Study Protocol

The delivery of chemotherapy at home: an evidence synthesis

1. Aims and objectives

The aim of this project is to investigate the impact of the delivery of chemotherapy at home on quality of life, safety, patient satisfaction and costs. Decision modelling will be undertaken to compare the provision of intravenous chemotherapy, led and managed from the oncology department, delivered either in the patient's home, in the community or in the hospital outpatient department. The impact on costs and benefits will be evaluated not only from the NHS perspective but will also be extended where possible to include the patient perspective.

2. Background

Historically, chemotherapy treatment for cancer patients was delivered in hospital. Just over ten years ago a BMJ editorial noted the shift in chemotherapy practice in the UK from inpatient to outpatient ambulatory therapy and highlighted the small body of growing evidence to suggest the safety and acceptability of chemotherapy administered at home whilst identifying the need for more evidence on patient selection and cost-effectiveness.[1]

Potential benefits to patients of receiving chemotherapy treatment at home include less travelling to in-patient or out-patient facilities, reduced risk of hospital acquired infection, receiving treatment in the comfort and security of the home, less disruption to family life and an increased feeling of control over treatment and illness.[2] However, there may also be potential concerns for patients, for example isolation, less contact with hospital staff (such as specialist nurses) and other patients, feeling less secure with less back-up outside the hospital setting and the possibility of lower continuity of care.[3]

Safety is a key issue, due to the toxicity of the drugs and the need for specialist skills to administer and monitor treatment. It is important to ensure that problems with toxicity are identified promptly and that concordance with treatment is good. Severe side-effects can be very disturbing and may influence a patient's decision to continue with treatment; this is true in any setting, but may have a longer term impact on patients when experienced at home. Health care professionals involved with the administration and monitoring of treatment need to have the relevant skills and expertise.

Throughout the NHS there is an increasing focus on developing service models of care which meet the needs of patients.[4] In the area of cancer services, the Cancer Reform Strategy has pledged that care will be delivered in the most clinically appropriate and convenient setting for patients.[5] The Department of Health Cancer Policy Team has produced guidance to develop chemotherapy services in the community (outside of cancer centres and units in facilities such as GP surgeries or in patients own homes),[3] which builds on best practice guidance provided in the National Chemotherapy Advisory Group report published in 2009.[6] These documents promote the consideration of opportunities to devolve chemotherapy from cancer centres and cancer units to community settings while maintaining safety and quality and delivering an efficient service. However, a report looking at how effectively strategies laid out in the Cancer Reform Strategy have been utilised to improve cancer services for patients found a lack of activity in the commissioning of services with only 26% of PCTs having undertaken a cost-benefit analysis looking at different ways of delivering cancer services.[7]

There is variation in chemotherapy delivery practices throughout the UK and a variety of systems exist, reflecting the different challenges of, for example, large cancer centres and district general hospitals.[8] Nurse-led chemotherapy is established in some centres but home delivery of chemotherapy is not widespread. Different geographic challenges exist for provision in remote and rural

communities compared with more urban-based centres. Although not currently widespread, the provision of chemotherapy at home within the NHS is increasing as community chemotherapy services receive attention. The Department of Health lists exemplars of NHS community chemotherapy services in Sunderland, Dorset, West Anglia, East Anglia and East Kent;[3] there are also healthcare companies who undertake chemotherapy in the community, offering services to both private and NHS providers e.g. Healthcare at Home, BUPA Home Healthcare, Baxter, Calcea and Alcura.

3. Existing research

A preliminary search of the published literature indicates that there is a limited evidence base evaluating home chemotherapy, no systematic reviews were identified. There are a small number of published trials which evaluate different populations (for examples see table below); these trials have been undertaken in a number of countries, but not in the UK. In general, results from these trials are supportive of home chemotherapy in terms of patient satisfaction, quality of life and compliance. However, the trials are small, and the measures used in the studies vary (for example, a variety of unvalidated study-specific quality of life measures). The protocol for the OUTREACH trial, a UK-based randomised trial comparing the delivery of cancer systemic therapy in three different settings (patient's home, GP surgery and hospital day unit) has been published,[9] and interim results have been reported;[10] publication of the final results is anticipated this year (Pippa Corrie, personal communication).

Table: Sample of published trials evaluating home chemotherapy

Study	Country	Population	Sample size	Comparator	Outcomes
Borras (2001)[11]	Spain	Adults with colorectal cancer	87	Hospital outpatient clinic	Toxicity Compliance Quality of life Satisfaction Resource use
Rischin (2000)[12]	Australia	Adults with cancer (breast, colon, NHL, pancreatic)	20	Hospital	Patient preference Costs
Stevens (2006)[13]	Canada	Children with acute lymphoblastic leukaemia	23	Hospital outpatient oncology clinic	Quality of life Effects on parental care givers Adverse effects Costs
Corrie (2011) (trial protocol[9] and interim results[10])	UK	Adults with cancer	Not stated in protocol. 55 of 97 patients recruited included in interim results	1. Hospital day unit; or 2. GP surgery	Patient perceived benefit Semi-quantitative interviews Service use and cost data Compliance

Questionnaires and feasibility or pilot studies have assessed patient satisfaction, as reported by patients, carers or healthcare professionals (for example[14-18]). Some studies have also examined professional and organisational issues surrounding the provision of chemotherapy at home. A

feasibility study that explored the issues around introducing a home-based service identified the need for leadership to implement change whilst highlighting the poor quality of cost data and the need for accessible robust financial information.[16] A prospective descriptive study of healthcare professionals' views (nested within a randomized crossover trial[13]) identified several issues related to service delivery and human resources: consistency in personnel and care; skills and knowledge requirement; communication and workload issues.[14]

Economic studies of home versus hospital delivery of chemotherapy have reported varying results, reflecting the difference in the location, content of the programs and the way in which patients' preferences and costs are incorporated into the analysis. A US study found reduced charges and costs from the perspective of the parents of children with cancer,[19] an Australian study found an increase in costs,[12] and a French study found marginal cost was significantly higher whereas the average cost was significantly lower.[20] No UK economic evaluation was identified, although a feasibility study addressed costing an NHS service.[16]

To date, this research has not been systematically identified, appraised and summarised to fully describe and evaluate the evidence base.

4. Rationale

Current government policy promotes patient choice and transfer of services closer to home, but it is not clear that there is a strong evidence base to support this recommendation. Also, it is unclear whether analyses taken from the NHS perspective are sufficient to inform decisions on these types of services. This research will bring together and assess the existing evidence surrounding the delivery of chemotherapy at home and provide a framework to evaluate alternative approaches.

It is anticipated that the research may identify gaps in the evidence base for the delivery of chemotherapy at home which will inform research priorities for the future. If feasible, a value of information analysis will be conducted to assess the potential value of further research.

The research will also identify gaps in the methodological evidence base, in particular the need to quantify the benefit to patients of particular models of care. It is anticipated that existing validated patient reported outcome measures, both specific (e.g. EORTC QLQC30) and generic (e.g. EQ-5D), may not reflect or measure the factors that are important to patients when considering where chemotherapy should be delivered. Therefore, novel approaches may be necessary to obtain patient reported outcomes.

5. Research Plan

5.1 Patient pathway

The starting point of the research will be to describe the patient pathway for the alternative approaches to delivering chemotherapy. We use the term patient pathway to refer to mapping the processes involved in delivering chemotherapy to ensure we consider the key events relevant to the different settings (home, community or outpatient). We plan to focus on the provision of intravenous chemotherapy led and managed from the oncology department, delivered either within the patient's home, in the community or on a hospital outpatient basis. It will be assumed that the clinical effect of chemotherapy, in terms of mortality and tumour response, will not differ between delivery settings except through the impact of side effects and concordance with treatment. However, effectiveness measured more broadly in terms of quality of life and patient benefit may differ between the delivery

settings. We will consider any appropriate chemotherapy agent as described in the current regimen list for the SACT chemotherapy dataset (http://www.chemodataset.nhs.uk/homepage.aspx).

To ensure relevance and completeness, the pathway will be generated in close consultation with our clinical collaborators; additional expert advice will be provided by a project advisory group (see below). To inform the project and gain insight into the variation in current practice in the NHS, we will undertake a survey of relevant professionals about the delivery of home chemotherapy. The survey is not intended to be a comprehensive and validated assessment of the provision of chemotherapy, rather it is intended to help describe the patient pathway which will inform and guide the development of the decision model. It will provide insight into the variation in current practice by collecting basic information on the structure of services, who is offered home chemotherapy and who receives it, as well as any information that may be available on resources. These questions will be generated with input from our advisory group to ensure the pathway and decision model will be representative and useful. The approach will be pragmatic, we intend to contact all NHS and private providers and we will also contact cancer charities. These will be identified using experts, relevant NHS contact database and appropriate NHS networks (e.g. cancer networks), also utilising the Centre for Reviews and Dissemination's (CRD) experience and existing contacts in this area. We anticipate undertaking the survey using the Survey Monkey web-based software (http://www.surveymonkey.com) and we will use email communication, with email and phone follow-up as necessary.

5.2 Advisory Group

We will establish an advisory group for the project which, alongside our clinical expertise, will ensure that all relevant stakeholders are involved. This group will include representation from cancer nurse specialists, pharmacists, primary care, patients and the public. We will involve the advisory group at key stages of the project, in particular developing the patient pathway and decision model. We already have the agreement of the following people to be part of the advisory group:

Dave Ardron, Chair of the NCRI Consumer Liaison Group (2008-2012) and a member of the North Trent Cancer Network Chemotherapy Strategy Group.

Pippa Corrie, Consultant and Associate Lecturer in Medical Oncology, Oncology Centre, Cambridge University Hospitals NHS Foundation Trust (and PI for the OUTREACH trial).

Jane Kelly, Procurement Project Pharmacists, Leeds Teaching Hospitals NHS Trust (and National Homecare Medicine Committee Member).

Una Macleod, Professor of Primary Care Medicine, Supportive care, Early Diagnosis and Advanced disease (SEDA) research group, Centre for Health and Population Sciences, Hull York Medical School.

Gillian Parker, Professor of Social Policy Research and Director of Social Policy Research Unit, University of York (and PI for the project Evaluating models of care closer to home for children and young people who are ill [21]).

Melanie Robertson, Oncology Nurse Consultant, Lead Cancer Nurse, Oncology Unit, City Hospital Sunderland NHS Foundation Trust.

Saskia Syms, PPI representative.

5.3 Decision Modelling

From the pathway, decision model(s) will be developed to estimate the cost-effectiveness of delivering treatment within the comparative settings. The model framework(s) will characterise patients' treatment and resultant outcomes from alternative perspectives. The specific modelling objectives will be: 1) to assess the cost-effectiveness of the alternative delivery settings with a view to informing commissioning decisions and 2) to identify key uncertainties and limitations relating to the cost-effectiveness analysis with a view to informing future research.

Modelling will evaluate the potential costs and effects, both positive and negative, attributable to the delivery of home chemotherapy; these will be evaluated not only from the NHS perspective but will also be extended, where possible, to include the patient perspective by incorporating costs incurred by the patient (for example, travel costs, childcare costs, informal support).

Given that we do not anticipate differences in treatment effectiveness, including compliance, modelling will be restricted to a time horizon reflecting the length of chemotherapy treatment.

5.3.1 Model development

Clinically relevant and appropriate decision modelling will be structured to map the patient pathway for the alternative approaches to the delivery of chemotherapy. The effect of treatment location on quality of life outcomes, compliance and adverse effects will be carefully considered. The clinical experts on the team will review the model structure(s) to ensure it has good clinical face validity.

5.3.2 Time horizon

We anticipate that any impact on patient benefit through the provision of chemotherapy at home will last for the duration of treatment. We will not attempt to quantify any sustained long-term benefit (for example, through improved mental outlook and general well-being) subsequent to treatment as formal measurement is unfeasible. Therefore, to facilitate modelling, we will assume that the long-term benefit of treatment is the same regardless of the setting in which that treatment is delivered. An appropriate modelling time horizon will be chosen that is long enough to capture the costs and associated outcomes relevant to the treatment time-frame; this time frame is expected to be one year or less to reflect the time that patients actively receive chemotherapy.

5.3.3 Populating the model

To inform the model, we will undertake a systematic review of both the clinical and economic literature to identify the existing evidence on the effectiveness, cost effectiveness, safety and patient benefit of the delivery of chemotherapy at home (see 5.4 below). Results from the synthesised evidence will be used to populate the decision model, either in the form of quantitative summary outcome estimates or individual study results when summary results are not available. Further searches will also be undertaken where necessary; the information specialist will work in close liaison with the health economists to identify the model questions. Information to answer these questions will be provided by focused searching of appropriate databases, statistical sources and other sources of relevant information. To further augment the evidence base and fully populate the model, routine hospital data sources and expert opinion will be utilised where necessary.

5.3.4 Measuring health benefits

Health benefits may be expressed in terms of quality adjusted life years (QALYs), however to ensure that all relevant patient outcomes (for example, satisfaction) are captured we will undertake additional analyses using other relevant benefit outcomes identified in the systematic review.

5.3.5 Uncertainty

The uncertainty in the data used to populate the model will be captured through the use of probabilistic modelling which requires that each input in the model is entered as a distribution rather than a fixed parameter. Using Monte Carlo simulation, this parameter uncertainty will be translated into uncertainty in the overall results. The results of this analysis will be presented graphically using cost-effectiveness acceptability curves which show the probability that each intervention is cost-effective conditional on a range of possible threshold values attached to an additional QALY.

5.3.6 Long-term Cost-effectiveness and Value of Information

Should the short-term modelling highlight differences in outcomes which may impact on longer-term outcomes and potentially long-term cost-effectiveness we will undertake further modelling, time allowing. Using published HTA reports we will identify a model which evaluates the lifetime impact of cancer treatment in an appropriate populations. Permission will be sought from the authors to augment their model with our *de novo* model to allow a full analysis of the costs and outcomes of treatment in the different settings to be conducted. Should this long-term modelling be relevant and feasible to undertake, the model may be used to undertake a value of information (VoI) analysis. Decisions based on existing information will inherently be uncertain. If feasible, we will conduct an expected VoI analysis to help estimate the cost of this uncertainty and identify whether it is of value to conduct further research in this area. If the expected value of perfect information for the population of interest exceeds the expected costs of such additional research, then potentially, it will be cost-effective for further research to be funded to better inform this decision in the future.

5.4 Systematic review

A systematic review of the clinical and economic literature will be undertaken to identify the existing evidence on the effectiveness, cost effectiveness, safety and patient benefit of the delivery of chemotherapy at home. The review will be conducted according to recommended guidelines[23] and the protocol will be submitted for registration on PROSPERO, an international database of prospectively registered systematic reviews in health and social care (http://www.crd.york.ac.uk/prospero/).

The review questions will be generated with reference to the key decision points in the model. As the initial scoping work suggests that the published evidence base to inform this area is limited, we will employ a broad search strategy to look for both quantitative and qualitative studies, unpublished and grey literature to ensure all the available evidence is identified.

5.4.1 Search strategy

Published and unpublished literature in any language will be identified from searching electronic databases, internet resources and consultation with experts.

The following databases will be searched:

- AMED (Allied and Complementary Medicine),
- British Nursing Index,
- Cochrane Library (including Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), NHS Economic Evaluation Database (NHS EED), HTA Database, Methods Database)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL),
- EconLit,
- EMBASE,

- HMIC,
- Inspec,
- MEDLINE,
- MEDLINE In Process,
- OHE Health Economic Evaluation Database (HEED).
- PsycInfo,
- PubMed,
- Social Policy and Practice.

In addition, information on studies in progress, unpublished research or research reported in the grey literature will be sought by searching a range of relevant resources including Conference Proceedings Citation Index: Science (ISI), Inside Conferences, Dissertation Abstracts, NTIS, ClinicalTrials.gov and Current Controlled Trials (metaRegister of Controlled Trials).

We will search relevant individual conference proceedings which are not indexed, for example the National Cancer Research Institute (NCRI) conference and hand search journals if appropriate; we will contact the Department of Health's Cancer Policy and Cancer Action teams to ensure we identify Department of Health evaluations and reports. We will also contact private providers of home care through the National Clinical Homecare Association (including Healthcare at Home, BUPA, Baxter, Calea and Alcura) to identify unpublished reports, evaluations, or resource information. We will contact the MHRA to explore whether it is possible to obtain relevant safety data.

Update searches will be undertaken 6 months after completion of the original searches to ensure that any recent publications are identified.

For comprehensive retrieval of all potentially relevant studies, no methodological filters will be used to restrict the type of studies we search for, nor will any language or date limits be imposed.

5.4.2 Study selection

Two researchers will independently screen all titles and abstracts obtained through the search. Full manuscripts of potentially relevant studies will be obtained wherever possible. No study will be excluded on the basis of language. Two researchers will independently assess the relevance of each study using pre-defined eligibility criteria. Discrepancies will be resolved by consensus, with recourse to a third researcher wherever necessary. The EPPI-Reviewer software (version 4) will be used to manage the study selection process.

The eligibility criteria are:

Population: Cancer patients receiving intravenous chemotherapy

Interventions and comparators: Studies comparing intravenous chemotherapy, in any two (or more) of the following settings:

- Home setting (includes mobile units and nursing homes)
- Community-based setting (e.g. GP practice, community clinic, community hospital)
- Hospital outpatient setting

Within-setting comparisons will also be eligible, but only if the study compares different organisational or management approaches.

Outcomes: Any of the following:

- Safety
- Patient quality of life
- Preference
- Satisfaction (including treatment compliance/adherence)
- Social functioning
- Clinical outcomes
- Costs
- Resource/Organisational issues (including access)

Study designs: Comparative studies - Any type of comparative study will be eligible.

Single-setting studies - To obtain information about patient quality of life, satisfaction, preferences and opinions, studies reporting results only for one eligible setting and qualitative research (in any of the three settings) will also be eligible, providing a stated aim of the paper is to evaluate (one or more of) the eligible outcomes, except for clinical outcomes and multi-domain quality of life scores. Given the review focus on home and community settings, and the potential diversity and likely volume of these studies in an outpatient setting, we will focus on studies of the home and community settings and then identify whether any similar studies have been performed in outpatients.

Case studies/case reports reporting any of these outcomes will be excluded.

Full economic evaluations comparing two or more relevant options which consider both costs and consequences (including cost-effectiveness, cost-utility or cost-benefit analyses) will be eligible.

5.4.3 Data Extraction and Quality Assessment

The quality assessment of studies will be conducted as part of the data extraction process using criteria relevant to the topic and study designs included. Data will be extracted into structured forms using the EPPI-Reviewer software, designed to capture all relevant information from the various study designs. The data extraction form will be piloted by each researcher involved with the process, and refined as necessary prior to full data extraction to ensure consistency. Data extraction and quality assessment will be conducted by one researcher and checked by a second researcher for accuracy, with any discrepancies resolved by discussion or by recourse to a third researcher if necessary.

Clinical studies: Data to be extracted will include: details of study methods, country and geographical region in which the study was conducted, whether it was single or multicentre, dates over which the study was conducted, patient characteristics, interventions, comparators where appropriate, all relevant outcome measures and results.

The quality of included comparative studies will be assessed using criteria appropriate to the study design, adapted from published checklists.[23]

Randomised controlled trials will be assessed using the Cochrane Risk of Bias tool which focuses on the domains shown to impact on the trial results in particular (selection, performance and detection biases and attrition).[24]

Non-randomised studies which include a comparison group will be assessed for methodological quality using criteria based on the Newcastle-Ottawa scale and those identified by the ongoing work of the Cochrane Collaboration (see recent publications in Research Synthesis).[25-26] These criteria will be operationalised for this review and the research team will consider their particular relevance for the specified outcome measures. Broadly, domains will include consideration of: selection of the groups, comparability of the groups, how the outcomes were assessed including follow-up and methods of assessment, relevant confounding factors and the potential for selective reporting.

Studies without a control group will not be quality-assessed however details will be presented in descriptive tables.

Qualitative studies will be assessed for methodological quality using criteria based on the work of Pope and Mays among others.[27-28] As with the quantitative studies, the intention is to focus on those domains which influence the reliability of findings. Areas to be assessed include transparency and documentation of the data collection and analysis processes, description and justification of sampling, validity appropriate to the method being used, reflexivity and clear distinction between data and interpretation.

Economic studies: Data extracted from economic evaluations will include: interventions compared, study population, dates to which the data relate, measures of effect, direct cost (medical and non-medical), currency used, utilities/measure of health benefit, results and details of any decision modelling applied. The purpose of the review will be to help inform the decision modelling, so any additional information that may aid the development or population of the model will also be extracted.

The quality of the cost-effectiveness studies will be assessed based on established checklists.[29-30]

5.4.4 Data synthesis

A detailed narrative synthesis that explores the methodology and reported outcomes of included studies will be undertaken. Key study characteristics, patient outcomes, and quality assessment will be tabulated to provide clear summaries of the included studies. The clinical and statistical homogeneity of the accumulated evidence will be assessed. Results from studies will be presented graphically, in the form of forest plots if appropriate. Differences between studies will be discussed in the text, and the potential impact of these differences on outcomes explored. The results will be interpreted in the context of the quality of the individual studies. Where possible, relevant subgroups will be identified (for example, adults and children) and the results synthesised in a narrative framework.

Ideally, for quantitative studies, summary estimates will be derived by pooling data from prospective controlled comparative trials, calculated using established meta-analytic and evidence synthesis techniques. However, data in this format is likely to be scarce or absent. Where such data are identified, the comparability of baseline characteristics of the populations recruited or the outcome measures used, will be investigated to assess their suitably for pooling.

The findings of the systematic review of full economic evaluations will be summarised in a narrative synthesis.

6. Project timetable

We propose to undertake the project over a 13.5 month period, beginning March 2013:

Project stage	**Duration/completion dates**
Protocol development	March to May 2013
Describe patient pathway	March to May 2013
Literature searching	March to April 2013
Development of the decision model structure	March to May 2013
Peer review of protocol by Advisory Group followed by protocol registration on PROSPERO	May to June 2013
Canvas opinions from UK oncology departments, private providers, and charities	May to July 2013
Screening and study selection	April to July 2013
Data extraction and quality assessment	June to September 2013
Data analysis from systematic review	September to December 2013
Development of the decision model	July 2013 to December 2013
Report production	December 2013 to March 2014
Draft report to Advisory Group for comment	Early March 2014
Deadline for comments from Advisory Group	End of March 2014
Submit final report	Mid April 2014
Implement dissemination strategy including drafting papers for peer review journals	

7. Patient and Public Involvement

It is important to ensure that the views and experiences of service users and carers are reflected in the development of the research proposal; this will be done through members of the project advisory group (see section 5.2 above). If appropriate, we will seek further input from relevant charities and patient groups during the project.

Where appropriate we will work with patient representatives to disseminate the findings of the project to relevant individuals and groups.

8. Team Expertise

The project team combines the clinical expertise of oncologists with the methodological skills and experience of national centres of excellence in evidence synthesis and health economics. The team members have methodological expertise in all the relevant skill areas including decision modelling, health economics, literature searching and retrieval and systematic review methodology. Additional expertise will be provided through the advisory group. The advisory group membership will provide representation of all relevant stakeholders, including cancer nurse specialists, pharmacists, primary care, and public and patient involvement.

Alison Eastwood will have overall managerial responsibility for the project and will supervise the evidence synthesis. Gerry Richardson will provide economic modelling expertise with Dawn Craig taking the lead in the development of the model. Mark Corbett, Morag Heirs, Micah Rose and Alison Smith will undertake systematic review and modelling work under the leadership of more senior analysts. Lisa Stirk will undertake the literature searches and provide bibliographic management. Dan Stark and Dan Swinson will provide clinical expertise. All applicants will contribute to the protocol development and the interpretation of results, and will be involved in the writing of the project outputs (final report and peer review publications).

Alison Eastwood is a Senior Research Fellow at CRD with responsibility for CRD's systematic review work. She has over twenty years experience of health services research, with a particular interest in the area of oncology. Currently her focus is on health technology assessments undertaken on behalf of the National Institute for Health Research (NIHR) to inform decision makers within the NHS. Prior to this, she was responsible for a programme of work to undertake systematic reviews to inform site specific national cancer service guidance, and has also undertaken work to support the National Cancer Research Network and to inform the Cancer Reform Strategy.

Dawn Craig is a Research Fellow at CRD and an experienced health economist who has undertaken economic modelling for a number of HTA projects including decision analysis in sampling infected diabetic ulcers, diagnosis of lower limb peripheral arterial disease, breast feeding in neonatal intensive care units and management of frozen shoulder. In addition, she has experience in Bayesian evidence synthesis methods and critical appraisal of economic evaluations.

Mark Corbett is a Research Fellow at CRD with five years of systematic review experience. He has worked on systematic reviews commissioned for NICE, the HTA programme and the Advisory Group for National Specialised Services (AGNSS). He has contributed to the study protocol and will provide input at all stages of the review.

Morag Heirs is a Research Fellow at CRD with eight years of systematic review experience. Morag has worked on reviews commissioned for NICE, the HTA programme, the Public Health Research Consortium, MacMillan Cancer Support and others. Morag has also conducted a mixed-methods synthesis of qualitative and quantitative sources including both primary and secondary data within her

doctoral research. Morag has contributed to the study protocol and will provide input at all stages of the review.

Micah Rose is a Research Fellow at CRD and a new member of a small team of CRD health economists. Micah has critically appraised economic modelling and conducted additional modelling for the NICE Single Technology Appraisal programme. Micah's MSc dissertation focused on the quantification of unassessed structural uncertainty in the NICE Single Technology Appraisal programme.

Gerry Richardson is a Senior Research Fellow in the Centre for Health Economics at the University of York. He has many years experience of conducting cost-effectiveness analysis alongside clinical trials and using the results of trials to inform economic models. He has conducted applied and methodological work valuing outcomes that are important to patients as well as being a successful co-applicant on a number of large trial based economic evaluations.

Alison Smith is a Research Fellow at CRD and a new member of a small team of CRD health economists. Alison has critically appraised economic modelling for the NICE Single Technology Appraisal program. Alison's MSc (Health Economics) dissertation comprised of a systematic review and meta-analysis for a breast cancer diagnostic test.

Dan Stark is a Senior Lecturer in Cancer Medicine at the University of Leeds and Honorary Consultant in Medical Oncology at Leeds Teaching Hospitals NHS trust. He has local and regional leadership roles in the multi-disciplinary management of teenagers and young adults with cancer and germ cell tumours; and 9 years consultant experience in the delivery of complex chemotherapy regimes for sarcoma and germ cell tumours, as well as in common and intermediate cancers. Dan is an experienced clinical trialist with expertise in the measurement of patient reported outcomes; he holds, as principal or co-investigator, a range of current and recent research grants through Cancer Research UK, the European Union, the National Cancer Research Institute and Macmillan Cancer Care.

Lisa Stirk is an Information Specialist within the Information Team at CRD with over 15 years experience in designing and running literature searches for reviews undertaken by CRD and other contracted organisations. She is involved in the production of DARE and the HTA database through running searches, screening results and indexing records. She will be responsible for devising the search strategy, carrying out the literature searches and maintaining the literature database.

Dan Swinson is a Consultant Medical Oncologist at St James's Institute of Oncology and Honorary Senior Lecturer with an interest in gastrointestinal cancers. He is the Chemotherapy Lead for Leeds Teaching Hospitals and has an interest in developing novel methods of delivering chemotherapy that may improve patient experience and prove cost-effective. He has a clinical research background, being the Principal Investigator for several Oncology clinical trials conducted at SJIO and the Chief Investigator for a phase 1B multicentre study approved by the CRUK New Agent Committee.

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Appendix

The following draft search strategy to identify relevant studies was devised for MEDLINE (Ovid interface). This strategy will be further developed and converted to run appropriately on other databases.

1 exp neoplasms/

2 (cancer$ or neoplas$ or tumor$ or tumour$ or malignan$ or oncolog$ or carcinoma$).ti,ab.

3 oncologic nursing/

4 or/1-3

5 drug therapy/

6 Antineoplastic Combined Chemotherapy Protocols/

7 chemotherapy, adjuvant/ or consolidation chemotherapy/ or maintenance chemotherapy/

8 administration, intravenous/ or infusions, intravenous/

9 chemotherapy.ti,ab.

10 systemic therapy.ti,ab.

11 intravenous drug therapy.ti,ab.

12 adjuvant therapy.ti,ab.

13 or/5-12

14 home care services/ or home care services, hospital-based/

15 *Outpatients/

16 *Ambulatory Care/

17 *ambulatory care facilities/ or *outpatient clinics, hospital/

18 community health services/ or community health nursing/ or community health centers/

19 general practitioners/ or physicians, family/ or physicians, primary care/

20 general practice/ or family practice/

21 ((service$ or therapy or treatment$) adj6 (home or community or outreach or out-reach or ambulatory or domicil$)).ti,ab.

22 (hospital at home or hospital in the home or own home$ or home care or homecare or closer to home).ti,ab.

23 or/14-22

24 4 and 13 and 23

25 home infusion therapy/

26 (chemotherapy adj6 (home or community or outreach or out-reach or ambulatory or domicil$)).ti,ab.

27 (chemotherapy adj6 service$).ti,ab.

28 (chemotherapy adj6 (general practitioner$ or family practitioner$ or family doctor$ or family physician$ or primary care physician$)).ti,ab.

29 (self-infusion adj6 home).ti,ab.

30 home infusion.ti,ab.

31 or/25-30

32 4 and 31

33 24 or 32

34 exp animals/ not humans/

35 33 not 34