And to think rather coyly that clinicians won't work that out I think is really not sensible."
>
> (HR6)

> "I mean should I be encouraging patients to get involved in trials, depending on what they are? … I guess one argument would be, and the end result of the trial is meant to be, is going to be greater good isn't it? But on a more personal level certainly more invasive trials and trialling new drugs or drugs which we don't know much about, I think there is a bit of a conflict of interest over what's going to be best for the patient, what's going to be best for my bank balance."
>
> (GP13)

> "I mean indeed the more you get paid the more you're going to… the more the impetus is to act unethically. You know, theoretically if I'm getting 10 grand per patient as opposed to £10, I want to give them the bloody disease, you know."
>
> (HD11)

Many respondents were concerned that the coercion of inappropriate patients to take part in clinical trials would lead to fraud, such as creation of imaginary patients, falsifying entry criteria and abuse of the system:

> "I think then you also start getting into ethical issues of whether undue pressure might be put on patients to participate because, in the hopes of the practitioner getting payment, on the basis of the more we get in the more we get. At its ultimate, although one would hope that this would be fairly unlikely, I guess there could be fraudulent, you know creation of patients. But … one has heard of cases where that kind of thing happens. So I think those pressures are there and … can't be denied."
>
> (HR4)

> "I think the problems clearly are fraud, of misuse of the system as there are with any form of benefit and I think fraud is the main one, either if patients are getting money, fraud on their part, or fraud from doctors, nurses or abuse of the system."
>
> (GP8)

However, the above respondent went on to point out that fraud is possible whenever money can be made, but that it was not a justification for not paying people "a decent amount for the work that they do".

Other negative aspects of incentives mentioned included: creating a 'market economy' where investigators would always expect to be paid (HD12, HD6), changing the nature of the relationship (HR5) and diverting GPs away from their clinical work (GP11).

Many thought that paying incentives would increase the cost of trials. More money would have to be found to pay incentives, which could result in fewer clinical trials. Additionally, research governance would have to be more effective to safeguard against possible fraud, further increasing costs:

> "Well first of all we have to find the money, and therefore if the cake is a certain size there will be less research done. That's the major implication. That's assuming the cake remains the same size and you can't find the incentives from outside the research budget, but it's unlikely to be the case."
>
> (HR5)

Respondents believed that not only would there be less research carried out, but also that investigators would be pushed towards taking part in trials funded by the pharmaceutical industry. Publicly funded trials would not be able to

compete with the more highly funded industry trials. The result would be a concentration of research money which would not result in advances for science and medicine, or the good of patients:

> "If you over-incentivise investigators, you will drive them more towards industrial-led trials and that may reduce the quality of trials in terms of gaining important new insights, because often pharmaceutical trials are designed to try to position drugs, and they are not going to generate important new insights. And so that is important because investigators, if they're paid a thousand or two thousand pounds per patient going into a trial, they would be very keen to do that in order to develop their research funds and so on. And that's fine and that may be an acceptable reward for the work they're putting in, but it's important that the trials that are done; those trials are not done in expensive public sector trials that often lead to more important new insights that could be more important for patients. And so I think that is something that's got to be kept an eye on."
>
> (HD6)

> "One of the big implications is that it will further concentrate the research that's done into the areas that are supported by the pharmaceutical industry, so truly academic studies will become relatively more difficult to do and the ones funded by industry relatively that much easier to do."
>
> (HR8)

Combined with the bureaucratic effects of research governance reported above, it was feared the UK was becoming less attractive as a location for clinical trials.

Altruism and financial incentives

We asked interviewees who considered that altruism **did** exist how they thought paying incentives would affect altruism. Most talked about the way it would change the relationships between collaborators, PIs and funders. Those who thought it would have a positive effect believed that paying investigators incentives would make them more likely to be committed to their role in a trial. Payments would value their time and make the transaction more formal and enforceable:

> "It might make it easier. If somebody is doing something for altruism – then you can only plead with them to deliver on what they said they would deliver on. If you are paying them and you are paying them a decent incentive to do it, then you can set a service level agreement and say 'you said you would deliver this number of patients – why are you not doing it' and that changes it to a much more business-like relationship and that, if you can get it set up and organised in a suitable manner and people are happy with that, then it is going to make the research easier."
>
> (GP10)

> "I would have thought, it's going to make you more wealthy, but it's probably more likely to make you comply and think about, can I be arsed. If you're sitting in outpatients and there's a patient sitting there and you know that there's a trial for which this patient is suitable; it's tempting to just let them go because it's more work for you, but if you're getting paid for it then it's clearly tempting to say, well hang on I will take some time to do this. Now whether that's altruism or not I don't … I don't think so because you've been paid. But you know being ethical or unethical is about plugging the gaps that allow you to be unethical."
>
> (HD11)

> "I think [*it still allows altruism*], because even if you're reimbursing people they're still going to run late for the rest of their surgery and get home late for their dinner that night, or they're going to have to rush other things that they're doing, so they have to have sufficient goodwill towards the project to endure that."
>
> (GP5)

Respondents who thought paying incentives would have negative effects on altruism felt it would taint research relationships:

> "I think it does change the nature of the contract as I said earlier between being a participant in the research. And I think if you're giving something, like I'm giving my time now, you're much more agreeable to it and you're going to have this all the time. Whereas if you're being paid, you know like the lawyer, you know the clock is ticking now and if you sit and talk to me for 30 minutes I'm going to charge you…That, and if you run over I'm going to charge you more, and it becomes that sort of different relationship."
>
> (HR5)

> "Because now if you like it becomes a transaction – if you pay me, I do the research for you, rather than actually a sense of you are joining in something that is of altruistic value of itself. But I don't think we can go back to those days, so, it's a bit of a shame that the culture has changed such that that's not possible but it isn't possible by and large. I mean you might get the odd unusual individual who would still do it if you didn't in effect offer money for the practices but not often."
>
> (GP11)

A GP who was not 'research active' described the way in which the new GP contract affected his attitude to altruism:

> "I think there's less and less. And I think in General Practice I think most people feel pretty low morale-wise in many ways and I think the new contract probably has veered away from … I mean underpinning part of the new contract is that any new work means new money and we're not going to continually have worked dumped upon us and just absorb it into our workload, and I think maybe that kind of overspills into stuff like research and I think I find myself doing it with letters coming through and I just haven't got the time, I'm doing other things so I suspect there's less altruism than maybe there was 20 years ago."
>
> (GP 13)

A hospital consultant warned of the effects of a move to a financially driven health system:

> "Oh yes. I think the minute that the average doctor loses his vocation then we're in for a very rocky ride, we're … teetering on the brink of that, somehow … I think if you ever moved to a financially driven health system then we're in for trouble."
> I: "Really? So, what? The altruism will go?"
> R: "Yeah. I think if you lose the altruism, I think medicine's a peculiar one in that you can be amply rewarded financially and still maintain an altruistic element to it."
>
> (HD4)

Principles for payments related to research

To overcome the negative effects of incentives, respondents suggested several principles: good study design, appropriate reimbursement of expenses, no payments to individuals and full transparency and disclosure.

Good study design

Good study design, it was suggested, could prevent many problems to do with payments:

> "… the only ethical issue is that you might finish up recruiting people who wouldn't otherwise be eligible and there are pressures on the edge, but again I think with strong study management you can get round that just by being very clear about what your protocol requirements are, and there are a number of elements for good practice in that, one is not over-recruiting from any one centre, another is making sure that you assess centres properly and making sure that the people there are trained properly and all those things reduce the potential for bad practice. But you have a place that's well organised and you are sort of giving them money that recompenses their, that covers their expenses, I think it is unlikely to be a place that is going to run into ethical issues."
>
> (HR5)

Appropriate levels of compensation

Respondents believed that the level of compensation for time and effort would make a difference to the quality of the study. There was a 'fine line' to be drawn between an appropriate and excessive payment that would not compromise the objectivity of researchers. When payments did not relate to the actual costs of carrying out trials the quality of research would be affected:

> "I think that if we can get the level right to encourage people to take part, then the research will be better and the practice will be better … Undue levels of payment as opposed to recompense, I think are an ethical problem. The profession's already fully paid, well paid for what we do and these kind of additional funds I don't think are reasonable … in a way they can be seen as a way to kind of bend the rules on recruitment in order to get payments."
>
> (GP5)

We asked respondents about the amount of money they considered appropriate. Respondents found it very hard to put a figure on what was a suitable amount. Most GPs started by saying £50–100 per patient depending on what was involved, but all respondents thought that the amount of money must reflect the cost of doing the research, with perhaps a little left over to plough back into other research or to fund conferences. However, exactly how much seemed to be impossible to say. This answer was typical:

> "I think it would be very difficult to put a number on that. I think it probably again depends on the disease area because for some patients, for some areas it's very simple to get patients to a study, but for others there's actually an awful lot of work that requires to be done, so I think really no, there isn't an upper limit or a lower limit. It has to be, probably again on a trial by trial basis."
> I: "So that means it's related to the actual cost … not a specific amount."
> R: "That's right. It has to be. There has to be some scale reflecting the effort that's been put in."
>
> (HR7)

Incentives should not be paid to individuals

We have reported that most investigators did not see compensation for time and effort as an incentive, but rather a necessary recompense for the work they do. However, it must be a realistic figure based on a proper costing of time and expenses. It must not be excessive. Some thought there was room for a small 'profit', but this should be paid to the institution rather than the individual. Problems would arise when incentives were considered to be a 'bribe':

"Well actually if I was choosing between a bottle of wine and a £5 note for completing a questionnaire I would feel that the … bottle of wine was a bribe or a reward or an incentive, whereas the £5 was a payment for the work I'm doing. So I guess, I think there's a qualitative difference."

(HD3)

"… it needs to be very clear about why an incentive occurs, how it, what the benefits are to the individuals. There needs to be a clear process, explicit process as to why it's happening, where the benefit is being seen. I think there is a significant danger in an individual receiving money … And that's the major one I think. What that money gets used … for me it would have to be used for the benefit of the NHS as a whole, be that patients or staff or environment or whatever. Not on somebody's jaunt to India to present or whatever."

(HD2)

"I think so far we haven't ever been involved in offering financial incentives directly to doctors for being involved in studies. It will always be by way of funding that will be payable to their research funds so there are no personal payments ever given to clinicians that are involved in studies."

(GP5)

"I don't think payments should be excessive and I think that's the difficulty – what is the appropriate level of payment that should be made. I also think that paying at the [*GP*] practice level means that there's less coercion, the potential for coercion is less. I think paying in that way also means that … I mean if a practice doesn't deliver we won't pay that fee, but if they do deliver, and they may not deliver hundreds in terms of recruitment, but we do know how hard they've tried or not tried because we are in close contact with them – then I think that has to be recognised."

(HR9)

Transparency and disclosure

Most respondents believed that, in general, transparency was an important way of overcoming some of the negative aspects of incentives. How this was to be achieved was difficult. We asked respondents whether they thought patients should be told the extent of payments to the health professional for recruiting them into trials. The responses to this question were mixed. Several thought it was too difficult to explain properly to patients. The situation could be complex, and patients might not be able to put the payment into the context of the costs of the trial. The main issue was whether or not the health professional was making a profit. One respondent likened paying incentives to taking out a mortgage:

"You need to be aware of what your agent is and what the incentives that agent has for pushing towards a certain policy."

(GP2)

"I don't think it would be helpful for most patients to be told the amount because I don't think the majority of patients would really understand. It would seem, certainly for an oncology study, it would seem like a huge amount of money. But I suspect the average oncology patient would have no idea how much a CT scan is, whether it's the NHS paying or privately paying, just the actual physical cost of doing a CT scan or a PET scan. And so I think they would just think oh that's an enormous amount of money without really understanding at all. And I think that would actually probably end up losing us patients because people would feel that actually they're making a profit out of them, where in actual fact they probably aren't making a profit out of them."

(GP4)

"… in a lot of the information sheets now – they won't say the amount of money but they will state that the investigator is being paid for this. And it tends to be to cover costs and all the rest of it. And I think most people understand that. And I think probably, I don't know – I would be very interested to know if you were to ask patients what level would they feel happy about the amount of profit that would go into it. I suspect most wouldn't mind a modest profit but then again seem … I think I would be extremely angry as a patient if I thought there were huge amounts of profits being made out of putting people in studies. So I think it's in our interest to keep those profit margins down to a reasonable level."

(GP6)

Several respondents remarked on the length of patient information sheets and because of the complexity of the information were reluctant to burden patients with any more detail. Other respondents talked about "the patient test" – if the investigator felt able to tell the patient how much they were being paid, this was an acceptable amount as these examples show. Respondents also believed that patients would not find payments to individuals acceptable:

"If you are embarrassed about the amount of money you are being paid for the job you are doing, then you are being paid too much. You know, if you are being paid £500 for recruiting this person into this study, and you're going to be embarrassed about that – well you are asking too, you shouldn't be doing it."

(GP10)

"Yes, I think that you have to be careful about it, I don't have a problem with an incentive even a financial one, that you can use indirectly for professional-related activities. I feel quite comfortable about that. I would

> have no problem, I think the ultimate test I've always applied is 'Are you, would you be comfortable discussing with a patient?' because if I'm doing [*name of condition*], it says what do we gain financially or why do you want to do it to gain financially, I feel quite comfortable saying 'Well, the reasons are as follows, these are the activities I support that we create', so I'd have a problem with it coming to me personally, I think that would put me into a rather difficult and unethical situation, but I think where the money is being used indirectly to support [*other research activities*] I have no problem with that."
>
> (HD8)

Some respondents argued that it was not necessary to tell patients about compensation paid for time and effort, since they were not told about other aspects of doctor's services, for example the cost of a consultation in the NHS.

During the interviews, it became apparent that many of the respondents were not entirely clear about their views on incentives for health professionals to recruit patients to trials. When analysing the interviews we noted contradictions, and in some areas strong personal views. This respondent illustrates the way that several of our respondents consolidated their opinions after discussing the issues with the interviewer:

> "… I've leaned away from incentives … but having spoken to you I think it's certainly not an absolute question. I don't think I would dismiss a study that had paid their participants or their researchers, you know, their – clinicians, to do that study, so it probably is O.K. to do it and as we move more and more towards payment by results out of maybe transparency these clinicians' time, the participants' time may in fact be a reasonable way to go which is probably directly opposed to what I would have said to you half an hour ago when I sat down on this seat."
>
> (HD5)

Summary and discussion

A key finding was the distinction between expenses and payment over and beyond expenses. The former were strongly supported while the latter were frowned upon. While the distinction between costs and prices (to use economics terminology) may be debatable, it does provide limits on what prices might be deemed reasonable. The key element may be the value attached to a clinician's time, which may differ between the clinician and others, such as employers, patients and possible commercial contractors. Payment for clinicians' time raises questions about scope for private work, which applies more widely to clinical practice.

Potential positive effects of financial payments to clinicians for research involvement included improved recruitment and validation of processes. Some lead investigators were moving towards paying collaborators an amount per patient recruited. Financial compensation to collaborators was seen not only as rewarding commitment but also enabling quality control.

On the negative side, it was feared that financial payments could erode altruism and encourage 'unsuitable' researchers who would provide lower quality research.

Ethical issues were raised, leading to some suggested principles for payments: good study design, payments to organisations rather than individuals and improved transparency and disclosure.

Chapter 9

Health professionals: motivations for research involvement

Introduction

This chapter reports on interviews with the same group as the previous chapter but to do with more general issues.

Interviewees were asked a series of questions, starting with 'why do some health professionals choose to take part in clinical trials, while others choose not to?' They were then questioned about the role of altruism and the role of non-financial incentives (such as recognition, reputation and publications). At the end of each interview we asked why each respondent had agreed to be interviewed. Successive sections below deal with the analysis of responses in terms of:

- motivating factors
- barriers to research
- contextual factors
- why interviewees agreed to participate.

Themes within each heading were identified primarily on the basis of frequency of mention but also on emphasis, sorted into major and minor themes. Some principles for payment for involvement in research, as suggested by the interviewees, are also summarised.

Non-financial motivating factors for being involved in research

The major factors that interviewees considered most important motivations for becoming involved in clinical research included interest in the question, intellectual curiosity and benefit to patients. Factors such as altruism, career progression, recognition and skills acquisition were mentioned as minor themes.

Interest in, and relevance of, research question (major theme)

Interest in the research question was one of the main reasons professionals took part in clinical trials. Almost all respondents considered an interest in the research question important if a clinician was to recruit patients to a study. This interest could be general, or specific to a disease or patient group. For some, an interest in the research topic was essential and could overcome a general lack of interest in taking part in research:

> "I think it's important … It needs to be quite concise and it will ring people's bell. Some topics are interesting to certain people and they are more likely to recruit to those."
>
> (HD7)

> "I think the reasons why people will take part: the subject interests them, so they are not interested in research generally but they are interested in the subject in particular …"
>
> (GP10)

Non-clinical respondents thought that some clinicians were interested in research that would help them to help their patients:

> "… for people who have this … interest, who have patients or see patients that they really don't know quite how to deal with, and they see lots of those, then they're really interested to know whether something works well or not and they're prepared to take part in a study to find that out. And I think that's an important driving force."
>
> (HR3)

> "I do think it's very important for them to be interested in the research question … generally speaking the reason they get involved in the research is that they have patients who present to them with a specific problem and they're looking for an answer to help in the treatment of their patients, and in that respect they have direct interest in the research question, because it's going to be of direct use to them once the results are known. So I would say it's paramount, really."
>
> (HR7)

A non-research-active hospital consultant who had been involved with one large clinical trial explained how the relevance of the research question had been crucial in motivating his participation:

> "It was absolutely the right study that needed to be done for this stage of development of treatment of this condition."
>
> (HD12)

Some participants gave examples of problems with recruitment caused by questions that did not have relevance:

> "I think another problem was that the topic of the research … in two trials the first … was just looking at different classes of [*drug*], but it wasn't a priority topic area for the practices or the practitioners. It was the [*funder*] decided that it was very important … to commission the research, but it wasn't big on practice – doesn't fit into any of the National Service framework, or the QOF Points or anything like that. So they had other things that were more important to them for all sorts of reasons … and then the patient lack of interest on top of all of that."
>
> (HR4)

In comparison with financial incentives, respondents often said that an interest in the research question would override the lack of financial incentive to the research:

> "At least in one of my studies that I was actually being rather mean about it because I just couldn't get any more cash … because I didn't really want it, but in two of the others … there's not a lot in this for us but we think it's an interesting topic so we'll do it, and yes, you're covering our costs, and that's generally the way it goes."
>
> (GP1)

Some believed that researchers looked for answers to specific questions that had arisen from their own practice:

> "I moved from a service career to an academic career because I got so annoyed that I could not understand what was going on – specifically about things in my area of research interest … I ended up doing research trying to find out what was going on. Now I realise that it was not my problem that I didn't know what was going on – but NOBODY knows what's going on; but as a consequence of that I made a move into an academic career largely based around [*specialism*]."
>
> (GP10)

> "I realised a lot of the things that we were doing we were doing because it had always been done that way, and I thought that was rather unsatisfactory really, so I guess it was curiosity to try and find a better way of doing things which REALLY led me into doing research."
>
> (HD1)

Intellectual curiosity (major theme)

A majority of respondents cited the importance of general intellectual curiosity as opposed to interest in a particular topic, with interviewees referring to: learning; satisfaction; furthering or developing knowledge; answering questions; stimulation; having an enquiring or inquisitive mind; solving problems; developing methods; developing understanding; and an interest in the research process:

> "I think it's just a personality thing … It's what drives people, some people are driven by money, other people are driven by curiosity, other people are driven by a desire to do good works – you know, it just depends how they're made."
>
> (HD1)

> "I think some people who are into research, it's just part of their make up, they're interested in asking questions. There are a lot of people who haven't got the intellectual energy or the drive to want to develop research themselves but realise this is an important thing to cooperate in research, and it's good professional activity to cooperate in research, and then there are other people who just want to plough their furrow every day backwards and forwards and they don't care about research."
>
> (HD6)

Others considered intellectual curiosity the realm of clinicians and altruism more the realm of patients:

> "Well, I think altruism applies more to patients in some senses. And having a sort of scientific enquiry view applied more to clinicians, so there's nothing in it for them personally, but there is something for science – so you could see that altruistically or you could see that as being wanting to further knowledge. I think there are a lot of people like that who do want to do it like that, and I meet them."
>
> (HR3)

For some, expanding the boundaries of medical knowledge was a way of getting more satisfaction from their work. Respondents expressed enthusiasm and excitement about research:

> "… I like asking questions and finding out things … I get a real like buzz out of asking questions and I hear a person 'maybe we could look at this, maybe we could look at that' and get ten million ideas and I forget to write half of them down and, so yes, that's where my, I enjoy it and it's sort of problem solving …"
>
> (HD5)

> "I think there is this issue about being inquisitive and wanting to break, sort of expand the boundaries; I think that it's fun undoubtedly – it's fun, it brings another dimension to the work that people are doing."
>
> (GP7)

Benefits to patients (major theme)

Roughly one-quarter of respondents reported that the potential for medical benefits for their patients

motivated clinicians to take part in clinical trials (a recent Cochrane review[61] has challenged this belief). They believed that patients in trials were more closely monitored, and received more attention than otherwise:

> "Well certainly the evidence suggests that patients who go into trials get better healthcare. That's certainly, well maybe not evidence, but it's certainly the anecdote, I believe there probably is some evidence there, but I haven't looked at it … You get, well that's something, you get more attention. And therefore if you get more attention one assumes you get better health care overall."
>
> (HR5)

> "In general it's acknowledged that if you participate in a clinical trial then the standard of care for the placebo arms tends to be of a higher level and so people do well in clinical trials, so actually doing lots of clinical trials is probably an activity which benefits your patients overall."
>
> (GP9)

Patients may also gain access to treatments or drugs that might not otherwise be available to them, making recruitment much easier, as these examples show:

> "So for example, if you're doing a randomised trial, say in that vaccine trial, the women – they were randomised the vaccine and they're protected against [*condition*] and they could see that as a health gain for the rest of their lives. If women taking part in the [*name of trial*] achieve control of a disease without any surgery then that's terrific for them, so we have no problem recruiting patients to those sorts of trials."
>
> (HD6)

> "The other motivating factor can be access to a service which is otherwise difficult to get access to. So trials which I find it easy to recruit to are where people get randomised to physiotherapy or something else but you can't get physiotherapy normally so if you recruit your patient with back pain and they get into the trial they've got 50/50 chance of getting physio so there's something in it if you like … ."
>
> (GP9)

Respondents gave examples of patients (and sometimes clinicians on their behalf), who were reluctant to be randomised into a non-treatment group:

> "Trials where the issues are more complex or some trials where there's a placebo, where if they've got an illness and the placebo represents non-treatment vs treatment, as in the [*name*] trial. Placebo controlled trials in patients like that could be much more difficult because of the disincentive there is that if you draw the placebo arm, for example, then they're not going to get any active treatment. This may be that there isn't any active treatment outside the trial for them, but nevertheless that's more difficult."
>
> (HD6)

> "The study of [*condition*], where we knew when we wrote the proposal, and the [*funder*] knew when we wrote the proposal, that you knew there would be a very strong patient preference for [*treatment*], by parents. So the design was such that it was a patient, or a patient preference trial design."
>
> (HR5)

> "I think that most people go into these trials thinking they would like to have the intervention. They go in to take a chance to have the intervention and they would be very happy to have the intervention."
>
> (HD12)

Altruism (minor theme)

NHS health professionals were asked about altruism as a motivation to take part in clinical trials. Most believed it existed but was diminishing; some thought it had gone. Altruism was variously defined as: "contributing to the greater good", "giving something back", "there was nothing in it for them personally", "goodwill", "good of mankind", "benefiting other people", "going the 'extra mile'", "working not just for the money".

Some participants argued that altruism was intrinsic to the medical profession:

> "I think it's part of what one would perceive automatically as part of the profession, I don't hear people expressing it."
>
> (GP7)

> "I think it runs through all, I think it runs through anybody who does a clinical research job, has an element of that in their make-up, otherwise they wouldn't do it."
>
> (HR6)

This observation that doctors could afford to be altruistic, that they are well rewarded financially anyway, was made by several respondents:

> "I think medicine's a peculiar one in that you can be amply rewarded financially and still maintain an altruistic element to it."
>
> (HD4)

> "I think there are people who are altruistic and they are just not influenced by the money in either direction. Usually that happens when you have got enough money, I mean, it's easier to be altruistic when you're not starving, you know, and not many doctors are starving."
>
> (HR3)

One respondent questioned whether it was altruism or enlightenment:

> "I see that as doing something really for nothing, for the greater good. I see that as an altruistic gesture. I see doctors who take part in clinical trials as really just being more enlightened. Because they're getting well paid for the job that they're doing, so I don't think it's so much an altruistic thing as just an enlightened thing."
>
> (HD6)

This consultant went on to describe doctors who were hostile to clinical trials as less good doctors. However, he then acknowledged that some doctors faced competing priorities, pressure of work or patients who were unsuitable for trials. Another made a similar point:

> "I think there is a large element of altruism in this in terms of the positive motivation in taking part in trials. In terms of why individuals don't, I think it's just overwhelmingly pressure of time, that taking part in research, even if it's putting your patients into a trial, does take time, it takes an increasing amount of time now."
>
> (HR8)

Altruism as the furthering of scientific knowledge was frequently seen as collective activity:

> "I think the incentive of being part of a bigger group, I think is part of the altruistic part of it. If you're prepared to go along and be open about what you've done and you're looking to learn from … not mistakes, but ways of doing things better… ."
>
> (HD4)

> "You often, you don't see [*altruism*] as being the paramount reason for getting involved, however, I think … I think it probably has to be there somewhere, especially when you're working in wide collaborative teams. I think there are still some … single centre, single-handed physician-type research which, for which altruism isn't necessarily a driver, but these big collaborative trials, altruism plays a part. I don't think it's explicit in there, coming across, but it is there."
>
> (HR7)

Those who felt altruism did not exist fell into two groups – the first challenged the meaning of altruism:

> "For doing research? – not really. No I think I'd be the first to say the reason I do it is because I'm being selfish. You know I think, intellectually I think, it satisfies and stimulates. I can't see I'm doing it to save the world. And I haven't seen many researchers who are doing it for that reason … I think really the altruistic people are out in Africa helping people out there. And they've probably got fairly selfish motives as well. Well not selfish in terms of it makes them feel good but I think the true altruistic people are actually doing that sort of thing rather than research … probably."
>
> (GP6)

The other respondents who did not believe altruism existed were more cynical, as this example shows:

> "Well, I suppose, because I'm an academic and I work with some of the academics, I rarely see… altruism, it's always about 'what's in it for me or my department?', I rarely work with anybody who is willing to give anything up for the good of man, just for genuine kindness, I mean people will always give you a bit of advice, but then as soon as you start asking for more they stop, unless there is something in it for them, and I do the same now, I don't go around giving advice unless I'm going to get something back … ."
>
> (HD9)

All those who thought altruism was diminishing linked this to a system increasingly driven by money:

> "Most of our work is obviously with primary care researchers and primary care clinicians and, you know, to be fair they are pretty much resource driven, so they won't do anything for terribly altruistic… It isn't to say they are out to make a lot of money out of it but they certainly don't want to be out of pocket for getting involved in things."
>
> (GP2)

> "I think practitioners are becoming much more hard-nosed now, they've been very cynical otherwise they wouldn't get out of bed if you didn't pay them … I think the other is increasing competing demands on people's time and goodwill."
>
> (HR4)

Another reason given for the demise of altruism was the increased regulation of trials, such as the GCP requirements.

Career progression (minor theme)

Several respondents believed that career progression was one reason for research involvement, though none believed it to be the prime motivation. The data were contradictory; respondents reported an expectation that clinicians should take part in research in order to further their career. Conversely, they also reported a lack of training in research methods among collaborators and colleagues. This respondent, a non-academic hospital doctor,

described the pressure on registrars to stand out from the crowd:

> "… an awful lot of Registrars do research because they see that as the only way that they will get on in their careers … Registrars, SHOs, and when they all turn out for jobs now you know they are all very, very similar, and they have to send their experience, similar jobs that they have performed, and one of the only ways that they can stand out from the rest of the crowd is by what they have presented and what they have published, so a lot of the sort of more minor research that is done, particularly in the NHS … is actually a career progression thing, it's got nothing to do with scientific interest in what's going on."
>
> (HD14)

Research was valued differently across disciplines and specialities. Research in 'fast moving' areas was more highly valued and carried greater prestige. Change in government policy and disease patterns affected respondents' motivation to engage in research:

> "The only way the recognition can come at the moment is if people make an active decision to leave one post that they're in and apply for a new post."
>
> (HR9)

> "Well my specialty is rather different. In order to be an academic [*specialty*] surgeon … you've got to train as a [*specialty*] surgeon and – there are quite a few [*specialty*] surgeons who commit time to academic work and do less clinical work. But it's fewer than in many other specialties … I am not sure why it is. I think academic [*specialty*] surgery is becoming more appealing to people now than it was … Perhaps because [*specialty*] surgery is changing. There's less [*disease*] about and I think people are perhaps thinking well this gives me another string to my bow as it were."
>
> (HD12)

These respondents also believed that there was an expectation within the NHS that clinicians participated in research. Several respondents reported peer pressure to do research:

> "You've got to experience something [*research*] to get the flavour of it. A lot of people get that flavour because they have to, they feel they have to do it because peer pressure rather than anything else."
>
> (HD2)

> "… he works closely with one or two other doctors who have managed to produce a number of papers, and they encourage their juniors to do it, they force their juniors to do it, and they regard it as part of their training."
>
> (HD13)

However, using peer pressure can have negative consequences for the quality of research:

> "On the other hand your boss, if you're more junior, may take a centre into a trial and that might mean the minion – the SHO or the Registrar or whatever – is involved in a trial, not because they agreed to it but because that's what's happening in their place. And so they may have been less asked but actually be doing the recruitment mostly on the ground, and they may show their unhappiness … by just missing the odd case or not asking very well, or whatever, and their recruitment rate won't be high. But they may not actually refuse because they're not in the position where they have been asked, they're just having to do it … ."
>
> (HR4)

> "You do it because you have to and your boss wants you to do it, not because you want to do it and a lot of research that's done certainly in hospitals I think and probably in academic research."
>
> (GP6)

The last two quotations highlight a recurrent theme of 'reluctant researchers' who it was feared could damage the quality of research. Respondents believed that investigators who were motivated by excitement, altruism and intellectual curiosity were more likely to be better researchers than those who were pushed into it for career progression or money.

This respondent was pessimistic about the future of research in the NHS, believing that careers in academic medicine were no longer attractive or encouraged:

> "… if you look at Modernising Medical Careers, there is a complete absence of any emphasis on the importance of doing research. Now when I trained in surgery basically you would not get a consultant job if you had not done either an MD or a PhD thesis – not required now, actively discouraged in fact – they want to train you quickly and get you to start shovelling coal, doing hernia repairs and seeing patients in clinic. And so we are going to have our hospitals populated by a group of people who have no experience and no interest in research. And if you look at most of the research active people in this Trust are over 50 and many of them are over 55 and most of them are keen to take early retirement. So if you actually look at the body of people who are going to be doing research in the future, massive crisis in clinical academics, and I'm talking about NHS consultants here, where there is a huge crisis in attracting people to universities to do clinical academic jobs."
>
> (HD1)

When probed, many respondents thought that health professionals should be encouraged to start

thinking about research early in their careers. Research training should start early and suggestions included starting at undergraduate and postgraduate level in primary care and catching clinicians before they became "bogged down" by clinical work and private practice. Research would then be seen as "normative behaviour" (GP5). Respondents pointed out that without knowledge of how research works they were ill-prepared to take part in trials:

> "I think it's a pity that there isn't more opportunity for NHS people earlier in their careers to have research, because I think if they get their hand in, so to speak, even for a short period of time, then I think that would be easier. But if you've been working in the NHS for 5 years or something and, you know, someone says, oh why don't you come back into doing some research, you know, first of all you have to think well one way, so what I give up … my private clinic which earns, you know, to do something which I'm not really up to speed with, you know I think its very difficult for them. And so I've met quite a few NHS clinicians who I think could have been allowed to do more research, could have been encouraged to do more but just feel overwhelmed by the NHS commitments …And then they also get quite comfortable in their consultant posts, with their private practice."
>
> (HR6)

> "I would have thought you'd have much more impact in really helping to form some view before they're finally solidified and ossified in people who just are – you know, 'we do service delivery and that's what we do, and we're interested in anything around that, particularly financial aspects around it'. You ought to get in much earlier in the formation of doctors about the importance of research."
>
> (GP8)

The discussion of early training led respondents to talk about how they became interested in research. After several people had mentioned this, it was included as a direct question. Health researchers also talked about how they thought the medical collaborators had become interested in research. Responses from clinicians suggested that they had more structured careers, whereas non-clinicians had often "drifted into" research (GP6), or started "accidentally" (HR3). They then found they enjoyed it. However, not all clinicians had planned their careers, for example one GP found himself "sucked into" research. Mentors were also mentioned:

> "… in fact it dates to when I was a medical student really, I could have had some good relationships with senior colleagues who were very encouraging, they encouraged my curiosity and you know, my first experiences in doing research were as a trainee general practitioner, um, and I was supported and encouraged with that, enjoyed both the challenge and the feeling of contributing to improving patient care, it sort of snowballed from there over the years!"
>
> (GP1)

> "I mean I wasn't particularly academic at university in my early training. I initially started, I guess to do research, because I felt it was going to progress my career, or it's been another set of hoops that should be jumped through to progress. I guess I had good mentors who were interested in this speciality which was, which is still rare but it was even rarer more than a decade ago. And I enjoyed it and I think one of the benefits of being a consultant is the breadth of things you can actually do within what's … well historically have been able to do within the breadth of a job plan and I've continued to do it. I started my … I had an MD when I was a recently appointed consultant. Again I don't know why, it was something that I got money for and there was an opportunity there and I felt I'd be stupid not to take it up to, and it's just sort of grown from there."
>
> (HD2)

Three GP researchers talked about 'always knowing' that research would be their career path (GP7, GP5, GP11). Other reasons given were the desire to be a "world expert" (HD11), and being in a top teaching hospital (HD9) with high-calibre research and research culture.

Recognition and reputation (minor theme)

Many respondents mentioned recognition as a motivation for taking part in trials, although none saw it as the main reason. The data can be divided into two perspectives – on an individual or institutional level.

On an individual level there was reference to self-promotion or "self-aggrandisement" (HR1). The first quotation is from a non-clinician who has led many large trials (after describing several other motivating factors):

> R: "They like – you know, being the great I AM and … ."
> I: "Recognition?"
> R: "Yes, yes, having papers published with their names on it and being seen by their colleagues as being a good researcher … ."
>
> (HR3)

The following two respondents had NHS contracts only:

> "Interest is probably what drives people to start off, reputation is then probably one of the biggest things

in that a lot of people see that if they are producing large amounts of research, actually that gives them prestige, and I have no doubt that an awful lot of research is done for prestige, secondly an awful lot of Registrars do research because they see that as the only way that they will get on in their careers."

(HD14)

"I think for some they have a genuine thirst for finding out information and want to know why things happen and how to change outcomes for people, others I suspect there's probably a little bit of glory involved in it … ."

(OHP2)

Some respondents talked about their personal desire to be an expert as a motivation to do research:

"… I like the feeling that you are at the forefront of your albeit tiny field within medicine that you become an expert on it and you've done research to find out and you can share that experience with other people. So it's not just the sharing, it's doing it as well. Finding out but becoming an expert in that particular field. I really enjoy that part of it."

(GP6)

"I mean I basically wanted to be a world expert in something, which is as simple as that. I wanted people to value my opinion and I wanted people to think that I was good at what I do and being in medicine and looking around the quickest way to get that is to be a researcher and build a reputation, and it was extraordinarily easy actually."

(HD11)

This researcher, a non-clinician, did not believe that being an expert was linked to taking part in trials:

"But I don't think in almost any field that I've worked in – being an expert in your field necessarily means being a trialist. You can get up the expert route from doing very different sorts of research and it may be also valuable or it may be just that you've shaken the right hands of the right people to get up the career route. I think research is only one component of that, sometimes not the biggest, or not even a big one."

(HR3)

Most references to reputation were made in the context of institutional recognition. Respondents talked about the value of being part of an important trial and positioning their organisation in a better way (HR5). However, a GP from a research practice felt that this made little difference to most GP practices, except for research practices which needed to justify their existence (GP11), a view that was echoed by several GPs. This consultant believed that acknowledging her collaborators was worthwhile:

"People who have agreed, have agreed because they're generally, some of the District General Hospitals (DGHs), I think they can see the benefit of being part of a study that will include them in some ways, like in this study that we're doing, it will include, we'd like to say special thanks to Drs So and So from each of the following Trusts who were collaborators on this study and helped us to recruit patients from their team, so they get, they will get something from that, they will get a mention and I think that's a worthwhile thing."

(HD9)

It was suggested that patients also valued the reputation of a doctor:

"Well, I would say again it's all part of the richness of the reputation of the professional that you're known to be someone who's involved, and patients do get to know that … in a vague sort of way, and they obviously like to imagine they are being treated by someone who has a national leadership role, so, it's all quite complex dynamically."

(HD4)

In general, recognition was considered to be a minor motivation. However, a few individuals were highly motivated by personal recognition, which they felt was higher with publicly-funded trials compared with those funded by the pharmaceutical industry.

Publications and conferences (minor theme)

The importance of publications varied by the type of work undertaken. Academic researchers felt pushed to publish by the Research Assessment Exercise (RAE) but for collaborators without academic contracts this mattered much less. Respondents believed that this kind of recognition was less important for GPs. One hospital clinician (HD10) pointed out that his faculty recognised publications as part of continuing professional development (CPD) – he had earned most of his CPD points through his publications. It was observed that authorship guidelines are strict and coordinating large numbers of authors can be difficult. Journals had become more willing to list collaborators.

One respondent argued against authorship as an incentive because only the few lead investigators could be authors:

"The other rewards are much more subtle in scientific means which are still there about authorship of the

> paper that comes out at the end, and I think that still needs to be explicitly made clear to all clinicians who take part, is that if they take part they will be named, because I think there is a little bit of variability of practice around that, that is it seen that two or three people at the core take all the kudos."
>
> (HR7)

A non-research-active consultant said that he sometimes doubted the quality of research that takes place – "the concept of producing papers for papers' sake was till apparent" (HD13). The responses suggest that commercially funded research (interviewees' views in the pharmaceutical industry are discussed more fully in Chapter 11) was of less value in terms of publications than publicly funded research:

> "One is the external perception that if you are doing pharmaceutical funded work that somehow it is going to be influenced by the drug company. To be fair my involvement with industry has been that they don't do that at all, they leave you alone – but there is certainly an external perception which then makes it more difficult to get things published. And in terms of academic credibility it's obviously better to have mainstream monies than pharmaceutical monies."
>
> (GP2)

> "So I think certainly there are pressures on the one hand to have more commercial studies for the revenue that they can generate, for the new drug you can get that you wouldn't get otherwise. But in terms of RAE brownie points the balance is towards research councils, big charities, the various NHS funding streams, the prestigious funding streams, and that gives you RAE rateable papers."
>
> (HR4)

Attending international conferences motivated some of our respondents:

> "I mean they're still partly for me because there's stuff I get interested in for [*specialism*]. I mean I can end up being a leading investigator for the country, you know in the UK for a trial and that enables me to go and talk about it in other parts of the world which obviously is great. And that carries on really from the non-commercial stuff. I'm still at the forefront of that particular bit of medical information. So that's one motivation."
>
> (GP6)

> "Yes, yes, and all the career – you know – there's stacks in it for us and it's not just the money thing, it's the kudos it's the international lecture circuit and all this kind of business. Not that I do international lectures, but you know – there's stuff in it for me."
>
> (GP10)

A few respondents had used money left over from lucrative pharmaceutical trials to fund attendance at overseas conferences.

Gaining skills and knowledge (minor theme)

The answers in this theme linked gaining skills and knowledge to intellectual curiosity. It was pointed out, however, that research skills could only be gained through taking part as an investigator, not as a collaborator. One researcher observed a lack of knowledge about clinical trials among health professionals:

> "… you can't assume any health professional knows and understands what a trial is or how to explain it to a patient. Because I've had long discussions with clinicians who really do believe in studies but when I tape recorded them talking about trials, you suddenly hear that, you know, they don't actually understand, they don't understand the intention to treat … or if they do understand randomisation they can't really explain why it's a, you know why it's a sensible idea and that's not surprising when you think how confusing the concepts are … I think it's the same with nurses as well. Again you can sort of assume that because of their training they understand the basics of a trial and how to talk about it, but actually they don't."
>
> (HR6)

Other answers related to improving practice or learning about a specific disease area (GP5) or new procedures (GP1). It did not appear that respondents took part in trials specifically to gain skills or knowledge, but sometimes this indirectly resulted from participation.

Barriers to taking part in clinical trials

During the interviews, respondents referred to barriers to taking part in research which are summarised in this section.

Bureaucracy (major theme)

This produced the strongest reaction from interviewees. Over recent years researchers have seen changes in ethics committee procedures; the introduction of the EU Directive on good practice in clinical trials, the Data Protection Act and the requirements of research governance. Many health professionals felt they were being overtaken by bureaucracy. The bureaucratic requirements of a clinical trial were believed by respondents to be a major obstacle.

Respondents reported that it took up to 1 year from writing a funding application and designing a study to set up the project. Delays of up to 2 years were reported. Two hospital doctors said that it was no longer possible for junior staff to take on research projects because they would have moved on to new posts before the study could start (HD2,HD5).

Bureaucracy – research governance

Respondents believed in principle that good research governance was necessary. Respondents made the point that in the past people had been "a bit free and easy" with handing over case notes (HR1) and that some researchers still had a cavalier attitude to research governance. Problems arose from inconsistent and conflicting interpretation of regulations by bureaucrats:

> "I think it's [*research*] become much, much more difficult to do as such because of research governance. I think that a lot of people in the NHS are completely baffled by research governance and they're terrified of doing the wrong thing. … So they say 'we'd like to help you but we don't know what we're allowed to do'. The R&D officers and the trusts often have very little understanding either and that causes very long delays, and clinical staff are uncertain whether you should have access to the patients' medical records because they've heard there is this thing about research governance, and they don't really know what it means … ."
>
> (HR1)

> "I think it's … great that it standardises and it certainly – we've had examples quite recently of how – it brings people into line. People still think that, you know, they're Prof of this and therefore they can write to GPs and do what they like and ethics – why ethics? I didn't have ethics when I did this as a medical student, sort of thing! So I think all of this has got to be good. And as long as the amount of bureaucracy doesn't exceed the goodness that can come out of this that's fine. I think that there's probably too many people at the moment involved in governance and that it would be better if it was streamlined."
>
> (GP7)

A few respondents thought that dealing with R&D departments in Hospital Trusts and Primary Care Trusts (PCTs) was beginning to improve, but the majority felt that it was getting worse or not improving. The main complaint was inconsistency: "Three different applications for research governance approval to three different primary care trusts or areas will result in three different forms and three different sets of requirements coming back" (GP1). Although some PCTs and Trusts were improving, others were still struggling, as this respondent explains:

> "Well, it's, I think overall it's getting better, however, it's the tail that's dragging at the moment and you almost have a black list of R&D offices that you think, 'Oh no, I have to go and speak to them again,' and I think that's unacceptable. Um, if you can get approval for a study across 20 centres in the UK and the 21st R&D office drags their feet, I think that's inappropriate, so yes, I would say R&D seem to be getting their act together. It's a lot better than it was, but really we need to sort out the dead-end Charlies … ."
>
> (HR7)

Others saw research governance as diverting resources from research (HR3, HD3) and encouraging defensiveness (HR3). Several respondents suggested that the new rules merely formalised what they were already doing: "it's a very big sledge hammer to crack a very small nut" (GP3).

There was consensus that the length of time taken to gain approvals was a disincentive to participate in research and was discouraging more and more health professionals from leading or even taking part in clinical trials:

> "I think it's been a really big switch-off for a lot of people, and I've heard people who, at the end of studies, have said, 'I'm not going to go through that again'."
>
> (HR8)

The EU Clinical Trials Directive was seen as having had a profound effect on academic research. Clinical studies have to be carried out according to GCP standards. Trusts were reported to have become reluctant to sponsor trials. The commercial sector has been following GCP for the past decade, but it was new to the NHS and expensive to enforce. A hospital consultant expressed views held by many:

> "I think the EU Clinical Trials Directive scared lots of universities and scared lots of Trusts about what are the roles of sponsorship, you know, we simply don't have the resources to really follow GCP as the private sector does – so what actually do you want us to do? I don't think there's a great deal of clarity on that … and I think most people think, I think the medico-legal environment in which we work is extremely unhelpful with people looking over their shoulders all the time, and certainly Trusts are doing that, Trusts are very, very medico-legal conscious and very reluctant to sponsor indemnity and such like. It's not so much a problem for commercial trials because

> obviously that's covered through the prior arrangements and such like – but if you want to do own account research and shoulder the responsibility; government bodies like the MHRA are a complete nightmare to deal with if you want to do a trial, a study involving a drug, even a licensed drug."
>
> (HD1)

Bureaucracy – ethics committees

Most respondents thought that the system of applying for ethical approval had improved. The centralised process of COREC and the on-line application form were seen as saving time. However, there were still complaints about the complexity and length of the form and its frequent changes. In common with research governance and R&D approval, researchers found it frustrating waiting for the next committee to meet, waiting months to approve minor amendments. Respondents pointed out that despite research proposals being peer reviewed, ethics committees could "stray into scientific issues" (HD7). Many criticised the length of the patient information form now required. This respondent reflected the views of many:

> "I think that some of the initial fears that people had are being overcome to some extent, that genuine effort is being put in to try to make life easier, but I get the perception that a lot of clinicians think it's one thing after another, that if it's not the new European legislation, then it's performance with GCP or performance with research ethics that are maybe becoming tighter and as soon as one hurdle has been dealt with and that problem goes away, something new comes in and I feel that it's water dripping on a stone for some people. They just don't see an end to extra bureaucracy coming in."
>
> (HR8)

Time – competing priorities and targets (major theme)

Lack of time was one of the main reasons why health professionals did not take part in trials. Respondents reported that clinicians had increasing demands on time and goodwill. Paying for health professionals' time was suggested by some as a way to increase participation in clinical trials. Some had signed up for a trial but found later the burden too onerous:

> "Some clinicians are tremendously overworked and with the best will in the world they would like to take part in research but can't. In some respects those people who say they can't at the start, it's more helpful because sometimes you find people who want to take part in research but really don't have the time to do it and it's that realisation down the line that they don't have the time to commit to it, and that's when it becomes potentially problematic for the trial. It's very well meaning but they really don't have the time."
>
> (HR7)

> "… but what happens is you kind of join up and don't foresee just quite how much time commitment it is and then you're in, even with the best will in the world, in your surgery and unless I've got spaces I just don't have the time to do it or else I will put all my patients back half an hour and you don't want to do that … So I didn't recruit any patients and it was a time issue."
>
> (GP13)

GPs emphasised the cost of recruiting patients to research in terms of patient throughput:

> "The GPs have often wondered, 'Is it worthwhile studying?' They're already running late in seeing these patients, and it's very difficult to explain what you're wanting to do and it takes a long time, so they default to just not bothering. Friends who've had to send back large sums of money to the research council because they just couldn't get patients recruited to studies in primary care … ."
>
> (GP6)

Some suggested that nurses or other members of the team could recruit patients outside the consultation time, with trials designed to cause the minimum disruption to practices. A secondary care respondent reported that in his department, patients were only on the premises for short periods, with no time to build rapport (HD2). A consultant (HD6) observed that recruitment was easier in teaching hospitals where doctors had time designated for research. In district general hospitals research was reportedly seen as a low priority.

The competition for clinicians' time was complicated by targets resulting from the new consultants' and GP contracts:

> "And I think doctors – think people perceive themselves in primary care as being really, really busy. I mean having this new contract has been a huge amount of extra work and taken kind of motivation. And it's taken your energy, if you like, your kind of extra spare intellectual energy has been devoted to working and how you can score your QOF points. So there isn't anything left over for research and I just think that's a reality really and I don't think it's the people don't want to do research anymore, I just think that genuinely they've been diverted from it."
>
> (GP9)

> "One of the problems we had with the recent piece of work which really floundered was because not only all

> the GPs had the problems of these contracts and therefore they hadn't got any time or they wanted resources. But secondly, and more importantly probably, that wasn't a very interesting subject anyway to them. It wasn't part of their contract."
>
> (HR5)

A consultant with 25% of his time allocated to research had difficulty devoting that time to research:

> "The job plans are very clear now what you should be doing and you are accountable to them. So that it does make it more difficult to take time out to do research on a regular basis, I mean a regular commitment, you can do something once or twice but a regular commitment you would need to think about that and probably renegotiate your job plan."
>
> (HD7)

Other reasons for not taking part in research were to do with payment. GPs could earn £175 an hour for private work. A hospital consultant explained that private practice paid more than clinical excellence awards:

> "Say you do two EPAs [*Extra Programmed Activities*] research if you want to do that, that's reasonable compensation, but if your main drive is to make money then it's not worth doing. You can earn a lot more in two EPAs outside in the private sector."
>
> (HD4)

Extra programmed activities are part of consultants' job plans, with agreed rates of remuneration. In general, consultants are allowed up to two additional 4-hour sessions per week.

Differences by specialty (major theme)

Differences in attitudes to clinical trials between medical specialties were highlighted by respondents. Several surgeons thought their speciality had difficulty with uncertainty and equipoise:

> "Surgery's quite an interesting area to do trials because it's very difficult to persuade surgeons about uncertainty and exploring uncertainty, so in the past we've tended to do cohort studies, which really are not randomised in that sense, so we're just looking at case–control or cohort studies over time, but more latterly we've had a bit of a breakthrough, I think, in that we've been able to use this pragmatic trial design that Adrian Grant's worked through up in Aberdeen. This is about allowing surgeons to randomise in quite narrow areas of uncertainty, so we've more latterly been running randomised controlled trials whereby we're able to persuade surgeons maybe just to be uncertain about one area in quite a complex operation."
>
> (HD4)

> "We're recruiting patients to study and it's taken a long time to recruit the right number. And it comes down to the patient in the end, some are happy that you genuinely don't know which way is the best and some find that difficult to accept and want to be treated along more conventional lines and therefore they don't end up going into the study … ."
>
> (HD12)

This PI, a clinician, explained another aspect of dealing with uncertainty, the professional rivalries and entrenched attitudes of clinicians and research centres:

> "We had some centres that said they wouldn't participate because their policy was to give intensive imaging follow-up to everybody. Then other centres who said they wouldn't participate because their policy was not to give intensive follow-up to anybody, showing that there's indeed clinical disagreement about whether you should or you shouldn't and basically that has led to different policies. Quite a lot of places have signed up and said they would do it, but then again are faced with the same problem. Surgical trials like that are very different from pharmaceutical trials. In the pharmaceutical trials – so let's say you have somebody on all chemotherapy; they normally see one clinician who deals with that. They will turn up, get recruited into the trial and they get given the package of stuff to take. And that's basically it. Surgical trial, there might be 10 or 12 surgeons in a major centre who are doing that sort of operation. Some of them might have signed up for the trial some of whom might have doubts about it's clinical worth, some of whom may have personal enmities with the lead investigator in that centre and there is no coordinated system of ensuring that those people get picked up by a research nurse."
>
> (HD10)

Contextual factors

The factors discussed here – clinical duties, research culture and communication – emerged from the interviews but were related more to social or institutional arrangements than individual incentives. Such contextual factors can encourage or hinder involvement in clinical trials.

Clinical duties (major theme)

The tension between clinical work requirements and research was a major theme that emerged from the interviews:

> "It's to do with their values. For some people every moment, every pound spent other than clinical care is a waste of time and money and for other people they think that engagement in other work, teaching, etc., is an essential part of their professional role and that

they should take part to the extent that they have opportunities and aptitude."

(GP5)

One respondent pointed out that some doctors with whom she worked felt that spending too much time on research activities could affect clinical skills:

"We don't have practising doctors here in this institution. And even at the [*anonymous unit*] most of the clinicians who were working there tried for quite a long time to keep a finger in and then felt they were being de-skilled on the clinical side and didn't want to carry on doing that indefinitely because they just didn't feel they were doing enough of it to be able to do it well."

(HR3)

The interviews showed that that within the culture of the NHS, clinical work took priority. It was reported that 'own-account' work in the NHS was discouraged because of financial and clinical pressures (HD7). One respondent said he had heard of people who had been told they must not do research because it interfered with their clinical workload (HD10). Both GPs and hospital doctors reported that clinical work took precedence:

"… but again, you have got to recognise it's taking time out of people's day job and so if you are not doing, unless you have got that built into your job description – say you must do this for part of your time, you have to justify what you are doing because if you are recruiting people into trials you are not healing the sick, and ultimately the NHS is about healing the sick."

(GP10)

"… no matter how hard I work there is always a pile of notes I need relating to patient care, and it is only lately that I have begun to argue in my job plan to get time off to do the proper audit work for instance … to monitor my own performance and my department's performance in [*procedure*] for instance … at last in the next few months I may have some dedicated time to monitor and appraise the performance of the [*procedure*] unit. As it's meant to happen, but it's only just become available. Clinical care has dominated."

(HD13)

Clinical work was seen as a priority, and came first in terms of time and job planning. This often left little or no time to participate in research, or to spend the extra time required to recruit patients to trials unless the time was 'ring-fenced'. Respondents often found themselves doing research work in their own time (e.g. HD9).

"You go out, you visit the doctors in their busy surgeries … you make the effort to go to them, you don't send them just a bit of paper through the post and say, please fill this in. Because it is hell out there as a GP, I know, they are fire fighting to keep on top of their clinical work. And in fact so competitive is it for the attention of the doctors' time, so many people compete for it, that some practices have a 'no research' policy…Time is a limited resource and when people are pushed, and particularly when they feel that their priority setting is for clinical care, they're just not going to deviate from that, and I really don't blame them because I think this is a very worthy aim, good clinical care."

(GP8)

"… there are lots of people in the NHS who I think might have taken the interest in research if they'd had more opportunity. I mean some of them seem to get so quickly into a completely overburdened NHS situation that they lose touch with research and then it's very hard then to get back onto the bandwagon. Both just because of the effort that it takes and because there isn't, there doesn't seem to be much allowance made in terms of their NHS workloads, and the academic clinical practices it's very hard to get into, it's very hard to sustain those two aspects."

(HR6)

This non-research-active hospital consultant, when asked what was needed for him to be more involved in research, exclaimed:

"More time, more time, I'd like to find myself on a Friday afternoon saying 'God, what am I going to do this afternoon, I've done everything, and everybody's letter is done, and everybody's been discharged and there are no problems and now, God, what am I going to do, let's do some audit, let's do the … O.K. we're not handling these patients, so let's intervene and try this and see what happens as a trial'. I'd like to have a dedicated time and I'd like to have a registrar to have a dedicated time … I have a free session tomorrow afternoon, it's my SPA, my personal study time, I can't remember the last time I had an SPA and I've got about three patients to see during the course of the afternoon who are unwell, and my clinics are full, and they'll have to wait until next week to see me anyway, and I can't see them then because they are full, and they need to be sorted out before the weekend … ."

(HD13)

One respondent with a full-time NHS contract, when asked whether he was ever tempted to go down the academic route, responded that research would distract him from his clinical work, his main job satisfaction:

"I love operating, I love looking after patients, and pure academia would distract me from it, would reduce my exposure to patient contact and without having a reasonable sized infrastructure to mean that

you're basically running it while other people are doing it."

(HD14)

Another respondent remarked on the kudos attached to clinical work and the demands that this type of work can make on a doctor:

"Perhaps research hasn't got, for many people, the same level of kudos as clinical care because … they get more money than researchers and I think because dealing with people, with their lives is extremely stressful, things go wrong, they can go badly wrong. And I think dealing with health aspects of care is stressful, demanding and also quite high kudos and pay."

(GP8)

This respondent pointed to the impersonal nature of research:

"But I'm sure when you're doing clinical work, you know, your altruism is much more directed towards the patient in front of you, whereas research of course is directed at patients that you don't see. So, I think … clinicians get used to and like the one-to-one patient contact, again doing research is a bit alien because it's, you know, you're suddenly talking about research, you know, for the future, also including a whole load of people that you've had nothing to do with."

(HR6)

Another interviewee warned against the view of research as a hobby:

"I think if you want to get more people into research, there's a very strong educational component which people, that perhaps it's got to really come across that … research isn't some sort of hobby of, you know the same relevance as moth collecting. You've got to show that actually it really does make a difference to clinical care and if you're committed to clinical care then you should be up to speed with, certainly in aspects of research, although you can't be up to speed with all aspects of research."

(GP8)

Research culture (major theme)

An overarching theme that arose from the interviews was the need for a culture that valued research within the NHS. For some this culture already existed, but many saw a need for an ethos which valued research [issues of training for research have been addressed in the section 'Career progression (minor theme)'. p. 44]. A 'culture of research' would extend to patients as well as health professionals. Respondents suggested that patients should be well informed about trials and actively encouraged to take part.

In some hospitals there was an expectation that every patient should be part of a trial (HD8), but this varied by specialty:

"I would love to see all the patients coming in to have heart operations, you know, getting a letter that says you should expect to be invited to take part in the study. It's because that's how this whole trust works and is conceived and the department works because that's the only way we make progress. You shouldn't feel this is abnormal or unusual and this is why we're doing it, and I think that would be wonderful, but all patients in the NHS should expect to get those letters."

(HR2)

Respondents said that patients were ill-informed about research and had little understanding of what it meant:

"The general public needs to be more cogent of research findings and less inclined to believe fairy stories."

(HD10)

In some specialties, particularly cancer, a culture that valued research already existed and most patients have access to trials. This respondent highlights the positive effect this has had on children diagnosed with cancer:

"… paediatric oncology practice is an example of an area of clinical work that has developed dramatically by the concept that effectively every patient comes in as part of a trial, and the outlook now for children diagnosed with cancer is vastly better than it was 20 years ago, simply because they have vigorously and methodically treated through trials in the last 20 years …."

(HD8)

Evidence-based medicine has been as widely accepted; this respondent made the point that clinicians must take part in research in order to provide the evidence:

"There is a little bit of a dislocation between evidence-based medicine and what that actually practically means for the NHS. People are very willing to become evidence-based practitioners but what they seem to realise less is that in order to develop evidence that also requires them to participate in research and to support research more generally … And sometimes it really takes just being able to make that personal connection with people and make them realise that actually all of this talk about evidence-based medicine and research isn't just something that happens outside of them, it is something that has to involve them, and they just need to wake up to that."

(HR9)

It was suggested that health professionals should see taking part in research as an essential part of their work. Some respondents believed it should be the duty of health professionals:

> "Within my ideal world I would be arguing that look this is altruism – it ought to be part of every clinician's job description – says you must do this … ."
>
> (GP10)

> "… I think it's a sense of professionalism and I would like to see that enshrined in statements about the role of a practitioner. General Medical Council Guide to Good Medical Practice for example, the Royal College of GP's training curriculum. I tried to get statements put in there about the importance of research and that it should be a professional's duty to take part in research just as they should regard it as a duty to take part in education. Because if they're not going to do that then they're undermining the basis for the development of their own profession."
>
> (GP12)

> "I don't think there should be any money that goes into somebody's pocket for joining a study. I think joining studies under the right circumstances should be seen as part and parcel or part of the obligation of anybody's job who's working in the NHS and that's what I thought we were moving to in 1991 when the NHS developed an R&D strategy and with work to educate people who work in the NHS about R&D and the need to answer questions … ."
>
> (HR2)

However, this respondent went on to note:

> "So yes we need an NHS that is completely research conscious, wanting research to happen but that doesn't mean that everybody needs to be a researcher."
>
> (HR2)

Some respondents favoured giving discretionary points linked to pay in consultants' contracts for taking part in trials would increase the importance to clinical trials (HD6). This could be underpinned by government pressure through GP appraisals to make research part of the ethos of the job (GP11).

Some interviewees wanted research to be included in QOF in the new GP contracts:

> "One of the problems we had with the recent piece of work which really floundered was because not only all the GPs had the problems of these contracts and therefore they hadn't got any time or they wanted resources. But secondly, and more importantly probably, that wasn't a very interesting subject anyway to them. It wasn't part of their contract. If it had been a disease category which fitted in with the contract they could have ticked a box here and said, yeah we'll do that research because it would help. And then when we did get to the patients eventually it's found that it wasn't really that, that wasn't the question for them."
>
> (HR6)

Communication (major theme)

Throughout the interviews, respondents referred to good communication as essential in running successful trials. Respondents talked about keeping collaborators informed, building rapport and creating good working relationships. Strong interpersonal and organisational skills were keys as well as keeping people 'in the loop' and sorting out problems as they arose:

> "In order for recruitment to be successful, communication between the clinical interface and the trial management team has to be top notch. Obviously having a person who has a regular appearance in a number of the different centres that you are recruiting to really helps to maintain the profile and they are fully aware of the whole context in which the trial is being conducted so that if there's an issue with recruitment across all sites or some sites, that information – with it lying within one person, is relayed very quickly back into the office and it's somebody who really knows their stuff. It works perfectly well if you have separated Trial Managers and Clinical Research Fellows provided that their communication is good. If you have poor communication between those individuals then you can end up in trouble and yes, recruitment will suffer for it, because the crux, I think, to getting good recruitment is that you act early on any early indication that recruitment is failing or that there is a problem and you've got to have good intelligence and then act early to stop a problem or to reverse a problem."
>
> (HR9)

> "(we've) always had very charismatic, well-organised people doing the day-to-day trial management, and I think, you know, if you've got somebody who can go in and talk to the practices, be receptive to their problems, problem solve, then that seems to work."
>
> (GP7)

Ways of building relationships with collaborators were suggested. One respondent set up an advice line (HD3) and others used newsletters and social gatherings. Face-to-face contact and creating "camaraderie" (HR3) were considered important, involving site visits, organised meals or meetings and study days. One respondent likened this aspect of trial management to a "pastoral" role (GP8) and another emphasised the importance of personal relationships:

> "Basically a personal relationship goes a long way with recruiting either patients or staff to help with

> research or pay out wages or whatever, you know. And treating them well, networking treating them well, and then keeping them in the loop. It is quite easy to miss out a bit of communication with somebody and that will hack them off, so we have face-to-face meetings an awful lot."
>
> (HD7)

However, respondents acknowledged that this was time consuming. Respondents claimed to work hard at this aspect of trial management. Keeping up good relationships within research teams and with collaborators was considered worthwhile and central to motivating clinicians to enter patients into trials. However, it was labour intensive and could be expensive, emphasising the need for good planning and interpersonal skills.

Why respondents took part in this study

At the end of each interview we asked each health professional why they had agreed to do the interview. Besides being of intrinsic interest this provided a way of exploring the extent to which respondents' reasons were congruent with their views. Most emphasised interest in the research topic, followed by personal contracts and obligation/reciprocity, as well as various minor themes (HTA Programme, not pharmaceutical company, 'asked nicely'). These reasons echoed and confirmed the reasons interviewees had given as motivations for being involved in research.

Summary and conclusions

Motivating factors

The major motivating factors were interest in the research question, intellectual curiosity and potential benefit to patients. Medical benefits for patients were linked to patients getting better access to treatments or drugs, as well as closer monitoring. Against this was the risk of being randomised to a non-treatment group. Respondents did not take part in trials specifically to gain skills or knowledge, but sometimes this was an indirect result of participation.

Minor motivating factors included altruism, career progression, recognition and publications. Most believed altruism existed, but was diminishing because of a system increasingly driven by money and the increased regulation of trials. The expectation that clinicians should take part in research was widely shared. Recognition and publications were of a minor importance.

Barriers to taking part in clinical trials

Lack of time was the main reason health professionals gave for not taking part in trials. Trials, it was suggested, should be designed to cause the minimum disruption to practices. The competition for health professionals' time was complicated by targets resulting from the new consultants' and GP contracts. Bureaucracy was seen as a major barrier to research involvement. The EU Directive on Good Clinical Practice, the Data Protection Act and research governance in PCTs and Hospital Trusts were seen as having discouraged research. Differences existed between specialties in the extent to which they were 'research friendly'.

Context

The NHS culture prioritised clinical work but some clinicians thought research provided a welcome alternative. The need for a culture that valued research within the NHS was widely stated. For some this culture already existed, but for many there was a pressing need to establish an ethos where research was valued within their work. Training in research should start early before clinicians got 'bogged down' by clinical work and private practice. Good communication at all levels was seen as essential: this meant keeping collaborators informed, building rapport and creating good working relationships.

Chapter 10

The views of patients and members of the public

This chapter reports on interviews with patients and members of the public about incentives in clinical trials. As discussed earlier, the inclusion of a patient/public element was a late addition to the protocol for this study. Eight people were interviewed, half of whom had been in a clinical trial. Each person was interviewed separately by the same interviewer responsible for all the other interviews.

All interviewees were asked about the incentives and disincentives to taking part in clinical trials, as well as the likely effects of payments to patients and to doctors. They were asked about disclosure to patients by doctors of any payments received for entry of patients to trials. Respondents were asked about their experience, if any, of involvement in clinical trials, and for those who had been involved what information had been provided relating to payments, expenses and feedback.

Incentives for doctors

The majority of interviewees were surprised to learn that doctors might be paid on the basis of the number of their patients who agreed to enter a clinical trial. They considered that the costs of extra procedures or tests and the salaries of research nurses should be reimbursed, but were less happy that a doctor (or practice) could receive any extra payments for enlisting patients into a trial. Concern was expressed about the ethics of such payments. Some confusion was expressed about what exactly a doctor would be paid for. Respondents saw research and improving medical knowledge as 'part of a doctor's job' or even as 'a duty'. Doctors were seen as well paid; references were made to recent pay increases. Other incentives such as career progression or professional status were seen as acceptable:

> "I think it's appalling, I think it's scandalous, and completely unethical … as far as I'm aware the doctors who were involved in the trial I took part in didn't receive payments, but I think there's a lot of kudos which goes with publishing research papers, you know publishing research papers is what helps them to get promotion and get ahead in their field, so although there may not be a financial incentive, there is a career incentive, and I think … . that can be bad enough … I felt at the time that I took part in that trial, there was already too much of … a pally, pally relationship between drugs companies and doctors, and to consider giving financial incentives, I think would just exacerbate a problem, an ethical problem within medical research that already exists."
>
> (PP1)

> "Well, I don't feel very comfortable about it really … because I think doctors are already paid to be doctors and part of being a doctor is to try and progress knowledge about health. I mean that is part of it. Whether they are doctors or doctors with an academic … slant or whatever and I don't think they should get extra reward for doing that. I don't think it's very difficult to put patients forward; they are your own patients anyway. And certainly I think there's a bit of an imbalance if you are not paying the participants but you are paying the doctors to produce a sample basically for you. I think it's … I think it's very indicative of the kind of culture we are now in, but I think it should be part of the expectation actually of being a doctor or a health professional that you are adding to the general good if you like or the general knowledge about health benefits of particular advances of drugs or whatever."
>
> (PP2)

> "But if they are doing it as part of their consultation – I am not so sure about that. I mean thinking of this study I suppose it probably took the GP maybe 5 minutes more to give me this and to ask me to take part. Perhaps 10 minutes more then, so in that case that's a double consultation isn't it, so the surgery should be paid for that I presume, actually, when you think about it. But I am not paid extra to do things in my job... But why do they need financial incentives?"
>
> (PP3)

> "Well I think if I as a patient don't expect to be paid. I am not sure that they should. And I'm not sure how much time and effort they put into recruitment because if this all … l happened as part of my natural dialogue with my consultant … I didn't get written to or, I didn't go and take any more time up, so I am not sure … what they would be being paid for."
>
> (PP4)

Some respondents were aware that doctors may receive financial incentives to participate in clinical trials. They took the view that if clinical trials are to be done successfully then doctors have to be paid to recruit patients:

"The only way to encourage and get the … work done is to pay them. Now, the morality of it … I can't give a view on, but I am sure if you didn't pay them something, they wouldn't want to know."

(PP5)

"You only have to know a doctor to know that (they get paid to take part in trials). Doctors demand money for signing passport forms, doctors don't do anything, they don't sneeze without money!"

(PP6)

Disclosure of any payments by clinicians

All interviewees felt that patients who participated in trials should be given full information including what payments are involved and how these payments were justified (extra staff, extra time, extra tests, etc.). These respondents thought that doctors would be reluctant to disclose because their motives may be questioned and/or patients may expect to be paid – or at least offered expenses:

"I think it's very important because it might make them question the motives of the doctor, which you know in some cases can be healthy."

(PP1)

"I think it should be clear to patients. I don't know whether either of the studies that I have been involved in other people have been paid extra to ask me these questions. I think perhaps if patients knew that doctors were being paid an incentive to ask the patients to be included, then the patients would think well actually I should be paid to be included then."

(PP3)

"Yes, well I don't think patients would be terribly happy if they thought that the doctor was being paid something and they weren't … I would be a bit miffed. Because … it's much more of a risk and a commitment and an out-of-the-ordinary thing for the patient to be involved than for the doctor to be involved in something like that … I think if people did know you might get quite a bad reaction so there's probably quite an incentive to keep it quiet, but that's not really proper either … ."

(PP2)

"Ignorance versus an open approach? Morally, maybe they should come clean, but on the other hand if they are being compensated purely for their time, and their time only, then that doesn't affect the patient on the trial, but if they were receiving a large sum which I cannot quantify what a large sum is … then from a moral point of view then maybe they should come clean."

(PP5)

Patient incentives

When talking about the incentives for taking part in a trial, respondents offered a variety of motivations: 'altruism' and 'getting better care' was cited by six out of eight. Other reasons for being involved included: having a good relationship with the doctor, assisting the researcher and helping the NHS.

All respondents considered trial participation as a form of altruism. Trial findings might not necessarily affect their own treatment but could further medical knowledge or the 'greater good':

"My first reaction was I was really pleased because I had already watched one of my friends die of breast cancer and I thought I was probably going to die so I was quite pleased to … be able to do something for other people so … at the time you're kind-of on a bit of a 'oh right yes well I'll do that'."

(PP4)

"I can see the fantastic benefit of identifying what state the liver is in by a blood test, not by intrusive liver biopsies which are very, very risky, so I could see, wow, this is really good … I'm 99% sure that it has produced good results, so I can feel pleased and proud in some ways that I've hopefully just played a part in doing non-invasive tests that will help so many people."

(PP5)

Another reason for participating centred on getting better medical care. The majority of respondents cited this form of self-interest as a motivation for participation. They expressed the view that trial participation might give them new drugs, better care or at least more medical monitoring and interest than otherwise:

"I think you'd do it for the greater good but also because you might get some better treatment that wouldn't otherwise be available to you."

(PP6)

"… people might not know that you are more likely to get better care … if you take part in a trial, so … for me that would be quite a big incentive anyway so I don't know how well that's publicised."

(PP7)

"The main incentive … in a very personal way would be if you really feel that what was being offered in the trial might add an alternative to what you would otherwise get conventionally … perhaps that is the main motivation that people might hope that for themselves as well they would get something out of it."

(PP2)

One respondent was more concerned with sustaining a good relationship with his doctor than with knowing about any financial payments:

> "I am more interested in the long-term relationship, I think if my GP asked me whether I'd take part in a trial, providing it is relatively minor and not particularly invasive, then if she or he asked me to take part I would probably agree simply because… I want to please them or rather I want to maintain that relationship which is good. So in saying no or whatever I would need a strong reason to … In principle I think there should be transparency but in practice I don't think I would ask what payment they were getting. And I think I know what the answer would be anyway, they would say they were receiving enough to cover their expenses."
>
> (PP6)

A respondent who worked for a patient organisation stated that she would participate in order to assist the researchers:

> "I know from the work I do that they are always desperate for people to go into trials."
>
> (PP7)

Another respondent described her motive as helping the NHS:

> "I wouldn't want to take money because I think we all know the NHS is in such a parlous state … so I just think anything you can do to help has got to be good hasn't it … ."
>
> (PP4)

Patient disincentives

While almost all (seven) respondents stated that they would consider taking part in the future trials, three reflected on how difficult this can be when feeling unwell. One respondent took part in a trial but was too unwell to understand fully:

> "But it wasn't really quite clear … what their best outcome was for me, but then perhaps I wasn't supposed to know that anyway. … at the time I felt really groggy with this, and they probably gave me more information, I read it but didn't absorb it at all and so I think it probably said to me if you can hang on and not take the antibiotics 'til tomorrow, then, you know, it will probably get better by itself. But when you are feeling really rotten and you have to go to work tomorrow, it's very difficult."
>
> (PP3)

The following respondents pointed out that a serious diagnosis such as of cancer could make it difficult to think about joining a trial:

> "Well, they told me exactly what would happen. I don't remember to be honest, I may well have signed stuff, I was poorly, I don't remember because I was quite stressed at the time I think."
>
> (PP4)

> "I think I was very focused on the immediate event. And I think that probably is a problem for people … their energy is kind of used up emotionally and mentally and just getting there, sitting there, doing it, coming home, going to sleep … it was such a shock … the last thing you probably want to do is, you know, within a matter of weeks of getting that shock to be asked to be part of some trial when you are trying to deal with the actual treatment and the kind of implications of it."
>
> (PP2)

These two respondents also raised the issue of 'being a patient' or being given a 'patient identity'. After the shock of a cancer diagnosis and treatment, they wanted to put their illness behind them. Taking part in a trial could remind them of their illness:

> "I don't want to … have that identity really, the cancer patient identity so I want to put it behind me … if you had asked me maybe at the very beginning of my treatment … that might not have come into it to the same extent, although probably then I would have said I feel too preoccupied with the actual treatment to take on something else which would seem like an additional burden in a way … I think it's very hard perhaps to think of the greater good when you're going through it yourself, which is probably mostly what clinical trials are about aren't they. I mean you are not probably going to benefit from it."
>
> (PP2)

> "To be honest I wanted to sort of put the whole thing behind me, I really didn't want any more. I didn't want to go to the hospital any more for any reason, so I actually didn't want to either, and they didn't pursue it."
>
> (PP4)

Patient expenses

All interviewees believed that patient expenses should be paid. They argued that being compensated for expenses would mean that more patients would participate. The cost of hospital car parking was highlighted:

> "I think reimbursing expenses is a good idea, especially if people have to go quite a number of times, maybe it's not very convenient for them and if they are really quite sick, you know, maybe can't drive and all sorts of things like that, I think expenses certainly can help. Especially with an elderly

population and parking costs at hospitals and stuff like that."

(PP3)

"No. No. Nor my parking, which was extortionate … I didn't ask for it, I didn't even think of it."

(PP7)

Payments to patients for trial involvement

Four of the eight respondents had been involved in a clinical trial. None of these four respondents recalled having been given any information relating to payment, whether to them personally or to any payments to their doctors for putting them into a trial. None received any expenses. All felt that expenses should be given to trial participants. Only one of the four respondents who had taken part in trials had received any feedback about the results of the trial.

Interviewees did not think that patients should be paid to participate in trials over and above reimbursement of expenses. Concern was expressed about 'getting the right people' and 'people just doing it for the money':

"I don't think so really but what I would be concerned about is that people need to have realistic costs covered, you know. You can't expect people to pay or subsidise it in any way and I suspect quite often they end up doing that because … I don't know whether they do, but I think they might because I know that in other areas of research where you end up with people you know paying their own expenses to get there or whatever. I mean I think that definitely is wrong, you know, they should certainly have that covered and I don't think you probably need to pay them over and above that."

(PP2)

"I am not sure about paying to take part … I suppose … I know people are desperate to get more people in trials and that some trials don't take off so it would work as an incentive … You know, I wouldn't have a problem with paying people although I could see that there could be and people might get involved for the wrong reasons."

(PP7)

One pointed out that if patients were made aware that doctors are paid then it would not be unreasonable that the patients should also be paid:

"I think perhaps if patients knew that doctors were being paid an incentive to ask the patients to be included, then the patients would think well actually I should be paid to be included then. It's me that's actually taking part, so I think that might influence the patient's decision about whether they should be paid to take part in a trial. It's an odd concept that somebody else is being paid for you to be a guinea pig."

(PP3)

Others felt that rather than paying patients to take part they should be given a token of some sort to value the participant:

"Maybe a nominal, you know, because a lot of people maybe might not take it seriously unless … unless they had some – well, you know, nobody is paying me for this so it doesn't matter if I don't actually follow it to the letter – so maybe a nominal."

(PP8)

"I really felt that people felt they were being a bit valued by getting that, even though it was quite a small amount … But it wasn't the monetary value really. So I suppose what I am coming round to saying is I quite like that as a sort of incentive and if so … said to me, you know, for sort of *X* amount of hours we would give you a £50 or £100 or whatever voucher for, you know, John Lewis that would be rather nice."

(PP2)

Principles

Several 'shoulds' were suggested by the interviewees: disclosure of any financial payments to doctors for involving patients in trials should be disclosed, patient expenses should be reimbursed and research results should be fed back to patients.

Summary

Respondents agreed that all extra costs for doctors involved in clinical trials should be met. Most were surprised that doctors could receive financial incentives to recruit patients to a trial. All had concerns about the ethics and impact of such incentives. They believed that doctors were well-paid professionals and that involvement in research should be their duty.

The motivations for patient participation suggested by respondents included 'the greater good', getting better care and new treatments, sustaining good relationships with doctors, helping researchers and assisting the NHS. Barriers to patient participation included feeling

too unwell, having 'too much to think about' after a diagnosis and not wanting to adopt a 'patient identity'.

Interviewees believed that patients who participated in trials should be compensated for all expenses. Although some suggested 'token' payments, they did not think that patients should be paid other than expenses to participate in trials. They favoured full disclosure to prospective participants of any financial payments. Full information should be given including whether and how much doctors received for recruiting each patient. They also favoured feedback of research results to trial participants.

Chapter 11

The pharmaceutical industry: its views on incentives and how it was viewed by NHS professionals

This chapter first outlines the views of pharmaceutical company interviewees before summarising the views that NHS professionals had of the pharmaceutical industry (the NHS professionals were the group whose interviews are reported in Chapters 8 and 9).

Views of pharma on incentives to clinicians and related matters

The interviewees were from six different companies, based in the UK, USA, Switzerland and Japan. Interviewees held fairly senior research management posts: a director of clinical research, a medical director, a managing director, a clinical projects lead, a study management director and a head of outsourcing.

The companies were split between those that did their own clinical research and those that contracted it out to contract research organisations (CROs). Their clinical trials covered primary and secondary care, with the bulk in the latter.

Payments for clinician involvement

All followed ABPI rules, which involve detailed costing of research including any additional tests and time inputs:

> "… everyone pays investigators for patients … what we pay them tends to be based on the amount of work that they have to do for that trial … you can … build up an estimate of what you should be paying based on what you are asking to be done, the tests you are asking to be done, etc., etc., so it's based on time … I say two key things really, one is it's not the investigator himself that gets paid, or it's very rarely the investigator himself gets paid, it's either a research fund which essentially ends up paying to employ people to do areas of research of his interest, or it may go directly to the hospital."
>
> (P3)

> "Well we take various guidelines. We obviously, we're aware of the ABPI and BMA rates for … advice on participating in clinical trials. We also … subscribe to various databases so it gives us an idea of financial compensation and really we sort of use those really."
>
> (P6)

These rules allowed payment per patient recruited to organisations but not to individual clinicians:

> "In terms of payments per patient … that's usually the basis for working out the sums involved, it … will be based on the costs of the study to a large extent."
>
> (P5)

> "… we certainly don't offer any incentives around like if you recruit 5 you will get more money on a per patient basis, or that sort of thing."
>
> (P4)

Costing

Costing was on a cost per procedure or per consultation basis with benchmarking from commercial databases of trial costs:

> "All the major companies know what the going rates are … for various types of studies. And that information is shared in an anonymous fashion anyway. There are databases that you can look at, if you subscribe to them, that will tell you what the going rates are for paying investigators for this type of study and that type of study, and any company can look at … Of course it doesn't tell you who it is, but, you know, if you want to run a Phase III study in, you know, hypertension, or something, you can look at the different costs associated with studies of different types and see what the going rates are for that type of study. And most companies would be similar again, I would think, in terms of the amounts that they pay."
>
> (P2)

> "Ideally we use … the Master Clinical Trial Agreement, which has been agreed by the ABPI and the Department of Health, and we … encourage sites to use that … we cost up the study ourselves based (on) time and events so we go through all the protocol and work out exactly what … . has got to happen in the study … But there's also what we call time-directed things – like patient consent, completing the electronic CRF [clinical research form] … So we go through and work out the numbers. For the procedural costs – they're just listed as these are all the procedures that are going to have to happen in this study and how many of them. And for the time, we allocate a time of how long we think it will take an individual to perform what we need them to perform. And then we allocate that to either physician time or nurse time, or sometimes depending on the study it could be other experts, like radiologists … or nuclear

physicists, or – yes, whatever … You usually use the ABPI rate for investigator costs, for physician costs, and then we usually use the nurse… we can't get like an average for the nurse time, so we tend to select a fairly high grade nurse because they tend to be quite high grade if they're a research nurse, for the nurse. And we just to be fair make a best guess if it's another – physiotherapy or radiologist or something. And that gives us an idea of what we think the study will cost to run. And our R&D organisation actually buys in benchmarking figures and so they will provide us with a benchmark cost as well. So that also again gives us an idea of whether we think we have calculated what we calculated correctly.

(P4)

"… there may be some upfront payment for a start for that centre, that particular hospital. Because often they've got to do quite a lot of work to get the study going, and often they employ other people as well – study nurses and so on – so there may be some element of upfront payment for them. And then the rest of it would be based on recruitment per patient."

(P2)

NHS costing

Large variations existed in research costs by Trust, with suggestions of arbitrary add-ons and overheads:

"… there is no transparency and no consistency across the R&D Trusts … And even quite recently we, we're setting up a study …… two, I'm obviously I'm not going to name the Hospitals, but two major … centres in the UK have costed the study … and one is twice the amount of the other one."

(P6)

"There are [*Hospital Trusts*] pricing themselves out of the market …… trials are expensive enough as it is, …, they all saw trials and thought 'oh, ready source of money, big fat pharmaceutical company, they've got loads of money, we'll have some of that' and that's when they started slapping on these massive overheads, but they very quickly get the answer 'well, I'm very sorry, I'm not going to pay that much, thank you very much, goodbye', and so they cut off their nose to spite their face … .'

'… these days, particularly in the UK, the dear old NHS puts on top overheads on top of what you are paying the investigator, and those overheads, I mean, it's meant to cover the facilities that investigators are using, so that's not unreasonable, but overheads can range from 40% to 100% of investigator fee in some institutions … actually the UK is the worst, because of course the NHS doesn't know how much it pays for anything, so if you say how much does it cost to get an ECG done you will get a massive range in costs, so it's actually quite difficult. In the US it's much easier because everything is itemised and there's a sort of going rate, and in some places like Germany and France, where the health systems are different, then they know pretty much what a test costs, but in the UK they haven't got a clue. It's frightening really."

(P3)

Clinical research in the UK was seen as facing considerable competition from other countries:

"We (UK) are seen as a good place to do research, a very good place to do research, but if it takes longer to get things approved and costs more, then there's a temptation for people to go elsewhere."

(P2)

"… to be honest, if you want patients enrolled in studies you are better off going to central and Eastern Europe. And all those countries are now in the EU. A lot of it is simply because of the way their healthcare systems are set up, because a lot of them, particularly in the East, still have centralised healthcare systems, so you get the clinics in hospitals with very large referral areas … excellent record keeping, very incentivised investigators. What you get from the UK is a bit piecemeal and is not actually very efficient … it will continue because the UK has got this reputation, and companies want to say that some of the patients came from the UK. It was in danger at one stage of getting squashed by the hospitals being greedy … and then they realised that they couldn't be greedy then I think they've stepped back a bit."

(P3)

"I think that there tends to be a range that's considered reasonable from within our European headquarters and I think consistently the UK will always be forced up into the upper reaches of that range and sometimes go beyond it because the investigators cost their involvement at a more expensive rate than many of the other European countries."

(P5)

Disclosure to ethics committees

Details of all payments have to be included in ethics committee applications and unduly high payments would be noted:

"… but I think another very important thing to realise which many people may not realise, is when you apply for ethics committee approval these days, you have to be transparent about what the investigator is getting paid, so ethics committees know how much they are getting paid, so they are sort of the ultimate arbiter, if they thought that you are paying too much as an incentive rather than just paying for the work, you'd get pulled up on that, so it's all transparent these days. That's why I say you very rarely pay the actual investigator…."

(P5)

"In the Phase I setting, because that information on how much a volunteer is compensated is broadly

similar, I think across units, and of course ethics committees would comment and could reject the protocol if it's thought that the compensation is too high for the inconvenience. I suppose, you know, one of the issues is the investigator fees in hospitals and general practice, which of course also has to go through the same system now."

(P2)

Payments to individual clinicians

Payments to individual clinicians were seen as unusual – instead, payments were to the host institution:

"It's not the doctors that are being paid … It's the trusts, so the money goes into the trust, theoretically then the consultant can, or the department can actually then dip into for funding various parts of the department. You find a lot of these, a lot of research groups actually, you are actually funding departments, you're funding personnel, you're funding equipment, so it's really taken out the hands of the physician."

(P6)

"… we will have an agreement with the investigator which will also include an element for their time and the time of their staff that should cover all the costs that are involved that are study related … I think the way that the clinicians view it is that they have all their costs covered plus what they would probably describe as a little bit of profit. And the profit I think is based on estimations of their time, and they do see the studies as a way of generating some income for their Departments, and I think that the majority of them would look at that as a way of supplementing their research funds in general so that they could then go ahead and do some of their own investigator-initiated studies, following up their own ideas."

(P5)

Other ways of rewarding clinicians

Other ways of rewarding clinicians were sometimes used but their scope was seen as having been much reduced:

"But of course there are other ways of compensating them, like for instance, you know, inviting them to come and present at some symposium in an exotic location. And this does happen and there's nothing wrong with that but it's an additional incentive, in addition to whatever fee they may get."

(P2)

"Sometimes we can work with our commercial teams because some of the commercial teams will invite people to attend congresses and conferences, and sometimes, you know, if we've got good recruiting physicians we will feed the names through to commercial and say, you know, these people have done very well in our clinical trial programme and we hope they will do well in the future, so if you're thinking about people that you would like to support in terms of an educational grant to go to a conference, this would be someone that we would suggest. But we don't control that budget, but we can just feed some names through and say if you … but they have limited funds so … but then that's usually funding them to … their transport costs and then their registration to the conference. We often get requests from nurses to be funded to a conference or part-funded to a training course, that sort of thing. … (Sometimes) things have gone wrong like a drug supply hasn't got out and they've had a patient waiting there, and we've managed to get the drugs couriered but it's meant a nurse having to work until 6 pm or something, or 7 pm or even 9 pm. We used to buy them boxes of chocolates or bunches of flowers almost like a personal thank you, we're not allowed to do that any more because they could potentially become a prescriber in the future or influence a prescriber. So it's been quite tough actually."

(P4)

"… if you are doing a study in Europe, then you have to get everyone into a succinct central spot to be able to do that, and you do it in the most logical place. There are actually guidelines, because we've just been reviewing some, issued by … the European Pharmaceutical Association … which again just says you have to be reasonable and sensible, so the location has to be logical from the logistics point of view and not some exotic place, you know not taking everyone off to Morocco, you take them to Prague because it is in the centre of Europe, people travel economy class and in fact these days you're not allowed to provide entertainment or anything, they are there to work."

(P3)

Primary and secondary care settings

GPs were considered to be different to some extent from hospital clinicians:

"These GP practices that have set themselves up almost as a business, you know they have clinics and it's almost a business … for private practice."

(P3)

"… some have joined groups, networks, where the administrative burden's taken off them. These SMOs as they are called, Site Management Organisations, that take a lot of the administrative work of the studies away from the GP just to allow them to get on with recruiting the patients, and obviously pay them as a normal pharma company would because the pharma company pays the SMO, the SMO pays the GP … There are a couple of big ones in the UK, they have been quite successful and have got networks. One of them has got a network of, I don't know, 600 or something GP practices I think throughout the country."

(P2)

"… there's always been incentives there for GPs to … prescribe medication or conduct research, there's always been some kind of incentive. I think they're under so much pressure these days, it makes you wonder how they actually manage to find time to conduct clinical research. And I think there's pressure on them to do more and more within their own clinical role and that has meant that they've had to, in many cases, employ or bring people in to run studies, and you see the better organised GP practices with a whole time study nurse. That has to be funded."

(P2)

Perverse incentives

The possibility of perverse effects of incentives was well understood:

"there is a … fine line to be drawn with regard to the level of incentives so that there isn't any sense that the objectivity of the clinicians would be changed in any way and that they might be tempted to recruit to studies that they otherwise would be more careful about … I think that the majority of doctors one would assume would not be influenced by that but I think it's something that should be guarded against so that doctors can remain protective of the patients that they might otherwise be recruiting … I think so far we haven't ever been involved in offering financial incentives directly to doctors for being involved in studies. It will always be by way of funding that will be payable to their research funds so there are no personal payments ever given to clinicians that are involved in studies."

(P5)

Reasons clinicians get involved in pharmaceutical company clinical trials

All interviewees saw access to new drugs or therapies as an important motivating factor for clinicians to enter their patients into trials:

"[*Patients*] often come with stuff pulled off the web I understand – certainly in oncology they're very informed and they will pick and choose what they think is the best study for them so I think you've got a much more informed patient. And in certain things like oncology I think there's probably been an increase in interest in doing a clinical trial because they have seen that that's the way to access things that they perhaps won't get."

(P4)

"… in all therapeutic areas that we're involved in that there will be people who are genuinely interested in the results of it and will see the possibilities of a new product as offering some hope for their patients and I think that's certainly striking in [*disease area*] where a product might have some advantages over an existing product … ."

(P5)

"A lot of physicians want to get involved purely to get their hands on the drug, you know, and the fact the drug's actually going to be provided free of charge."

(P6)

Altruism was not seen as particularly important:

"… I suppose it depends what interests them, and they are just sensible, practical people, so they may well do a publicly funded study … they probably don't get paid as much as they would for a pharmaceutical study, but they balance it, and they say, 'well I want to do this because I'm interested, so I'll do this publicly funded one because I'm interested, but I've got to make a living, and I've got my own research interests, so I'm going to do pharmaceutical company studies to fund that part of it'."

(P3)

"There is obviously also an inherent distrust of the industry amongst some physicians. A lot of physicians want to get involved purely to get their hands on the drug, you know, and the fact the drug's actually going to be provided free of charge … ."
I: "Do you think altruism comes into it?"
R: "Sometimes. I don't think it's that, again maybe it reflects the therapeutic areas that we work in. There's a lot of therapeutic areas which are rather specialist. And you know … it's almost a camaraderie rather than anything else."

(P6)

"Altruism … in all therapeutic areas that we're involved in that there will be people who are genuinely interested in the results of it and will see the possibilities of a new product as offering some hope for their patients … The problem is that people are very busy and sometimes these altruistic motives are not enough and they need to be in a position to justify to others their involvement in research activities and that's when some of the more practical considerations that we've already mentioned I think are also relevant."

(P5)

Unnecessary bureaucracy

Bureaucracy within NHS organisations was seen as a recurring problem:

"… there was obviously one time where ethics committees were quite inconsistent and seemingly uncontrolled, at least from a distance. You know the good news is with COREC which is the Coordinating Ethics Committee body, that the ethics committee process is incredibly good, very well streamlined, very open and you know everybody's happy with that. But what's happened now is that the R&D Trusts have taken over and that they are now causing the delays and the problems."

(P6)

"I think the only attitude is they realise they have to do a hell of a lot more work now in terms of filling in bits of paper, and that puts some people off, the amount of documentation they have to do … and we have to document everything and we, you know, after a monitoring visit we have to write to them and tell them what we found and blah, blah, and they have to file it all."

(P3)

EU Clinical Trials Directive

The EU Clinical Trials Directive and its implementation in UK law were seen as having increased the regulation of clinical research, and particularly academic research:

"Everything is much more regulated than it used to be. I mean there weren't any regulations in those days, not in terms of setting up and running the studies, although companies were doing things in similar ways, you were never exactly sure. And now of course everything has to be run according to the Directive across Europe … (which) has had some benefits on clinical research because it sets a pattern across the whole of the EU countries for clinical research. But it has made some things more difficult conducting studies, particularly in academia. Not as much in the commercial setting, although there have been problems there as well … there have been problems certainly in academia in conducting studies because it imposed on them a lot of additional requirements which they didn't have to comply with before. And a lot of the things the commercial companies were already doing."

(P2)

"The implementation of the EU Clinical Trials Directive has made trusts much more aware … especially for where they act as sponsors, they're much more aware of the implications of … actually supporting a study … it's not just financially but legally the legal documentation is really getting quite excessive … academic research which is again a very, very important aspect of research in clinical research within the UK; that's becoming more difficult with the hurdles that have been implemented by the EU Directive."

(P6)

UKCRC and research networks

Most but not all interviewees had heard of the UK Clinical Research Council (UKCRC) and the NHS research networks. Slow processing of requests and excessive bureaucracy were criticised:

"For oncology … a lot of the centres we use are part of the National Cancer Research Network. … Sometimes … the NCRN studies can really hurt us recruitment-wise, because they tend to be given priority at the site. And if we know that they're a leading light in one of an NRCN study, we may actually elect not to go to that site … (NHS research networks) will get there but they are painfully slow … we can't wait 3 months for something to go in for a peer review. Our company expects us to have that study up and running and recruiting patients within that time frame. So to actually wait 3 months for a peer review before the Network will agree to think … they even have an interest in participating in this study is not going to work."

(P4)

I: "Do you think this UKCRC initiative is going to be helpful?
R: "Possibly. Possibly, as long as it's not too bureaucratic."

(P6)

Payments to patients

Any payment of patients for trial involvement was seen as unethical (which needs to be distinguished from payment to volunteers in Phase I studies.):

"It's not ethical. Basically we don't, as far as I'm aware, not only do we in industry not pay patients but also I think … it's considered totally unethical to pay patients for participating in studies. There are obviously situations where patients receive travelling expenses but not, no incentive to participate in studies because that obviously goes totally against the ethics of the study."

(P6)

I: "Do you pay the patients any expenses?"
R: "Travel expenses only."
I: "And do you find people take it up?"
R: "Yes on the whole. Certainly for some of these studies where we're um … you know, people are quite poorly, and we say well look you know you don't have to come on the bus and you don't have to fight for a parking space, you can come by taxi and that sort of thing. So yes, people do use it."

(P4)

Disclosure

Mixed views were expressed as regards disclosure to patients of payments to clinicians:

"Well, I think they should know that there's compensation. I'm not sure they need to know how much that is. I mean, because for instance for volunteers of course the doctors that are putting them in the trials are paid a salary so it doesn't really count there. So, ignoring the volunteers and talking about the patients, I think they need to know that this is a commercial study for a compound that intends to be marketed and sold and the doctors are being paid a fee for their participation in the study and that if they complete the study correctly, i.e. the patient completes the study correctly, and that's a responsibility of both the patient and the investigator, then they will be paid a fee. I'm not sure that they

need to know how much that is, I'm not sure how useful that would be to them to know whether it is, you know, £500 or £700 or whatever it may be."

(P2)

"And in fact really to be quite honest I think it would be so useful for patients to know that for example (company *X*), they are involved in the study and (*X*) is actually paying for the nurse who is actually looking after them, you know, from that aspect I think that would be incredibly positive and build up good relationships and awareness with patients for them to appreciate what industry does do as far as supporting clinical departments… I think a lot of patients don't appreciate exactly how much it costs to develop a drug. You know, and then obviously they hear in the media about a particular drug costing seemingly a hell of a lot of money, and it is a lot of money for some drugs, but it's putting that in context, it would be very useful really because there's a lot of bad publicity out there regarding the financial aspects of the pharmaceutical industry."

(P6)

Quality of research

The quality of company sponsored research was seen as high but often unfairly denigrated:

"Well, there is this highfaluting idea that in some way academia is good and the pharmaceutical industry is bad, but my own observation is quite frightening what's done in academia, with virtually no controls whatsoever. The pharmaceutical industry is highly regulated, we document everything, everything is paramount to protection of the patient, we must have written informed consent for every patient, we must know we've got written, informed consent, we must prove we've got the written, informed consent, we must have ethics approval, regulatory approval, everything under the sun documented, we have to prove that the patient exists, we cross-check data that is written in the report forms that we have, check that it exists in the patient records, it's highly monitored, everyone on earth is looking at it, we can be audited, we audit ourselves, regulatory agencies audit us, national authorities audit us, it's highly regulated, extreme high level of professionalism I think, the analysis of the study, you have to write the statistical analysis plan and say 'this is what I'm going to analyse', you can't search afterwards for the only answer that you want, um, I think pharmaceutical industry's trials are the highest, highest standard. What I've seen occasionally coming out of academia, and what I know academics do is not controlled at all, it's more controlled now because of the clinical trials directive, but historically, they made it up as they went along. They know people keep on doing *t*-tests, Student *t*-tests, or they get a *p*-value they like and say 'ah, that's interesting so we'll report that', we would be shot if anyone found us doing that, and so I get really upset, and it's the elite journals as well, the editors of these esteemed journals, spouting from the rooftops that somehow academia is better than pharmaceutical industry, and I very much doubt it indeed. We have to validate databases, prove that what was written on the case record form is what's on our database is exactly the same and that validate the statistical analysis that was done as well, um, highly complex databases that have to be proven to work. A lot of academia, academic studies are done on Excel spreadsheets which is frightening, because it's not protected, it's not validated, all sorts of things can go wrong, yet in some way academic studies are meant to be better."

(P3)

Finally, some interviewees suggested that those with experience of commercially funded trials changed their views:

"… I think the investigators who participate in pharmaceutical funded studies are the ones with common sense, who recognise what they are doing, understand what they are doing, understand what the relationship is, no one's bribing anyone to do anything, um, they almost see it I suppose as a business, I think they understand what the industry is about, what the trials are about, and it's only those on the outside as usual who don't participate and therefore don't know what is going on who are the ones that stand on the outside and criticise. And you know, you're back to academic studies, you know, they, they try to criticise, but if you actually looked at what they did themselves you could drive a coach and horses through it probably, it's quite frightening, but because he wears a white coat and he's academic and he doesn't work for the pharmaceutical industry he must be O.K."

(P3)

Views of NHS professional on pharma

This section reports on the views of the researchers on the pharmaceutical industry, which emerged in the course of the interviews with the health professionals discussed in Chapters 8 and 9.

Discomfort

NHS researchers were almost all uncomfortable working with pharma:

"Commercial … it's like a dirty word really doing commercial research … And certainly I think the NHS hasn't really come to terms with where does this fit in – this commercial research?"

(GP6)

"I don't like working with drug companies, I don't like the way they operate and my limited involvement with being, tempted to be enticed to do various things by a company has just reinforced that view … ."

(HR6)

"I mean I did tinker, when I was an SpR [specialist registrar], there were lots of drugs reps and they used to take you out to dinner and pay you for giving talks and things like that, I did tinker with it and try it out, I just started feeling uncomfortable about whether I was prescribing a certain drug because this drug rep had taken me out or, if I questioned myself. That's why I stopped, and I don't do it any more."

HD9

"… as far as I'm concerned there's a clear cut between research that is sponsored by the research bodies, be it Wellcome, MRC, whoever and the HTA, and commercial. If it's commercial they are in it to make money so I want to make money as well."

(HD11)

The reasons given were varied, but many had to do with seeing commercial trials as biased and pharmaceutical companies as manipulative.

Commercially funded trials were perceived to be biased

"I don't think I would ever say never, never say no, but I would feel very uncomfortable about being part of a study that was drug funded …. Because we cannot ensure that biases are not being introduced … all research should be epidemiologically sound because patients participate in these studies … if you do badly designed studies, I just think that is outrageous … that case of that academic in Sheffield who wasn't allowed access to the data, … I just don't want to be manipulated …"

(HD9)

"I do tend to read who funded it. I think …. there's more openness and clarity about it now. Certainly in the *BMJ* … it's all very clear who has been paid what. It's not that I don't believe anything that a multinational drug company produces it's just that you've got to realise where they are coming from haven't you? I mean obviously they want their product to succeed so there's always going to be some conflict on one side I guess."

(GP4)

"… it was easier than being funded by a drug company where there's a concern that you might be biased … you certainly look when you are reading a paper to see who funded it."

(HR3)

Pharmaceutical companies were seen as manipulative

"I think the drug companies … clearly have a lot of experience of how to get clinicians to do what they want."

(HR6)

"You only need to read a few articles to realise that drug companies use … highly sophisticated techniques in working with patients and health professionals."

(HD9)

"… there's been a general move away from being manipulated by pharma companies … in general practice myself and all my colleagues near me don't see anywhere near the amount of reps we used to see because we do perceive that kind of threat and the way that pharmaceutical companies do manipulate both the market and both drug prices and the way that changes what we prescribe."

(GP13)

The types of questions asked by pharmaceutical companies were seen as inherently biased:

"I'd have a slight innate bias against pure pharmacological research from a pharmaceutical company that was out just to provide another possible 'me too' kind of preparation."

(GP4)

"If you over-incentivise investigators, you will drive them more towards industrial led trials and that may reduce the quality of trials in terms of gaining important new insights … often pharmaceutical trials are designed to try to position drugs, and they are not going to generate important new insights. … investigators, if they're paid a thousand or two thousand pounds per patient going into a trial, they would be very keen to do that in order to develop their research funds and so on. And that's fine and that may be an acceptable reward for the work they're putting in … Fortunately in this country the public sector research is very healthy and there's plenty of money for research so people are not driven necessarily in this country to rely on [*commercially funded*] trials."

(HD6)

"There's two camps at the [*hospital*] … the people that do a lot of biological research, and pharmacological research, they have quite close links with the drug companies. … (in the) epidemiology and social psychiatry department … drug companies tend not to be interested in funding us because we tend to look more at risk factors."

(HD9)

"I would be very happy to (be) … doing commercially funded trials … when it's in an area that I'm interested in … the key thing is that actually if I'm investigating it I want to have control of the data and the company doesn't have control of what analysis I do … Most of my stuff is about the balance between self-help and managed care, by-and-large trying to encourage people to look after themselves and drug companies really aren't interested in that sort of research at all."

(GP11)

Pharmaceutical companies were seen as driven by profit

"When you're involved in a commercial company you know that their priority is not research, it's not good for patients, you know patients' health, it's not what I call altruistic outcomes. Their bottom line is the money … I feel really lucky that I don't have to deal with those kind of issue …"

(HD3)

"I think, it's a difficult one, yes – I think so, yes [*that the patient knows that the doctor is receiving money for putting them into a trial*] … And the problem with drug companies is you don't know how honest they're being because at the end of the day they are marketing their sales aren't they? And it is hard because we are all doing it from different points of view aren't we?"

(GP6)

Pharmaceutical companies were seen as engaging in poor practices

"I've been asked to do all sorts of things which I think are appalling. I was asked to edit a book, for example, for a company and I said no I didn't want to do it and then they offered me a £200 fee or something, and I said no I wouldn't do it. And then they rang me up and offered me £500 to £800 and then, and then they offered me £800 pounds and said I wouldn't actually have to do anything at all, they'd do it all for me … and I was astonished because I wasn't actually playing that game …"

(HR6)

"There have been numerous examples of pharmaceutical clinical trials where clinicians haven't – you know – tried to generate money by getting patients in and perhaps, you know, massaging the data, not being as accurate as they might have been … . So they are trying to give the drug company what they think the drug company wants."

(GP2)

Non-research-active consultant:

"I have never in my whole medical career been seduced by a drug company, asked to do something that I thought was a bit dodgy, or undue emphasis on anything, I'm always surprised, not surprised, I'm sure it does happen … short of getting a few biros and pads, I've never really seen anybody, or myself benefit in any way from … proper or improper seduction by a drug company. I find it, I mean I'm sure it happens; I just find it a bit of a surprise when it does."

(HD13)

But pharmaceutical company studies were also seen as rigorous …

"I participated [*in commercially funded trials*] with my partner … in the early days and that did involve us doing some checks and going through protocols with patients and we were paid you know an adequate amount per head, certainly probably hundreds of pounds to get each patient through … I was impressed actually, the degree of probity, the careful approach of the company and the paperwork was quite considerable and it was all done in triplicate. You know there were checks and balances and we were kept an eye on basically to make sure we weren't fabricating it which was perfectly reasonable. And I've still got the documents actually locked up somewhere in a box because we obviously were asked to keep it for 10 years I think."

(GP4)

"… generally speaking it's my experience that commercial trials they are run extremely, almost irritatingly, what's the word I'm looking for, professionally … they are absolutely clear, absolutely everything if a patient wants to take up a trial, it must be reported, good clinical research practice and you have no choice, so generally speaking with the companies I've dealt with I think have worked highly ethical, extremely well organised trials, to be honest with you I think always run to a better degree in terms of professional governance than the non-commercial trials, partly I think because of resources, you know companies are much better resourced and there's been too many examples perhaps in not that distant history where companies have got egg all over their faces and these days I think they are very, very careful about what they do."

(HD8)

Pharmaceutical companies studies were seen as well funded …

"But I think if you have got a problem with recruitment it becomes even more of a problem. But on the other hand I accept there are limited amounts of money and public bodies do not have the vast sums of money that big pharma have."

(HD1)

"But I was involved in another drug company trial a while ago which was with [*describes trial*] … for us it was an example of actually being, you know, a well funded trial – we really weren't scrimping and saving, and it doesn't half spoil you for going back to public sector funding. I don't want to be beholden to the drug companies, but having money without having to think too much about it is terrific. Well, it just means you can make things look good, get proper materials in and good staffing instead of crossing or cross-borrowing all the time. So, but that was financially good but politically got quite difficult when the drug became licensed, because then they wanted to sell it, because they wanted to be part of a trial, and so luckily we had very water-tight lawyers who worked with us and they had to give us the drug and the money until the sample size got to its end. But it was a sort of a tricky situation."

(HR3)

…or too well funded

"I know obviously from pharmaceutical trials that the amounts that pharmaceutical companies pay is often in, often completely disproportionate to the amount of effort that goes on in providing information to the patients they recruit. I'm not going to change that, I think it should be disclosed to patients … I'm pretty horrified if people are improving their personal take home income by that method. I personally don't know situations where that's happening and I would have thought RECs [Research Ethics Committees] should stop it happening. I mean, you've got payment coming into a institution and being used for un – what's it called, unrestricted educational purposes or whatever, is one thing, paying school fees out of it is quite another thing."

(HR7)

"The drug companies often pay hundreds of pounds or sometimes even a thousand pounds per patient involved. And that seems to get GPs on board, but whether they're the sort of GP's we necessarily want is another matter."

(GP12)

Some changed their views after working for pharmaceutical companies

"Well, one is the external perception that if you are doing pharmaceutical funded work that somehow it is going to be influenced by the drug company. To be fair my involvement with industry has been that they don't do that at all, they leave you alone – but there is certainly an external perception which then makes it more difficult to get things published."

(GP2)

Summary and discussion

Pharmaceutical companies did not generally pay clinicians directly for being involved in or recruiting patients to trials. Rather the host organisation, the NHS Trust or GP practice, was paid an amount reflecting the cost of the research. These costs were estimated from benchmarking databases, with ABPI/BMA rates per hour of clinician time. Payments to organisations were sometimes on a per patient basis. Some limited scope remained for non-financial incentives such as conference or seminar attendances but these were becoming more controlled. NHS costing was seen as variable and NHS costs were high by international standards, making the UK less competitive.

All pharmaceutical company interviewees saw payments to patients for trial involvement as ethically unacceptable and illegal. Company interviewees were aware of, and frustrated with, their poor perception in the eyes of academic researchers. However, they thought some of these perceptions had been changed by working with the industry.

The views of the academic and NHS researchers on the pharmaceutical industry were highly critical, with many stating they would avoid working with the industry if at all possible. Industry was seen as driven by profit, manipulative, engaging in biased research, and paying disproportionate amounts to those clinicians who worked with them. A few who had worked on pharmaceutical company-sponsored research had, however, been impressed by the rigour of the studies.

The differences in views between the two groups were striking and fairly well understood by each side. The pharmaceutical companies were critical of the quality of academic research and the academic researchers distrusted the pharmaceutical companies. The only sign of reconciliation had to do with the few academic researchers who, after working with a company trial, adopted a less critical stance.

Chapter 12

Summary and discussion

This chapter briefly summarises preceding chapters before discussing the broader implications of the work and suggesting what further research might be useful.

Summary

Chapter 4 reported on a systematic review of the literature on the effects of financial incentives to healthcare professionals for recruiting patients to clinical trials. The literature was very limited in quantity and quality. No controlled trials of incentives were identified. Three surveys considered recruitment rates and reimbursement; two in the primary care setting and one hospital based. These examined the association of demographic characteristics and perceived motivating factors of clinicians with recruitment.

One of the primary care studies reported that successful patient recruitment was determined more by the research group and the research topic than by financial incentives. The other concluded that patient recruitment by GPs could be aided by a range of strategies including financial reimbursement. The hospital-based study found that reimbursement to the participating clinicians was of minor importance for participation in trials or for recruiting patients. The scientific aims of the study were considered to be the most important factor, followed by ethical considerations and communication between participants and researchers. The evidence from this literature was inconclusive as to the effects of financial incentives on recruitment.

Chapter 5 outlined the background codes of practice for clinical research that arose from the historical abuses of human experimentation. The Nuremburg code expanded by the Helsinki Declaration and later international guidelines[26] provided the basis for GCP in research, subject of an EU Directive[27] in 1999 and made law in the UK in 2004.[28] Although payment to clinicians for their involvement in research or for recruitment of patients to clinical trials did not feature specifically in these guidelines and codes, the latter provided the framework for regulating any such payments. Relevant headings in the guidelines included potential conflicts of interest and full disclosure of any such potential conflicts, including financial. These codes have been widely interpreted (Chapters 6 and 11) as prohibiting payment (other than expenses) to patients to join trials. This is distinguished from payments to healthy volunteers to join Phase I trials, which is permitted.

A scoping literature review identified papers exploring ethical issues to do with recruitment to clinical trials. Most papers considered the ethics of funding medical research in general. Fifteen papers[28–42] mentioned ethical issues relating specifically to financial incentives to healthcare professionals for recruitment of patients to trials. These ethical issues reflected the GCP guidelines,[57] specifically potential conflicts of interest, the disclosure of financial incentives to potential trial participants and the likely impact on the informed consent procedure and the doctor–patient relationship. None provided examples.

Chapter 6 outlined how payment of clinicians were dealt with in the UK guidelines, specifically those of the ABPI,[46] the Department of Health[48] and the GMC.[45] Key features included a general prohibition of payments to patients for involvement in clinical trials, but with scope for payment of travel expenses.

The payment of clinicians for involvement in clinical trials whether as investigator or collaborator was more complex. Clinicians could be employees of pharmaceutical companies or contract research organisations, in which case recruitment was part of their normal job. However, given the predominance of the NHS in the provision of healthcare in England, commercial companies generally work closely with NHS clinicians to recruit patients to trials. Rules for payments to NHS clinicians are tightly regulated under the ABPI[46] and other guidelines.

GMC guidelines and NHS research governance regulate clinical staff. All NHS staff are required to record any financial interest in organisations funding research in the NHS. NHS providers are expected to recover the full costs of any research for commercial purposes. The regulations steer

payments toward the host employing NHS Trust rather than the individual clinician. Clinicians can be paid on a per-hour basis for involvement in research but not per patient recruited. NHS Trusts could be paid per patient recruited but bonuses for achieving targets are not acceptable. Although GPs are bound by the same rules, their self-employed status allows greater scope for payments from commercial research. However, GPs are increasingly involved in research networks which pay practices rather than individuals.

Chapter 7 described the methods for the qualitative research. Thirty-eight interviews were conducted with NHS healthcare professionals, identified mainly through NCCHTA records with 'snowballing' to identify other interviewees. All had experience as principal investigators. They comprised a mix of clinical (mainly medical) and non-clinical researchers, drawn from primary and secondary care, and distributed geographically and by specialty and hospital type. Six non-research-active clinicians were included. Two other groups were interviewed, one made up of members of the public, the other research managers from major pharmaceutical companies. The same interviewer conducted all interviews using the same framework. Interviews were analysed using NVivo software[60] by CK and SH with assistance from JR.

Chapters 8–11 described the findings of the primary research. Chapter 8 outlined the views of healthcare professionals on financial incentives, showing that they generally supported paying expenses incurred in research to clinicians and related staff. Payments in excess of expenses were not favoured due to concerns over potential impact on the quality of research, such as in the type of persons attracted or the processes followed. Broadly, interviewees were 'knights' rather than 'knaves', motivated more by altruism than payment, but this was hardly surprising given that they had agreed to be involved in this research free of charge. Many thought payment to clinicians for recruiting would become more common. None thought they themselves would become 'knaves', but they worried that others might.

Payment to organisations rather than to individuals was seen as an important way of limiting the adverse effects of payments. Some clinicians favoured payment to team members such as nurses, partly on equity grounds (low pay) and particularly when those team members did much of the extra work required for the research. Clinicians tended to favour recognition of research activities in how they were paid (Quality and Outcomes Framework for GPs, Clinical Excellence awards for consultants), but some pointed to the possibility of perverse effects.

NHS professionals felt that disclosure to patients of any payments for patient participation in research was important, both in limiting the levels of payments they felt they could accept and as a test of probity. However, even when payment to clinicians was based on cost, they considered this might be difficult to explain to patients. Since few interviewees received payments for involving patients in research, the issue had not arisen much in practice. Full disclosure of financial interests is of course part of GMC guidelines. How well observed this is in practice is not known.

NHS professionals (Chapter 9) were mainly motivated by factors other than money for being involved in research, including interest in the topic, the scientific value of the study and its potential contribution to improved patient care. Professionals valued good communication with the research team and feedback of results.

Chapter 10 reported on the views of members of the public on incentives in research, providing a different but coherent perspective. They agreed with the healthcare professionals on several matters, including an acceptance of cost reimbursement but not of payments above that level. They shared the concerns of health professionals that payments other than expenses might lead to reductions in quality. They differed from the professionals in being unaware that such payments existed – most were shocked at the existence of payments. All were strongly in favour of disclosure by their doctor of any payments whatsoever linked to patient recruitment into trials. On payments to patients, they tended to be 'knights' rather than 'knaves', as was likely given the lack of payment for the interview. None of those who had been involved in trials had been offered expenses.

Chapter 11 dealt with the views of those working for pharmaceutical companies. This group saw matters from a different perspective. Payment by pharmaceutical companies for recruitment of patients was common but was to organisations, both GP practices and NHS Trusts, rather than to individuals. The requirement to disclose details of payments to ethics committees had been important in limiting amounts paid. Concerns were expressed that the prices charged by the

NHS varied widely with no clear relationship to costs. Trusts were also seen as having highly variable prices and some were seen as exploiting the pharmaceutical companies. Where payments were linked to expenses, they were reported to be generous and not subject to checks. Concern was expressed that some clinicians, particularly GPs who were reportedly charging up to £1000 per patient recruited, were pricing themselves, individually and as a group, out of the market.

Pharmaceutical interviewees were highly critical of the standards of publicly funded research, which they saw as *ad hoc*, struggling to meet the standards laid down for GCP, but often unfairly treated as superior when it came to publication of results. They considered that while their protocols and research plans had to be agreed prospectively, publicly funded researchers often engaged in retrospective analyses, which could lead to unreliable results.

Health professionals interviewed were very suspicious of research funded by pharmaceutical companies. Pharmaceutical companies were viewed as having different objectives to do with profits, and many interviewees cited negative experiences with company studies, whether personal or reported. The few who had experience of industry studies had however been impressed by their standards.

Discussion

Both the literature review and the qualitative research reported here confirm previous work on factors that matter to clinicians in recruiting patients to trials. Good research questions were widely cited as critical in this and previous work. Good networking and communication between the researchers and collaborating clinicians were also important. The interviews indicated that failure to pay reasonable expenses to doctors and/or to patients might prevent recruitment, and that payment to incentivise clinicians to recruit patients is fraught with difficulties.

One clear conclusion from the systematic review is the lack of evidence on the impact of incentives on research activity. No attempts appear to have been made to experiment with different ways of motivating clinicians to collaborate or patients to join trials. Despite the large number of trials and widespread reports of difficulties in recruiting patients, the way in which trials are reported does not provide data on those factors known to affect recruitment, such as if and how clinicians were paid, how important they thought the topic to be and if and to what extent patient expenses were met. These themes are picked up below.

Another striking finding is the lack of transparency on guidelines for payments for involvement in research. This is partly due to the issue being consigned to the detail of most guidelines. Our survey of guidelines from key organisations on payments for involvement in research drew a blank. Only a close reading of the ABPI guidelines provides an indication of the rules on payment (see Chapter 6). The Department of Health guidelines focus on commercial research. The GMC guidelines were by far the most specific on payments. However, the levels of payment allowed are not stated in any publicly available document that we could locate. Interviews with NHS health professionals showed little awareness of current practice with such payments and patients/members of the public were unaware of the existence of such payments. Yet interviews with the pharmaceutical research managers showed that not only were payments common, but also they made numerous complaints about prices charged by the NHS being too high. Companies commonly used commercial databases to benchmark the costs of trials.

Payments by companies tended to be to employing organisations rather than to individual clinicians (except sometimes to GPs). Payments to individual clinicians appeared to have been more common in the past. The requirement of full disclosure of financial arrangements to ethics committees appeared to have been particularly important in ending individual payments. This may point to the power of regulation as opposed to guidelines.

Given that the results of interviews with three different groups have been reported, the similarities and differences between these groups are worth considering (or triangulating). Similarities included:

- Beliefs by all three groups that all expenses incurred by researchers and patients to do with research should be reimbursed.
- Awareness that payments could lead to perverse or undesirable effects was shared by all three groups but was strongest among NHS professionals.
- Transparency and disclosure of details of the financing of clinical trials was seen as necessary by all three groups, although some NHS clinical researchers expressed concern that patients

might not understand the basis of the costing. Patients tended to be more strongly in favour of disclosure.
- Agreement between NHS healthcare professionals and pharmaceutical company research managers that two key motivating factors for clinical research involvement were interest in the question and scope for benefiting patients. Other shared motivating factors included minimal bureaucracy, good communication and facilitative research cultures. Altruism was not seen as an important motivation for clinicians.

Differences between groups included:

- Different funding methods for publicly and privately funded clinical research. Payment for all clinical inputs, including treatment costs, was normal in company-funded research. NHS-funded projects were costed in less detail and had treatment costs funded separately.
- Payments to patients, other than for expenses, was seen as unethical and illegal by the pharmaceutical interviewees but NHS healthcare professionals and especially patients had less emphatic views on this matter. Patient expense reimbursement seemed more common in industry-funded studies.
- Members of the public, by contrast with the other groups interviewed, tended to cite altruism as the main reason for participating in clinical trials.

Although payments for participation in commercial research have become more transparent at the level of NHS doctor and host organisation, less transparency exists between doctor and patient. Although the guidelines emphasise patient benefit as an overriding goal and require disclosure of any possible conflicts of interest, none of the patients interviewed with trial experience had any knowledge of the financial arrangements between their doctors and the research funder. NHS clinicians stated that they would find it difficult to disclose financial arrangements to patients. Most believed it should be the norm but worried about how best to explain these payments to patients who might not understand the basis on which amounts were set. Against this, many believed that a useful probity test was whether or not one could comfortably tell a patient how much the doctor was being paid.

Very few data are available on the extent of reimbursement in research projects of patient-borne expenses, such as travel and opportunity costs of time, whether time off work or leisure time. Although many research patients may not be employed due to age or illness, this is not always true, particularly when younger or less ill patients are involved. Although guidelines for health economics encourage inclusion of all costs whether public or private in cost-effectiveness analyses, the perspective encouraged by NICE, that of the NHS and social services, excludes private costs. Collection of data on the extent to which patients are reimbursed for expenses is considered below.

The role of payment to patients (whether expenses or other) needs to be considered in the planning of research alongside other initiatives, particularly those which encourage patient and public involvement. The latter is strongly supported by both NHS R&D and pharmaceutical companies, through organisations such as INVOLVE.

Should payments others than expenses be taboo? Clinical trial involvement by patients, and to some considerable extent by doctors, joins the list of items deemed unsuitable for pricing in a market. This view is inherent in the GCP research guidelines, which are based largely on historical abuses in the 1940s. GCP has been criticised for failing to meet criteria for guideline development, including lack of an evidence base. The view that payments to patients were unethical was stated strongly by interviewees from the pharmaceutical companies, and to some extent by NHS professionals. The members of the public interviewed were more concerned that patients' expenses were reimbursed than with the possible ill effects of payments.

Other healthcare products widely deemed unsuitable for market transactions include body parts for transplantation, blood and reproductive tissue such as semen and gametes. These differ in that there is an increasingly active debate on whether or not markets should be allowed. Such a debate seems overdue in relation to payments for participation in clinical research.

The boundary over payments or not for participation in clinical research is blurred by the acceptance of expense reimbursement, linked to the notion of a 'fair' or 'just' price. This is a concept which most economists would dismiss, arguing that the right price is that required for the market to match demand to supply. Applied to clinical trials, the right price would be that which led to target recruitment within time. Expenses, it should be noted, are difficult to define unambiguously as they can be limited to costs

incurred or extended to include payment for the opportunity cost of time, such as time taken off work or leisure.

The fears about payment have to do with attracting the wrong patients and/or for the wrong reasons, and that patients may not act in their own best interests. However, the acceptance of payments for healthy volunteers in Phase I trials (see Glossary) implies a strong difference in decision-making capacity between healthy people and patients, regardless of disease and severity. Not all patients suffering from any disease are equally at risk of making poor decisions. Although the embargo on patient payments for participating in clinical trials is enshrined in GCP, the issue deserves not only debate but further research, such as patient views on when and if payments might be acceptable, and also what the impact of different levels of payment might be. The current position might be caricatured as seeing patients as uninformed altruists unable to understand how costs are estimated.

The position with clinicians' involvement in clinical trials is broadly similar but with some differences. These include payment being more common in commercial trials, for expenses incurred but often also for clinicians' time. As noted above, payments for commercial trials tend to be to organisations rather than to individual clinicians. A key difference from patients has to do with the power of a clinician to influence patients to join a clinical trial. Patients may rely on their doctors' views on whether or not to join a trial. The ethical issues involved tend to come under the GMC headings of conflicts of interests and disclosure of same, rather than specifically on payments. Again this raises the question of the status of these guidelines. Clinicians might be caricatured as 'knights' in publicly funded clinical trials but 'knaves' when involved in commercial trials. The extent to which these different approaches to payment affects trial recruitment is not known and arguably deserves to be researched.

Turning to the future, greater transparency will be required if NHS clinical research networks are to host both commercial and non-commercial trials. All trials in the NHS in future will have to be run through Clinical Research Networks. Such networks already exist for key areas (cancer, mental health, diabetes, stroke, elderly, children, neurodegenerative diseases) in addition to the planned comprehensive network to include all other diseases. "A key characteristic of the NHS networks will be to support and conduct randomised controlled trials and well designed studies for commercial and non-commercial sponsors. This will include pivotal licensing studies undertaken for industry on a full cost recovery basis." (Para 6.31, *Best research for best health*, 2006[62]).

The funding of commercial and non-commercial trials in the NHS research networks may differ in three main ways. Collaborating clinicians will be costed and paid for only in commercial trials, if existing practice continues. Non-commercial trials rely largely on unpaid contributions from collaborating clinicians, although support staff tend to be funded. Treatment costs will continue to be included in the cost of commercial trials, but in publicly funded trials these have to be sought from separate PCT budgets, often involving delays and uncertainties. Commercial trials will be higher cost, with tighter deadlines and often run by professional contract research organisations. The conduct of non-commercial trials is seldom contracted out but tends to remain the responsibility of the principal investigator. These differences can only be brought into sharp relief when both types of trial are run side by side. The differential progress of these different types of trials could usefully be monitored and researched.

Assumptions, limitations and uncertainties

Strengths of this report include the following:

- It is an independent academic study. Although funded by NHS R&D, there was no interference of any kind with the design of the study, its implementation, interpretation or conclusions.
- The views of pharmaceutical research managers were included, as far as we know, for the first time.
- The report brings together the published literature on the effectiveness of payments to healthcare professionals to recruit patients to trials, with primary research on the attitudes, beliefs and behaviour of healthcare professionals on these matters.
- The literature review was guided by the principles for undertaking a systematic review with methods set out in a research protocol (see Appendix 1).
- The 'triangulation' of interviews between three groups, professionals, patients/members of the public and the pharmaceutical industry, helped to identify both common themes and differences.

Limitations to this study included:

- The sparse literature on trials of incentives, with only three studies identified, none of which was in the UK.
- The three studies were observational rather than experimental, and limited to exploring factors correlated with patient recruitment.
- Identifying the interview groups as planned proved impossible and led to use of a list of principal investigators in clinical trials funded by the HTA Programme.
- It proved difficult to interview inactive researchers. Snowballing led to other principal investigators, rather than to clinicians who might participate as collaborators.
- Although many of the research-active clinicians interviewed had been collaborators in other studies, it is not clear how well their views reflect those of clinicians who act mainly or solely as collaborators.
- Since all those interviewed did so without payment, they were more 'knights' than 'knaves'. Their views may not be representative of those who might respond favourably to financial incentives.
- Determining the point at which saturation was reached in the qualitative interviews was difficult as decisions had to be made before the results of previous interviews had been fully analysed. As noted above, these decisions were made by JR and CK on the basis of weekly discussions.
- An inevitable limitation had to do with the extent to which people interviewed revealed what they truly believed or, perhaps more importantly, how they might behave in practice.

Self-consciousness and reflexivity

In addition to being systematic, qualitative research should also be 'self-conscious', that is, it should consider the impact of the research design and of the researchers on the processes of data collection and analysis.[63] Intellectual and personal biases should also be outlined. To meet these requirements, the backgrounds of each of the researchers are outlined along with the roles played in design and analysis. We also consider what biases might have been introduced and reflect with the benefit of hindsight on how the project specification might have been improved.

The research was designed by JP, a public health physician, and JB, a specialist in systematic reviewing. The research was stimulated by JP's concern with lower-than-planned recruitment to clinical trials commissioned by the NHS HTA Programme and interest in how participation by clinicians might be increased. The context was one in which clinicians, particularly GPs, were being increasingly subjected to financial incentives, notably in the Quality and Outcomes Framework. The research was seen as clarifying the role of financial incentives for the range of 'NHS professionals', largely clinicians who might recruit patients to trials. Although the pharmaceutical industry was not planned to be included in the research, the bid for funding stated that payments were common in research funded by pharmaceutical companies. The inclusion of the views of the patients and/or members of the public was added by the HTA Programme at a late stage.

JP and JB were responsible for the systematic review. Neither JP (who changed posts) nor JB was actively involved in the interviewing or its analysis, which were led by JR with help from CK, who carried out all the interviews. JR's professional background is health economics, with considerable experience of clinical trial involvement. As an economist, he shares that discipline's view that incentives, both financial and otherwise, matter. He suggested the inclusion of pharmaceutical companies in the research and provided initial contacts with the companies. CK and SH, as sociologists with experience in qualitative research, tended to share that discipline's view that individual decisions might be socially mediated. Thus a wide range of professional backgrounds were involved, with different emphases at different stages of the project. All contributed to the discussions on the various drafts of the report, with JR responsible for drafting.

Since the entire team were active researchers, one obvious bias was towards recommending more research. The research recommendations have been formulated with this in mind. Another had to do with the focus on the public sector researchers, although this was altered by inclusion of interviews with the pharmaceutical sector. Nonetheless, a high proportion of interviewees had links to NHS R&D and plausibly reflect its preoccupations. Another bias towards active researchers might be identified in the selection of those interviewed. The original protocol envisaged interviewing clinicians who were active and inactive in research. In practice, it proved very difficult to obtain interviews with the latter group. Thus the qualitative research largely reflects the view of the former group, mainly principal investigators. Further, the fact that these interviewees were not paid meant that there was an implicit bias against including those who might only agree to be interviewed if paid. It should be

noted that none of those approached for interview requested payment.

How might these biases have affected the conclusions? First, we can conclude little about how financial incentives might affect clinicians not currently involved in research, except insofar as they are represented by those interviewed. Further, the context is changing. A strong background theme from the qualitative research is the extent that GCP and ethics committees have made financial payments more transparent and less to individuals than to organisations. The development of the clinical research networks will change the way that trials are run in the NHS. Understanding how non-research-active clinicians in NHS Trusts might be incentivised to join clinical trials will probably require much more focused research.

Second, the interviews with the pharmaceutical companies may be biased due to the small number interviewed and the reliance on personal contacts. Against this, those interviewed were not the personal contacts but rather spokespersons for the companies. Inclusion of these interviews provides a very different flavour to the qualitative research, which was largely consistent across the companies. One company spokesperson who insisted on seeing his interview transcript had to be omitted as he refused all further communication – his interview responses were little different from those of the other companies who were happy to proceed without sight of the transcribed interview.

Third, as noted above, the patient/public group comprised a small group known to have had recent use of NHS hospitals and who might thus have been asked to participate in a clinical trial. They were selected initially on personal contacts of JR and CK, with some leads generated by the first few interviews. Again these provided a different and consistent perspective, but which could be subject to bias.

With hindsight, key terms might have been defined more clearly. Work published[59] since this study started has shown that the term 'incentives' is variously interpreted by professional groups. The term 'healthcare professionals' might have clarified that this included clinical and non-clinical participants, who might be investigators or collaborators (see Glossary). The distinction between the motivations of investigators and collaborators is returned to below as a research recommendation. Overall, despite some lack of clarity to do with the terms, the focus in this research was fairly clear, to do with the potential role of payments to clinicians for recruitment to trials. On balance, we consider the evidence sufficient to formulate implications for practice and recommendations for further research.

Implications for practice

Given the major changes in the past decade to the regulation of clinical trials, more monitoring is required. While progress has been made in registering clinical trials, such as the Current Clinical Trials (CCT) database, few data are available with which to monitor recruitment. Policy changes such as GCP, Public and Patient Involvement (PPI) and revised ethics committee requirements have changed the regulation of clinical trials. Events such as the Northwick Park tragedy in which participants in a Phase I trial suffered serious harm may have altered public perceptions.

As noted in Chapters 8–11, mandatory GCP from 2004 is likely to have impacted particularly on non-commercial trials. Since trials generally take considerable time to complete, these effects are not yet evident. Slower starts, delayed completions, reduced recruitment and higher costs might be expected. Whereas precise comparison with trials pre-GCP would be challenging, crude overall rates would provide some indication of the effects of GCP. Similar points can be made in relation to the growing role of patient involvement, the changed ethics committee requirements and events such as the Northwick Park trial. Although establishing the impact of each of these on trial recruitment would be very difficult, the lack of any ongoing monitoring data on trial recruitment makes it impossible to know if recruitment has become harder or easier.

Monitoring the progress of recruitment in clinical trials should be the responsibility of funders such as the National Institute for Health Research (NIHR) and MRC. These bodies may already do such monitoring: if so the data should be made more widely available. Extension of the CCT database to include regular recruitment updates of registered trials there would be worth considering.

While more attention is required for monitoring, it will be hindered by lack of adequate reporting. The scope for a CONSORT-like statement[64] of how clinical trials should report in relation to factors known to be linked to recruitment has been raised above. We recommend that NIHR consider the scope for developing such a statement and for testing its acceptability and value in practice. Key

items on such a list might include: the extent to which all relevant costs are covered, the payment (if any) for any clinician (doctor or nurse) time. Other relevant items might include: collaborating clinicians' perceptions of interest in the topic and its scope for patient benefit, and of the quality of communication between lead and collaborating clinicians. Collection of routine data on these factors would require tighter specification and operationalisation of these headings and also estimation of any increased costs to trials. A standard classification of the organisation and context of clinical trials could permit reporting of the relevant information at low cost. Although developing a CONSORT-type list of requirements is beyond the scope of this project, the idea deserves serious consideration by research funders.

The gap in knowledge on the extent to which patients are reimbursed for any extra costs should be filled. Research funders should identify studies in which patient-borne costs are more likely to be important. Given that the HTA Programme can pay up to £20 for patient expenses, data should be routinely produced on the extent to which these payments are made. Within such studies, the effects of different levels of reimbursement might be explored.

Monitoring data should include costs. Clinical trials cost millions of pounds and constitute the largest share of the cost to pharmaceutical companies of bringing new drugs to market. Whereas pharmaceutical companies reported that they benchmarked the costs of trials using commercial databases, this is not the practice in the public sector. It should be. Public funders should explore the use of existing databases but may well have to develop their own. More generally, cost data should be published on all publicly funded clinical trials.

Research recommendations

One obvious research need has to do with analysis of the factors associated with more or less successful recruitment to clinical trials. Retrospective research on the portfolio of publicly funded trials might helpfully assess whether or not recruitment has become more difficult, and explore salient differences such as between specialties, single- and multi-centre trials, the importance of expense reimbursement to patients, the role of patient and public involvement and so on. Although databases such as CCT include some pertinent data on RCTs funded by NHS R&D and the MRC, a research project dedicated to the task might enable more relevant and complete data to be assembled for a range of trial types.

Prospective research comparing the progress of different types of trials through the NHS research networks would be valuable. Comparisons of the progress of commercial with non-commercial trials may indicate the relative importance of these elements in which they differ. Running both types of trials through the NHS clinical research networks is a natural experiment that may illuminate the relevant features. Not only will funding of commercial trials differ from that of non-commercial trials, the organisation of each may differ, with commercial trials having stricter protocols, and often being subcontracted to contract research organisations. Where new and not yet widely available drugs are involved, commercial trials offer the prospect of faster access to these drugs. Although these factors might plausibly facilitate recruitment in commercial trials, several other factors may work in the opposite direction. To the extent that collaborating clinicians see the questions asked in publicly funded trials as more relevant, as might be expected, for instance, in those that reflect the needs of the NHS, they may be more willing to participate. It is not clear if communication will be better in commercial or publicly funded trials. Hence not only will many of the motivating factors differ between public and commercially funded trials, some may work in opposite directions. Given this diversity collection of basic data on the progress of different types of trials would be helpful and would go with the grain of extended reporting on other aspects of trials.

More research may be valuable comparing the roles of collaborators as opposed to principal investigators. As noted above, the interviews with health professionals focused mainly on principal investigators. Collaborators are often the clinical leads in subsidiary sites in multi-site studies. Although sometimes credited as authors, collaborators are more often acknowledged as part of a collective, on whose behalf authors claim to publish. The research reported above indicates that collaborators are more likely to be funded for their inputs in commercial trials than in publicly funded trials, but this needs to be established, particularly in the changing context of NHS research networks. The extent to which the time of the lead clinician is required for the study may vary by type of study. In some studies much of the requirements (measurements, interviews) may be carried out by a research nurse. Arguably, what is

required is a typology of collaborator and further research on what might motivate each type. We recommend further qualitative work specifically with collaborators within the NHS research networks, both those who currently collaborate and those who might (this proposed research might be linked to or part of the proposed work on the NHS research networks or could stand alone).

Qualitative research on the experience of being involved in clinical trials would be valuable. This could be from different perspectives, both healthcare practitioners and patients, in order to draw out factors facilitating and hindering recruitment. Such studies might usefully be considered as add-ons to existing trials.

The ethical conduct of clinical research raises many questions to do with the appropriateness of the various guidelines. These questions are likely to become more pressing as health technologies expand to include controversial topics such as stem cell and other transplantations. Qualitative research with healthcare practitioners, patients and members of the public might usefully be funded.

Finally, scope exists for experimentation within trials of different types and levels of incentives. Method of funding might be randomised, such as to payment per patient recruited versus cost recovery. The level of patient disclosure might be randomised. The growing complexity and regulation of trials may inhibit exploration of this type of experiment within trials. Against this, an indication from funders that inclusion of such elements would be welcomed could lead to novel add-on experiments within trials.

In summary we recommend:

- Improved reporting of those organisational aspects of trials that are known to affect recruitment, including the type and extent of payments.
- Retrospective analysis of the factors associated with different levels of recruitment to RCTs, including payment of expenses to patients.
- Prospective comparative research on trial recruitment including between commercial and publicly funded trials within the NHS research networks and also between the roles of investigators and collaborators.
- Qualitative research on participants' experiences of being involved in different kinds of trials, and also to do with the appropriateness of the guidelines on payment for participation.
- Consideration by funders of clinical trials of proposals to include within trials experiments with payments methods, comparing different levels of disclosure and of payment.

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Contribution of authors

John Powell (Fellow in HTA/Consultant in Public Health) developed the research protocol, assessed studies for inclusion in systematic review, extracted data from and quality assessed included studies, synthesised evidence, obtained ethics approval for primary research, was principal investigator in the successful research bid and drafted the report. Jackie Bryant (Senior Research Fellow) developed the research protocol, assessed studies for inclusion in systematic review, extracted data from and quality assessed included studies, synthesised evidence, obtained ethics approval for primary research, was an investigator in the successful research bid and drafted the report. James Raftery (Director of WIHRD) was principal investigator from June 2005, directed primary research, drafted parts of Chapters 5 and 6 and Chapters 7–12 and edited the final report. Chris Kerr (Research Fellow) undertook primary research, analysed primary research data and helped to draft the report. Sheila Hawker (Research Fellow) undertook primary research and analysed the primary research data.

Paper published in another peer-reviewed journal relating to this research

Bryant J, Powell J. Payment to healthcare professionals for patient recruitment to trials: a systematic review. *BMJ* 2005;**331**:1377–8.

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Appendix 1

Research protocol

Research method for systematic review

Research question

The principal research question is: should NHS healthcare professionals receive financial incentives for recruiting patients to clinical research? To answer this question, three specific questions to be answered by reviewing the existing literature are:

(a) What is the effectiveness of payment to healthcare professionals for patient recruitment to trials?
(b) What do guidelines say in this area?
(c) What are the ethical issues?

Inclusion criteria

(a) What is the effectiveness of payment to healthcare professionals for patient recruitment to trials?

Interventions

- Financial incentive strategies to healthcare professionals with the aim of increasing recruitment to clinical trials. Incentives include both direct and indirect payments.
- Payments may be to an individual, a research team or a health service organisation such as a hospital, primary care practice or clinic.

Participants

- Any healthcare professional involved in recruiting patients into clinical trials.

Study designs

- Systematic reviews, RCTs, quasi-RCTs, controlled clinical trials, cohort studies, before-and-after studies, interrupted time series, cross-sectional studies and qualitative studies.
- An emphasis will be placed on studies including an appropriate comparator group, such as people/institution receiving some financial reward with those that do not. Where there is evidence from different types of study design for different types of financial incentive, only studies with the more rigorous designs will be included and extracted.

Outcome measures

- The primary outcome will be levels of patient recruitment.
- Other outcomes will include other measures of recruitment, such as achievement of sample size, proportion of patients with full follow-up, and qualitative measures of professional attitudes and of effects on participants.
- The primary outcome measure will be used for judgements regarding the inclusion or exclusion of studies. However, both primary and secondary outcomes will be extracted from the included studies and analysed in the systematic review.

(b) What do guidelines say in this area?

- We will include guidelines produced by UK research funding institutions (public and private sector) that address the issue of payment to healthcare professionals for patient recruitment to trials.

(c) What are the ethical issues?

- We will search for peer-reviewed papers addressing the ethical issues of payment to healthcare professionals for patient recruitment to trials. This will include research papers addressing ethical issues (mainly qualitative investigations) in addition to commentaries and discussion papers.

Search strategy

Relevant literature will be identified from a range of sources, including electronic databases, bibliographies of articles, grey literature sources and experts in the field. Databases will be searched for published and unpublished studies from their inception to current date (unless stated otherwise).

- Electronic databases will be searched for:

Journal articles and reviews: Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effectiveness (DARE); Cochrane Controlled Trials Register (CCTR); Health Technology Assessment Database (HTA); NHS Economic Evaluation Database (NHS EED); MEDLINE; PubMed (previous 6 months): EMBASE; Science Citation Index (SCI); PsycINFO.

Conference proceedings and meeting abstracts: NLM (National Library of Medicine) Gateway Databases; Conference Proceedings Index.

Other grey literature and books: HMIC (Health Management Information Consortium): Index to Theses; Dissertation Abstracts; WorldCat, British Library Public Catalogue.

Research in progress: National Research Register (NRR); Current Controlled Trials; Clinical trials.gov.

Guidelines: NeLH guidelines finder (http://rms.nelh.nhs.uk/guidelinesfinder/); Agency for Health Care Policy and Research; National Guideline Clearinghouse; Internet searches.

- Bibliographies of relevant papers will be checked for additional studies.
- Experts in the field and key organisations will be contacted to identify additional published and unpublished references. Experts will be identified from authorship details of key articles. Organisations will be identified from lists of UK research funding bodies. This direct contact will be particularly useful for identifying guidelines.
- The search will be restricted to English language studies. This is because the aim is not to provide an exhaustive review of all published literature in all languages, but to provide sufficient systematic evidence from relevant effectiveness literature, current guidelines, and ethical discussions, to inform future practice in the UK. We think the resources required to translate potentially relevant articles could be better spent elsewhere.

Quality criteria

Included studies will be assessed using recognised quality assessment scales and checklists. Systematic reviews will be assessed using criteria developed by NHS CRD (University of York). Experimental and non-experimental studies will be assessed using the Jadad quality score for RCTs, and the modified version of the Spitzer criteria for non-RCTs. Qualitative papers will also be judged against standard criteria.

Analysis

Studies will be synthesised using a narrative approach through subgroup analysis based on types of financial incentive strategy and quality of studies. If appropriate, a meta-analysis will be undertaken of the effectiveness studies. This will be judged in relation to the *a priori* quality and inclusion criteria, as well as study heterogeneity. Papers exploring ethical issues will be subject to a critical narrative synthesis. Identified guidelines will be synthesised as an overview of current policy in the UK. All syntheses will be undertaken by the two principal reviewers working in collaboration.

Application of review methods

- Inclusion criteria will be applied independently by two reviewers, with any disagreements resolved through discussion by the two reviewers, and referral to independent assessment by a third reviewer if necessary.
- Data extraction will be undertaken independently by two reviewers using a standard data extraction table, with any disagreements resolved through discussion by the two reviewers, and referral to independent assessment by a third reviewer if necessary.
- Quality criteria will be applied independently by two reviewers, with any disagreements resolved through discussion by the two reviewers, and referral to independent assessment by a third reviewer if necessary.

Research methods for primary research

Research questions

(d) What are the attitudes, beliefs and behaviour of healthcare professionals in relation to financial incentives for recruitment to trials?

(e) How are financial incentives viewed in relation to other barriers and facilitators to healthcare professionals recruiting patients to clinical trials?

(f) What is current UK practice regarding the payment of financial incentives to healthcare professionals for recruitment of patients to trials?

Method

In order to answer primary research questions (a)–(c), a qualitative approach will be taken. The qualitative investigation will involve semi-structured interviews with purposive samples of healthcare professionals and healthcare consumers.

The semi-structured interview schedules for professionals and for consumers will be devised by the research team based on the findings of the literature review. A semi-structured approach has been chosen in order to cover specific questions of interest while allowing for in-depth discussion of issues as appropriate. There will be flexibility in this approach to allow for emerging findings from the interviews to influence the issues explored in later interviews.

Purposive sampling will be used to identify health professionals with a range of experience in relation to clinical research and the receipt of incentives, and healthcare consumers with a range of experience of healthcare settings and involvement with clinical research. Maximum variation sampling will ensure all perspectives are considered and to sample individuals with varying characteristics in terms of gender, age, ethnicity, professional and social background, and geographical location within the UK. Health professionals and health consumers who have chosen not to participate in clinical research trials although they would be in a position to do so, will also be included in order to understand their perspective.

The sampling of health professionals will use databases of completed and ongoing research trials to identify clinical investigators. The principal source will be the NRR. This a public register of trials which gives details of trials and the lead investigator including contact details. Professionals who do not take part in trials will be identified by 'snowballing' with study participants, asking them to identify other individuals.

Sampling of healthcare consumers will initially start through contact with two key consumer organisations. These are CERES (Consumers for Ethics in Research) and INVOLVE (formerly Consumers in NHS Research). Further sampling will be guided by the need for a maximum variation sample. Consumers who have experience as participants in clinical research trials, as well as those who have declined to participate, will be included. Also consumers with current health problems who are accessing different parts of the UK health system, and members of the public who are not currently accessing health services, will be included. Potential participants will be identified by 'snowballing' from initial study participants.

To strengthen validity, negative or deviant cases who report data which might contradict emerging findings, will be sought. Interpretation of why these cases are deviant will provide further insight to the findings.

Multi-centre Research Ethics Committee (MREC) approval for interviews held with NHS staff, and for interviews held with healthcare consumers, will be sought.

The total number of semi-structured interviews carried out will be guided by the emerging findings which will determine when saturation is reached, that is, when new data add little to the findings already identified. The aim is to conduct interviews in a face-to-face setting where possible. Telephone interviewing will be used if a face-to-face meeting cannot be arranged. Interviews will be audio-recorded and transcribed for analysis. All eligible participants will be given written information on the study. Also, participants will be asked to give their written consent for recording, transcribing and analysis of the interview.

In order to answer research question (f), a brief questionnaire will be sent to all major UK funders of health research. This will ask whether they have a policy regarding payment to healthcare

TABLE 9 *Framework approach to analysis of qualitative data*

Stage of analysis	Description
Familiarisation	Immersion in the raw data by listening to tapes, reading transcripts, studying notes, etc., in order to list key ideas and recurrent themes
Identification of a thematic framework	Identifying all the key issues, concepts and themes by which the data can be examined and referenced. Carried out by drawing on *a priori* issues and questions derived from the aims and objectives of the study and also issues raised by the respondents themselves and views or experiences that recur in the data
Indexing	Applying the thematic framework systematically to all the data in textual form by annotating the transcripts with numerical codes from the index
Charting	Rearranging the data according to the appropriate part of the thematic framework to which they relate, and forming charts. The charting process involves a considerable amount of abstraction and synthesis
Mapping and interpretation	Using the charts to define concepts, map the range and nature of phenomena, create typologies and find associations between themes with a view to providing explanations for the findings.

professionals for patient recruitment to trials, what this policy is and whether they can supply us with relevant documentation. The wording of this questionnaire will be developed from the literature findings. It will be piloted on a convenience sample of individuals before being posted to named individuals in relevant organisations. Two reminder letters with copies of the questionnaire will be posted to non-respondents.

Analysis

The interview transcripts will be analysed using the framework approach.[65] This is a grounded method for analysing qualitative data consisting of familiarisation with the data, identification of a thematic framework, indexing, charting and mapping and interpretation. It provides a systematic and comprehensive way of analysing interview transcripts.[66] This five stage approach is summarised in *Table 9*. Two investigators will undertake this analysis.

To ensure the methodological rigour of this project, we will employ the following techniques:

- purposive sampling
- thorough description of methods of data collection and analysis, including description of study sample to allow generalisability of study to be assessed
- grounded approach to analysis including multiple coding
- reflexivity, that is, consideration of the investigator's role in the research.

Replies to the survey of UK funding bodies will be analysed descriptively in tabular form using SPSS software.

Appendix 2

Sources of information, including databases searched and search terms

The databases and search strategies in *Table 10* were searched for published studies and recently completed and ongoing studies. Details of search strategies are available on request.

Searches were restricted to the English language. Bibliographies of related papers were assessed for relevant studies.

Search terms used for payment to healthcare professionals to recruit patients to trials were Incentive$, motivat$, payment$, remunerat$, barrier$, physician$, doctor$, clinician$, nurse$, researcher$, ((healthcare or health care) adj3 (professional$ or worker$)), (subject$ or patient$ or participant$ near recruit$ or participat$ or enlist$ or enrol$), patient selection.

Additional search terms for ethics searches were ETHICS, ethic$, MEDICAL/ or ETHICS, RESEARCH/, CLINICAL/ or ethic$, PROFESSIONAL ETHICS/.

The process of identifying and including studies for assessment of effectiveness is illustrated in *Figure 1*. The primary reason for excluding studies was that they did not meet the inclusion criteria (e.g. they did not pay healthcare professionals to recruit patients to trials). A list of studies excluded at various stages of the process can be found in Appendix 3.

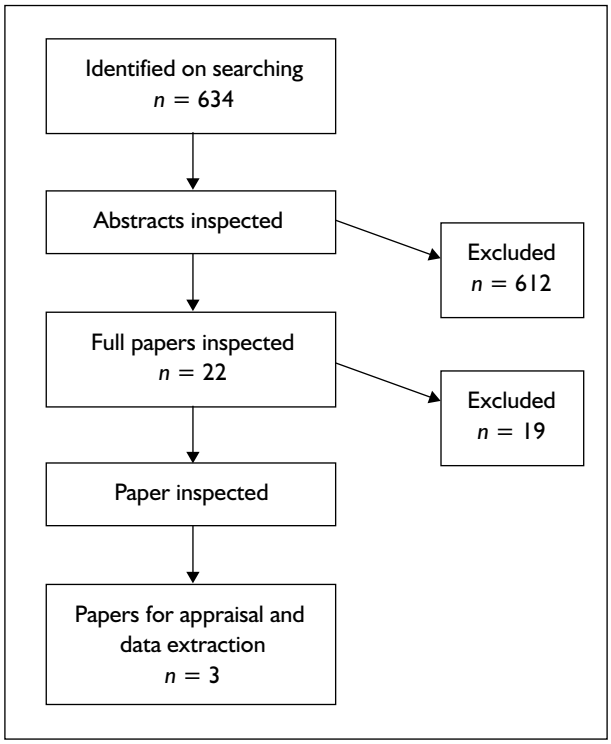

FIGURE 1 *Flowchart of identification of studies on effectiveness of incentives to healthcare professionals to recruit patients to trials*

TABLE 10 *Databases searched*

Databases searched	Effectiveness and ethics, issues or dates searched
Cochrane Library (Database of Systematic Reviews and Controlled Trials Register)	Cochrane Library, Issue 2, 2006 (06/2006)
MEDLINE (OVID)	1966 to 02/06/2006
EMBASE (OVID)	1980 to 02/06/2006
CINAHL	1982 to 02/06/2006
PsychINFO	1985 to 02/06/2006
Web of Science, ISI SCI/SSCI	1981 to 2006
Web of Knowledge ISI Proceedings	1990–2006
Medline in Process (OVID)	June 2, 2006
Conference Papers Index	1982 to current
Current Controlled Trials	http://controlled-trials.com/ (02/06/2006)
Clinical trials.gov	
HMIC Health Management Information Consortium	June 2006
National Research Register	Issue 2, 2006 (02/06/2006)

Appendix 3

List of excluded studies

Asch S, Connor SE, Hamilton EG, Fox SA. Problems in recruiting community-based physicians for health services research. *J Gen Intern Med* 2000;**15**:591–9. (systematic review of different interventions)

Ball JG, Snell ES. Payments to doctors and the responsibilities of ethics committees. *Br Med J Clin Res Ed* 1983;**287**:1884. (comment)

Bell-Syer SEM, Klaber Moffett JA. Recruiting patients to randomised trials in primary care: principles and case study. *Fam Pract* 2000;**17**:187–91. (no financial incentive)

Borgiel AE, Dunn EV, Lamont CT, MacDonald PJ, Evensen MK, Bass MJ, *et al*. Recruiting family physicians as participants in research. *Fam Pract* 1989;**6**:168–72. (paid physicians to recruit physicians)

Deehan A, Templeton L, Taylor C, Drummond C, Strang J. The effect of cash and other financial inducements on the response rate of general practitioners in a national postal study. *Br J Gen Pract* 1997;**47**:87–90. (survey; bibliography used)

Dickert N, Grady C. What's the price of a research subject? Approaches to payment for research participation. *N Engl J Med* 1999;**341**:198–203. (discussion article)

Donaldson GW, Moinpour CM, Bush NE, Chapko M, Jocom J, Siadak M, *et al*. Physician participation in research surveys. A randomized study of inducements to return mailed research questionnaires. *Eval Health Profess* 1999;**22**:427–41. (survey)

Foy R, Parry J, McAvoy B. Clinical trials in primary care; targeted payments for trials might help improve recruitment and quality. *BMJ* 1998;**317**:1168–9. (comment)

Foy R, Parry J, Duggan A, Delaney B, Wilson S, Lewin-Van Den Broek NT, *et al*. How evidence based are recruitment strategies to randomized controlled trials in primary care? Experience from seven studies. *Fam Pract* 2003;**20**:83–92. (non-systematic review)

Hutchison B, Woodward CA, Norman GR, Abelson J, Brown JA. Provision of preventive care to unannounced standardized patients. *CMAJ* 1998;**158**:185–93. (not recruitment to trial; USA preventative care programme)

Keinonen T, Keranen T, Klaukka T, Saano V, Ylitalo P, Enlund H. Investigator barriers and preferences to conduct clinical drug trials in Finland: a qualitative study. *Pharm World Sci* 2003;**25**:251–9. (no financial incentive)

King KA, Pealer LN, Bernard AL. Increasing response rates to mail questionnaires: a review of inducement strategies. *Am J Health Educ* 2001;**32**:4–15. (survey; bibliography used)

Lovato LC, Hill K, Hertert S, Hunninghake DB, Probstfield JL. Recruitment for controlled clinical trials: literature summary and annotated bibliography. *Control Clin Trials* 1997;**18**:328–52. (overview)

McIntosh S, Ossip-Klein DJ, Hazel-Fernandez L, Spada J, McDonald PW, Klein JD. Recruitment of physician offices for an office-based adolescent smoking cessation study. *Nicotine Tob Res* 2005;**7**:405–12. (no financial incentive)

Ross S, Grant AM, Counsell CE, Gillespie WJ, Russell IT, Prescott RJ. Barriers to participation in randomised clinical trials: a systematic review. *J Clin Epidemiol* 1999;**52**:1143–56. (not effect of financial incentive)

Taylor KM. Physician participation in a randomized clinical trial for ocular melanoma. *Ann Ophthalmol* 1992;**24**:337–44. (no financial incentive)

Taylor KM. Integrating conflicting professional roles: physician participation in randomized clinical trials. *Soc Sci Med* 1992;**35**:217–24.(mail survey; bibliography used)

Tognoni G, Alli C, Avanzini F, Bettelli G, Colombo F, Corse R, *et al*. Randomised clinical trials in general practice: lessons from a failure. *BMJ* 1991;**303**:969–71. (no financial incentive)

VanGeest JB, Wynia MK, Cummins DS, Wilson IB. Effects of different monetary incentives on the return rate of a national mail survey of physicians. *Med Care* 2001;**39**:197–201. (survey only; bibliography used)

Appendix 4

Summary of literature on incentives to healthcare professionals to recruit patients to trials

Reference and design	Incentive	Participants	Outcome measures
de Wit *et al.*, 2001[20] Survey within RCT and cohort study of dyspepsia treatment in primary care The Netherlands	Financial reimbursement: US$25 per patient recruited to cohort study US$70 per patient recruited to RCT All received project bulletins throughout project	2000 FPs in academic network of Utrecht University invited to participate (one-third of all Dutch FPs) 165 FPs signed research contract 132 FPs returned questionnaire 128 FPs data analysed	Questionnaire 5 months after project on: 1. demographic and practice data 2. initial motivation to participate 3. evaluation of project logistics 4. motivation to participate in future projects Number of patients recruited to study *Analysis*: Association of demographic data, motivating factors and number of recruited patients expressed as OR with 95% CI. (No. of recruited patients per FP was dichotomised: 0 to 4 versus 5 or more for cohort; 0 or 1 versus 2 or more for RCT) Factors associated with recruitment at $p < 0.25$ plus 7 factors from the literature (sex, list size, years in practice, practice location, research experience, high specialisation, financial incentive-driven motivation) entered into logistic regression model Determinants of maximal inclusion reported as adjusted OR with 95% CI

Results

Demographic results	Male responders	87%
	In practice more than 5 years	50%
	Semi-urban areas of The Netherlands	68%
	Involved in other professional activities (e.g. CME/CFP)	77%
	In group practice	50%
	Practices 'specialised'	>60%
	Participants with previous research experience	57%
Motivation for participation	Participation of the academic research group	63% FPs
	Research topic	59% FPs
	Professional obligation	39%
	Personal appeal by the research group	37%
	Presentation of the project	28%
	Financial incentive	15%
	Participation of the sponsor	11%
	Participation of a clinical research organisation	10%

Evaluation of project	Positive (%)	Acceptable (%)	Negative (%)
Overall satisfaction	56	24	20
Consider future participation	60	nk	nk
Quality of correspondence	93	–	7
Project bulletin	83	–	17
Quality of questionnaires	70	27	3

continued

Evaluation of project	Positive (%)	Acceptable (%)	Negative (%)
Quality of planning meetings	28	28	44
Acceptability for patient	17	69	14
Impact of GCP guidelines	16	53	31
Monitoring by CRO	15	72	13
Total time investment	2	51	47

	Number of patients recruited and FP characteristics (univariate analysis): OR (95% CI)	
	Cohort study	**Clinical trials**
Practice details		
Type of practice	0.60 (0.3 to 1.4)	0.7 (0.4 to 1.5)
Number of colleagues	1.0 (0.9 to 1.0)	1.0 (0.9 to 1.1)
Time in practice	0.8 (0.5 to 0.4)	0.7 (0.4 to 1.1)
Location of practice	0.9 (0.5 to 1.5)	0.8 (0.5 to 1.4)
Phase of practice	1.6 (0.5 to 5.8)	1.0 (0.3 to 3.9)
FP characteristics		
Years in practice	1.2 (0.7 to 2.4)	1.2 (0.7 to 1.9)
Sex	1.2 (0.4 to 3.9)	0.7 (0.3 to 2.1)
High specification	1.1 (0.5 to 2.3)	1.1 (0.5 to 2.3)
Active in CME/CFP	2.5 (1.0 to 6.0)*	2.1 (0.9 to 5.0)*
Research experience	1.4 (0.6 to 3.6)	1.5 (0.6 to 3.6)
Number of projects	1.1 (0.4 to 2.8)	1.5 (0.6 to 3.7)
Motivating factors		
Research topic	0.9 (0.4 to 2.0)	1.0 (0.5 to 2.2)
Research group	2.8 (1.2 to 6.6)*	2.2 (1.0 to 4.8)*
Sponsor	2.0 (0.4 to 9.7)	3.1 (0.7 to 14.7)
Clinical research organisation	4.2 (0.5 to 33.8)	2.8 (0.6 to 13.4)
Financial incentive	1.2 (0.4 to 4.1)	2.0 (0.6 to 6.4)
Presentation	0.9 (0.4 to 2.3)	1.3 (0.6 to 3.1)
Personal appeal	0.3 (0.1 to 0.7)	0.4 (0.2 to 0.9)
Professional obligation	1.9 (0.8 to 4.5)	1.7 (0.7 to 3.7)
Patients recruited by 128 FPs		
Total number of patients	793	527
Mean (SD) per FP	6.3 (6.6)	4.2 (4.9)
% FP recruited 0 patients	15	21
% FP recruited 4 or more patients	59	Not reported
% FP recruited 2 or more patients	Not reported	65

Multivariate analysis

Active in CME/CFP* and motivation by research group* associated with number of recruited patients in univariate analysis entered into multivariate analysis with 7 factors (sex, list size, years in practice, practice location, research experience, high specialisation, financial incentive-driven motivation) to give factor which predicts number of patients recruited

Motivation by the participation of the academic research group	Adjusted OR (95% CI) 3.5 (1.4 to 9.0)	Adjusted OR (95% CI) 2.9 (1.2 to 6.9)

Methodological comments

- Study design: survey within RCT/cohort, no comparisons between groups with/without financial incentive
- Data analysis: OR (association between demographic data, motivating factors and number of recruited patients), logistic regression to give adjusted odds ratio. Dichotomising subjective choice

General comments

- Generalisability: All 2000 academic FPs approached (33% of all Dutch FPs), 165 took part, data analysed on 132. May not be generalisible
- Outcome measures: appropriate and objective. Poor measurement of motivating factors; FPs can only choose 3, which does not mean they were not motivated by more than 3
- Inter-centre variability: not assessed. Multicentre
- Conflict of interests: Janssen Cilag sponsored the project

Quality assessment (modified DuRant checklist[19])

	Yes	U/I/S	No	DK/NR	NA	Comments
Is problem clearly stated?	✓					
Are objectives/hypotheses clearly stated?	✓					Objective stated, no hypotheses
Are methods appropriate to test hypothesis?			✓			No comparison group
Is study design clearly described?	✓					
Is study sample appropriate?	✓					All in particular group approached
Is sample size adequate?				✓		No power calculations. Only 8% of group approached
Are study sample demographics described?	✓					
Are outcomes objective?	✓					
Was blind assessment of outcomes used?			✓			
Did questionnaire undergo validity/reliability testing?				✓		
Was attrition reported?	✓					80% response rate
Are adequate summary data presented?	✓					ORs and 95% CI
Were appropriate statistical tests used?	✓					Logistic regression
Generalisibility		✓				

DK/NR, don't know/not reported; NA, not applicable; U/I/S, uncertain/incomplete/substandard.

Reference and design	Incentive	Participants	Outcome measures
Hjorth *et al.*, 1996[21] Survey within RCT of melphan–prednisone vs melphalan–prednisone + interferon for myeloma by the Nordic Myeloma Study Group, 1990–4 Sweden, Norway, Denmark	Financial reimbursement: SEK1000 (US$150) per patient recruited to RCT, with stepwise increase to maximum of SEK 3000 for patients with follow-up time exceeding 18 months Paid to clinic for research and educational purposes Schering-Plough paid costs for study administration and costs of interferon therapy Hospital-based clinic setting	PI at 99 participating clinics 93 investigators responded 3 investigators in Sweden, 2 in Norway and one in Denmark did not respond 92 (31% of those eligible to participate) referred patients	Questionnaire of 66 questions, 32 (42?) questions designed to explore attitudes of investigators to patient accrual Individual responders' conceptions of most important factors for decision to participate in trial explored by ranking list of 5 prespecified alternatives, from 1 (most important) to 5 (least important). Investigators' subjective opinions on important factors for trialists to participate explored by 9 questions Responders' conceptions of most important factors for their participation explored by ranking 8 prespecified alternatives, from 1 (most important) to 8 (least important) 21 force-choice questions concerning process with 2–5 response options which were dichotomised to reflect a positive or negative attitude to the trial Patient inclusion rate Characteristics of main investigators *Analysis*: Student's *t*-test for comparisons of inclusion rate between groups of centres. Mean inclusion rate with 80% CIs (to equate to two means test with 5% significance level)

continued

Results

Demographic results	Main investigators (no.)
University hospital	13
County hospital	80
Specialty – internal medicine + haematology	36
Specialty – internal medicine	54
Specialty – oncology	3
Academic degree beyond MD	16
Not PhD but spending 25% of working hours on research	3
Male	80
Female	13
Age (median)	46 years
Patient accrual	
Patients recruited	1014
% of expected newly diagnosed cases	72
% reported cases included in trial	54
Reported cases not eligible for trial	37%
Eligible but unwilling to participate	8%
Eligible but excluded for physician-related reasons	2%
Inclusion rate	
Mean (80% CI)	40% (38 to 43%)
Danish vs Sweden vs Norway	24% vs 43% vs 41%

[Inclusion rate based on number of entered patients divided by expected newly diagnosed cases (using crude incidence of myeloma multiplied by time period multiplied by population)]

Investigators' perceptions of factors of importance for patient accrual in multicentre studies	Very great or great importance	Little or no importance
Conviction of importance of scientific aim of study	90	3
Simplicity and comprehensibility of study protocol and forms	87	6
Conviction of rightness of ethical aspects of study	77	16
Communication with study organisation by telephone/email	77	16
Participation in regional investigators meetings	77	16
Conviction that study does not bring about any appreciable increase in workload	59	35
Sense of participation in the elaboration and implementation of study	57	35
Improvement of academic qualifications through participation	26	67
Monetary reimbursement for entered patients	14	79

Correlation between investigators' attitudes and inclusion rate	Dichotomised response	Inclusion rate (%), mean (80% CI)	*p* (t-test)
Importance of quality of life analysis in main study:			
Very important (65)	65	44 (41 to 48)	<0.01
Somewhat important (26), not important (2)	28	31 (28 to 34)	
Any preference as to treatment arm patient would be randomised:			
Several times (8), single occasion (41)	49	47 (43 to 51)	<0.01
Never (42)	42	35 (31 to 38)	
Complying with study protocol:			
Very easy (12), fairly easy (50)	62	44 (40 to 47)	<0.05
Neither easy or difficult (26), difficult (5)	31	34 (29 to 39)	
Extra work generated by study:			
Very much, onerous (3), some, acceptable (50)	53	45 (41 to 49)	<0.05
Fairly little (38), very little extra (2)	40	33 (28 to 37)	
Participation of regional meetings for investigators:			
All of them (31), >50% but not all (29)	60	45 (41 to 49)	<0.01
About 50% (17), <50% (4), no meetings (12)	33	33 (28 to 37)	
Benefit to clinic in terms of care given to myeloma patients:			
Very great benefit (9), fairly great benefit (52)	61	43 (40 to 47)	<0.05
Rather little benefit (26), almost no benefit (5)	31	34 (29 to 39)	

continued

Correlation between investigators' attitudes and inclusion rate	Dichotomised response	Inclusion rate (%), mean (80% CI)	*p* (*t*-test)
Did you hesitate to participate in the study due to anticipated increase in healthcare expenses?			
Yes (17)	17	51 (43 to 58)	<0.05
No (75)	75	38 (35 to 42)	
NB: for questions in which the total number of responses is less than 93, all respondents have not answered the question			

Methodological comments
- Study design: survey within RCT. No comparative group
- Data analysis: no logistic regression analysis performed. Student's *t*-test. Dichotomisation subjective choice. Choice of categories to be grouped together seems poor (e.g. low and adequate grouped together)

General comments
- Generalisability: Myeloma Study Group based in Sweden, Norway and Denmark
- Outcome measures: appropriate and objective
- Inter-centre variability: not stated. Multicentre
- Conflict of interests: Schering-Plough paid administration costs and supplied free interferon therapy

Quality assessment (modified DuRant checklist[19])

	Yes	U/I/S	No	DK/NR	NA	Comments
Is problem clearly stated?	✓					
Are objectives/hypotheses clearly stated?	✓/?					Objective stated, no hypotheses
Are methods appropriate to test hypothesis?			✓			No comparison group
Is study design clearly described?	✓					
Is study sample appropriate?	✓					All in particular group approached; self-selected took part
Is sample size adequate?				✓		No power calculations
Are study sample demographics described?		✓				
Are outcomes objective?	✓					
Was blind assessment of outcomes used?				✓		
Did questionnaire undergo validity/reliability testing?				✓		
Was attrition reported?	✓					93/99 responded
Are adequate summary data presented?			✓			Means and 80% CI
Were appropriate statistical tests used?		✓				Students *t*-test. No logistic regression
Generalisability		✓				Nordic Myeloma Study group

DK/NR, don't know/not reported; NA; not applicable; U/I/S, uncertain/incomplete/substandard.

Reference and design	Incentive	Participants	Outcome measures
Pearl *et al.*, 2003[22] Survey within RCT to determine usefulness of BNP in diagnosis of heart failure in the community 1999–2001 New Zealand	Financial reimbursement: NZ$150 per patient recruited to RCT Participants received bimonthly one-page newsletter on study progress Participating GPs acknowledged as co-investigators Participating GPs could receive Maintenance of Professional Standards points for their involvement in study	327 Auckland GPs from 135 practices sent introductory letter and invited to participate 294 GPs eligible to participate (working more than 0.4 wte) 186 (63% of those eligible) agreed to participate 92 (31% of those eligible to participate) referred patients	Questionnaire following completion of study, one for GPs who recruited and one for those who did not recruit. Both consisted of rating scales to determine GPs' attitudes to aspects of study and research in general (some elements common to both): 1. sociodemographic characteristics of GPs 2. process evaluation – study communication, study organisation, patient involvement, GP participation Number of patients recruited to study *Analysis*: Wilcoxon unpaired test for continuous variables and Fischer's exact test for categorical variable in comparison of characteristics of recruiters vs non-recruiters Multivariate regression analysis of questionnaire – statements tested by rating 1–5 (1 strongly disagree, 5 strongly agree); consistency and parsimony were sought from the models. A probability of 0.15 considered sufficient for inclusion in model; statistical significance threshold set at 5% Analyses performed using SAS

Results

	All GPs approached	GPs agreed to participate	Referring GPs
Demographic results			
Male responders	59% (193/327)	61% (113/186)	58% (53/92)
In solo practice	9% (29/327)	9% (17/186)	7% (6/92)
Years since graduation, median (IQR)[a]	18.5 (14, 24.5)	–	19 (15, 23)
FTEs worked, median (IQR)	–	–	0.9 (0.7, 1.0)
Patients referred			
Total patients referred	–	–	307
Median per GP (range)	–	–	1 (1–14)
Median days involved (IQR)	–	–	332 (161, 452)
0 patients referred	–	50.5% (94/186)	–
1 patient referred	–	–	18.8% (35/186)
2–5 patients referred	–	–	20.4% (38/186)
6–10 patients referred	–	–	7.6% (14/186)
>10 patients referred	–	–	2.7% (5/186)

Evaluation questionnaire	Non-referring GPs	Referring GPs
Response rate	27% (25/94)	64% (59/92)
Agreed or strongly agreed that GPs should participate in research	92% (23/25)	97% (57/59)
Agreed or strongly agreed that Dept of GP should be involved in research based in GP	NA	93% (55/59)
Agreed or strongly agreed that GPs should be reimbursed for involvement in trials	76% (19/25)	85% (50/59)
Agreed or strongly agreed that could not participate in research without reimbursement	36% (9/25)	46% (27/59)
Agreed or strongly agreed that bimonthly newsletter helpful	NA	80% (47/59)
Agreed or strongly agreed that MOPS points important	NA	39% (23/59)
Agreed or strongly agreed good study to be involved in	NA	97% (57/59)
Multivariate analysis – overall satisfaction independently related to: involvement of Dept of GP patient benefit		partial r^2 = 25% partial r^2 = 17%
Main reason for not referring	No patients met study criteria	–

continued

Methodological comments
- Study design: survey within RCT
- Analysis: a variety of iterative (stepwise, forward and backward) multivariate regression analysis. No correlation with recruiting rates, just assessment of agreement with statements (including about reimbursement)

General comments
- Generalisability: New Zealand primary care setting
- Outcome measures: appropriate and objective
- Inter-centre variability: not stated

Conflict of interests: not stated

FTE, full-time equivalent; NA, not applicable; IQR, interquartile ratio; wte, whole time equivalent.
[a] No significant difference between GPs approached and GPs referring ($p = 0.77$).

Quality assessment (modified DuRant checklist[19])

	Yes	U/I/S	No	DK/NR	NA	Comments
Is problem clearly stated?	✓					
Are objectives/hypotheses clearly stated?		✓				Objective stated, no hypotheses
Are methods appropriate to test hypothesis?					✓	No comparison group
Is study design clearly described?	✓					
Is study sample appropriate?	✓					All in particular group approached; self-selected took part
Is sample size adequate?				✓		No power calculations
Are study sample demographics described?	✓					
Are outcomes objective?	✓					
Was blind assessment of outcomes used?				✓		
Did questionnaire undergo validity/reliability testing?			✓			
Was attrition reported?	✓					63% of eligible agreed to participate
Are adequate summary data presented?		✓				Means and percentages. No CI
Were appropriate statistical tests used?	✓					Multivariate analysis
Generalisability		✓				Primary care in Auckland

DK/NR, don't know/not reported; NA, not applicable; U/I/S, uncertain/incomplete/substandard.

Appendix 5

Interview schedules used for professionals and users

Incentives for healthcare professionals for patient recruitment to trials

Introduction

Ask whether they've read information sheet

Get consent form signed

Turn on tape recorder and check

Demographic information

- Occupation/role (if appropriate percentage time clinical/research)
- Year of qualifying

[Experience of clinical research]

- **Have you ever taken part in a clinical trial, as an academic researcher or as a clinician, or as a participant?**

  Could you please describe the studies briefly?

  Who funded them?
  (commercial, public?)

  Have you had any experience of incentives and if yes what were they?
  (personally or clinic, how much, what, etc.)

  Primary/secondary care?

[Research participation: motivating factors]

- **Why do you think some health professionals take part in clinical trials and others choose not to?**

  [Prompts]
  What about the recognition it might bring – prestige, awards, promotion?

  Interest in the research question?

  The opportunity to gain knowledge?

  To gain skills?

  Altruism?

  Strengthening links between academics and clinicians?

  *** Effects of GP/consultant contract (QOF points/Clinical Excellence Awards)

[Personal views, including ethics of incentives]

- **It seems to be clear that incentives (financial or otherwise) are increasingly necessary. What are your views on the implications for clinical research?**

  [Prompts] What about *financial* incentives?

  And *non-financial* incentives?

  Incentives for clinicians?

  How about incentives for patients?

  And organisations?

- **And ethically?**

  [Prompts] The amount of money? (What's an appropriate amount? What's too much?)

  Does the type of incentive matter?

  Does the identity of the provider of the incentive make a difference?

  Does the identity of the recipient of the incentive make a difference?

  Can you describe situations where a conflict of interests might exist?

  How important is the disclosure of the presence of financial incentives?

  Informed consent?

  Trust within the doctor-patient relationship?

[Depending upon experience of respondent]

- **How have attitudes towards participating in research changed during the last five years?**

And finally –

- **Why did you agree to do this interview?**

AFTER: ask for leads, non-active, cooperative

Incentives: people who have NOT taken part in a trial (people who have a long-term illness or have been ill recently)

Demographic information
Occupation/role; age; disease condition

Discuss what they know about clinical trials – have they read the handout?

When you were seeing doctors about your [condition], were you asked to take part in a clinical trial?

Did you think about being part of a clinical trial at all?

Have you ever tried to find out about trials for [illness condition]?
[Yes] – how did you make enquiries?
Probe – Internet/GP/specialist
[No] –
Probe – Any reason why?

How would you feel about taking part in a Phase III clinical trial investigating treatment for [illness condition]?

More generally, why do you think some people take part in clinical trials?
Probe – to obtain treatment/drugs; more attention/surveillance

What are your views on paying patients to take part in trials? (Phase III)
For, against

What could be the effects if patients are paid to take part in trials?
Practical issues
Ethical issues

Up to now much clinical research in the NHS has relied on the goodwill and academic interest of doctors, alongside non-financial incentives such as recognition. However, increasingly health professionals such as GPs and consultants receive incentives (including payments) for recruiting patients

What are your views on doctors receiving financial payments to put their patients into trials?
Realistic expenses vs incentives
How much is too much?
Nurses (e.g. in GP practice)

How important is it for patients to know what incentives their doctor is receiving to recruit them to a trial?

Equipoise? –
In order to recruit patients to a clinical trial, it is necessary for the doctor to be uncertain about the outcome (i.e. the treatment might not work). How do you feel about that situation?

Probe uncertainty/doubt, etc.

What about being involved in trials for other conditions as well as your current condition –
Intervention like fish oil, supplements
Change in behaviour, e.g. exercising, diet
Drug trial
Surgical procedure

Anything else about incentives and clinical trials that I haven't mentioned?

Finally, why did you agree to this interview?

Incentives: people who have NOT taken part in a trial (people who have no illness condition)

Demographic information
Occupation/role; age
Discuss what they know about clinical trials – have they read the handout?

How would you feel about taking part in a Phase III clinical trial?

Intervention like fish oil, supplements
Change in behaviour, e.g. exercising, diet
Drug trial
Surgical procedure

More generally, why do you think some people take part in clinical trials?
Probe – to obtain treatment/drugs; more attention/surveillance

What are your views on paying patients to take part in trials? (Phase III)
For, against
(expenses?)

What could be the effects if patients are paid to take part in trials?
Practical issues
Ethical issues

Up to now much clinical research in the NHS has relied on the goodwill and academic interest of doctors, alongside non-financial incentives such as recognition. However, increasingly health professionals such as GPs and consultants receive incentives (including payments) for recruiting patients

What are your views on doctors receiving financial payments to put their patients into trials?
Realistic expenses vs incentives
How much is too much?
Nurses (e.g. in GP practice)

How important is it for patients to know what incentives their doctor is receiving to recruit them to a trial?

Equipoise? –
In order to recruit patients to a clinical trial, it is necessary for the doctor to be uncertain about the outcome (i.e. the treatment might not work). How do you feel about that situation?

Probe uncertainty/doubt, etc.

Anything else about incentives and clinical trials that I haven't mentioned?

Finally, why did you agree to this interview?

Incentives for healthcare professionals for patient recruitment to trials – people who have taken part in a trial

Demographic information
Occupation/role; age; disease condition (if applicable)(ask for details if necessary)

I understand you have taken part in a clinical trial, as a participant –
Could you please describe the study(ies) briefly?
What was involved – what did you have to do?

Do you know who funded the trial?
Commercial, public

Were you paid expenses?
If yes, how much?

Are you aware of any incentives (financial or other) paid to the doctor?

Who asked you to take part?

Why did you agree?

What concerns did you have before agreeing?

How were these concerns dealt with?

What are your views on paying patients to take part in trials? (Phase III)

What could be the effects if patients are paid?
Practical issues
Ethical issues

Up to now much clinical research in the NHS has relied on the goodwill and academic interest of doctors, alongside non-financial incentives such as recognition. However, increasingly health professionals such as GPs and consultants receive incentives (including payments) for recruiting patients

What are your views on doctors receiving financial payments to put their patients into trials?
Realistic expenses vs incentives

Would you take part in a trial again?
Intervention like fish oil, supplements
Change in behaviour, e.g. excercising, diet
Drug trial
Surgical procedure

Equipoise? –

Probe uncertainty/doubt, etc.

Anything else about incentives and clinical trials that I haven't mentioned?

Finally, why did you agree to this interview?

[Personal views, including ethics of incentives]
- **It seems to be clear that incentives (financial or otherwise) are increasingly necessary. Do you have a view on the implications for clinical research?**

What about *financial* incentives?

And *non-financial* incentives?

What are your views on incentives for clinicians?

How about incentives for patients?

And organisations?

- **And ethically?**

The amount of money? (What's appropriate?)

Does the type of incentive matter?

Does the identity of the provider of the incentive make a difference?

Does the identity of the recipient of the incentive make a difference?

Can you describe situations where a conflict of interests might exist?

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AFTER: ask for leads, non-active, etc.

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We look forward to hearing from you.

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@hta.ac.uk
http://www.hta.ac.uk

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