The delivery of chemotherapy at home: an evidence synthesis

Mark Corbett,1 Morag Heirs,1 Micah Rose,1 Alison Smith,1 Lisa Stirk,1 Gerry Richardson,2 Daniel Stark,3 Daniel Swinson,4 Dawn Craig1 and Alison Eastwood1*

1Centre for Reviews and Dissemination, University of York, York, UK
2Centre for Health Economics, University of York, York, UK
3Leeds Institute of Cancer & Pathology, University of Leeds, Leeds, UK
4St James’s Institute of Oncology, Leeds Teaching Hospitals Foundation NHS Trust, Leeds, UK

*Corresponding author

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Background

Throughout the NHS there is an increasing focus on developing service models of care which meet the needs of patients, with care being delivered locally wherever possible to maximise convenience and centralised where necessary to improve outcomes. For cancer treatment, recent policy and guidance has focused on chemotherapy services being offered not only in cancer centres and cancer units but also in community and home settings, while maintaining safety and quality and delivering an efficient service.

Many hospitals across England and Wales are delivering chemotherapy services at full capacity, with increasing demand for services putting a strain on NHS capacity resources. This can have a detrimental effect on patient experience as a result of longer waiting times. Delivering chemotherapy closer to home may be an approach by which the NHS could relieve demand for outpatient services while maintaining or even improving patient care. Nevertheless, the clinical and economic implications of delivering chemotherapy closer to home are uncertain.

Objectives

This aim of this study was to compare the impact of delivering intravenous chemotherapy in different settings (home, community and hospital outpatient) on a range of outcomes, including quality of life, safety and costs.

Methods

A systematic review of clinical effectiveness, qualitative and cost-effectiveness studies was undertaken. A decision model was developed to explore aspects of cost-effectiveness. Data from published and unpublished studies were sought systematically from 16 electronic databases (including MEDLINE, EMBASE and The Cochrane Library, searched from inception) in March 2013; updated searches of the most relevant databases were undertaken in October 2013. Reference lists and Google (www.google.co.uk) searches were used to identify any further studies.

Studies of cancer patients receiving intravenous chemotherapy in two or more of the following settings were eligible: home, community based (e.g. general practitioner practice, mobile bus, or community hospital) and hospital outpatient. Within-setting comparisons were also eligible. Studies had to report at least one of the following outcomes: safety, quality of life, preference, satisfaction, social functioning, clinical outcomes (such as self-rated health), costs or resource/organisational issues. Any type of comparative design (including economic evaluation) was eligible. Single-setting studies were also identified and included, but were used in the review only where they might usefully supplement the comparative study evidence (this happened only for qualitative studies). Quality assessment tools, specific to particular study designs, were used to evaluate the validity of the included studies.

Two reviewers independently screened all of the potentially relevant studies, and data extracted and quality assessed those included. Discrepancies were resolved by discussion. Clinical effectiveness and cost-effectiveness studies were summarised narratively; qualitative studies were synthesised using meta-ethnography.
To supplement the published evidence and to gain insight into the variation in current NHS practice, a survey was undertaken, canvassing views from relevant professionals about their experience of providing home and community chemotherapy. The results of the survey were intended to help to describe the patient pathway and inform the development of a decision model. A lack of evidence led to a simple model based on one UK trial (OUTREACH) being developed. The aim of the model was to assess the cost-effectiveness of intravenous chemotherapy delivered in the home, community or outpatient setting in a population considered eligible for home treatment. The model was conducted from a NHS perspective using a 12-week time horizon. The summary measure of benefit was quality-adjusted life-years.

**Results**

The literature searches identified 4272 references and 245 potentially relevant full papers were screened. A total of 67 studies were included: 25 comparative studies and 42 single-setting studies. Of the 25 comparative studies, 10 were randomised controlled trials (RCTs) and 15 were non-randomised studies; nine of the comparative studies included a concurrent full economic evaluation. Most studies evaluated adult populations and compared home and hospital outpatient settings.

The 10 randomised trials recruited 482 participants in total. Several trials were appropriately designed to minimise avoidable biases. However, slow recruitment rates and the non-participation of eligible patients for setting-related reasons meant that trial sample sizes were small and populations were inherently biased to favour the home or community settings. This bias was evident in the results for the preference and satisfaction outcomes, although these data were limited as only one trial studied strength of preference. Perhaps surprisingly, there was little evidence to suggest differences between settings in terms of quality of life, clinical outcomes or psychological outcomes. Adverse event data also did not suggest any important differences between settings; these data were limited by the small study sizes. The 15 non-randomised studies added little to the randomised trial evidence: the main limitations were the small populations and a high risk that the study results were biased as a result of confounding.

All nine of the economic evaluations were judged as being of low or uncertain quality. Most were cost–consequence analyses, which presented cost outcomes alongside clinical trial results but derived no summary measure of benefit. Only one evaluation assessed patient health-related quality of life and reported utility outputs (many studies used patient preference as an outcome measure). Poor reporting of resource use and use of different perspectives across different settings made the results difficult to compare. High levels of uncertainty made it difficult to ascertain whether or not costs or outcomes differed between settings. In general, these studies provided limited evidence from which to draw an overall conclusion regarding cost-effectiveness or to inform or populate a decision model.

The 17 qualitative studies evaluated the opinions and experiences of more than 450 participants in total, including patients, family members and health-care professionals. Generally, study quality was moderate to good but most studies did not appear to consider the impact of the researcher on data collection and analysis. Overall, data were grouped under three main lines of argument: barriers to service provision, satisfaction with chemotherapy and making compromises to maintain normality. The last of these was seen as key to being able to survive a difficult time and look forward.

Most patients made explicit trade-offs to maximise their resources (such as time, money and energy). Normality was maintained more easily when family life was minimally interrupted, the impact of cancer on daily life and family members was controllable, and patients were able to participate in activities of value. Time spent travelling and waiting for treatment meant less time and energy for normal life. Outpatient settings were most often associated with increased confidence in staff ability to deal with adverse reactions, but there was evidence that good, visible communication between an expert centre and a community or home location could alleviate some safety concerns. Based on available data, the time and energy consumed by outpatient treatment reduced overall quality of life such that patients preferred
alternative treatment settings. These themes were particularly evident in accounts from patients receiving palliative treatment and from parents of children with cancer.

We circulated the survey widely and it was passed on further by initial contacts. This made it impossible to calculate a response rate. Twenty-two NHS organisations (all in England) and nine private providers responded to the survey. The results suggested wide variation in the ways in which home and community chemotherapy was delivered. It was evident that more patients were eligible for community treatment than home treatment and that chemotherapy regimen and patient performance were important determinants of eligibility. Private providers were frequently used to deliver treatment in the home setting and appeared to use more selective eligibility criteria (e.g. treating patients only after two or more cycles had been delivered in hospital). Several NHS organisations highlighted that value-added tax savings associated with home chemotherapy were a significant motivator for providing such a service.

We anticipated that we would be able to develop and populate a robust decision model through combination of the published evidence and the survey. However, limitations of the available data meant that results from the cost-effectiveness model were highly unstable and should be viewed as exploratory rather than robust.

In the base-case analysis, intravenous chemotherapy in the community setting was the most cost-effective option, but none of the settings had a high probability of being the most cost-effective. Sensitivity analyses highlighted the fragility of the results to parameter changes. Adjusting cost values within plausible ranges also altered the preferred treatment setting. There was significant uncertainty over which treatment settings were cost-effective. Robust data to inform cost-effectiveness modelling would be needed to resolve this uncertainty, as well as further consideration of service configuration and appropriate patient pathways.

Conclusions

The results of this study highlighted not only avoidable study design and reporting limitations but also inherent and sometimes unavoidable difficulties that arise during primary studies of chemotherapy settings. Several studies were designed appropriately to minimise avoidable biases but implementing randomised trials in this area appears difficult in terms of patient accrual and recruiting unbiased populations. These issues impacted on the concurrent economic evaluations and were further compounded by poor reporting of cost and resource data. Consequently, few robust conclusions can be made about the clinical effectiveness and cost-effectiveness of different settings. High uncertainty remains owing to trial sizes that were potentially too small to detect effects reliably. It was unclear whether or not the quality-of-life instruments used in the studies were sensitive enough to detect differences in quality of life between chemotherapy settings. Accordingly, the results of the exploratory cost-effectiveness model based on the OUTREACH trial were not robust and the cost-effectiveness results of the model should be interpreted with caution.

Qualitative studies were more informative. They indicated that decisions and preferences about intravenous chemotherapy treatment setting are strongly influenced by a desire to maintain normality. Patient time and energy required for outpatient chemotherapy reduces overall quality of life enough for patients to prefer alternative treatment settings. However, compromises were needed to balance competing factors and patient preference for specific locations reflecting individual situations. Limitations of the qualitative studies were that all evaluated a new or proposed service against an existing (perhaps struggling) hospital outpatient setting, and participants were drawn from biased samples.
**Implications for research**

Considering the likely challenges involved in performing further RCTs using conventional study designs, a better design might be to nest a RCT within a larger observational cohort of patients: ambivalent patients could be randomised and patients with preferences could receive their preferred setting. Such a study might also incorporate (into questionnaires) the qualitative data themes identified in this review. Efficacy estimates would result from the randomised component of the study. Any additional influence of motivational factors could be studied by comparing randomised and non-randomised patients treated in the same setting. The results from this nested design should also indicate whether or not there are any clinical or demographic differences between the different populations at baseline, and produce estimates of likely rates of uptake of the different settings, to help inform future service provision. Such a study should more clearly identify and quantify issues such as setting-related adverse events, waiting times, anxiety and transport problems, and indicate how their prevalence and impact might vary according to patient characteristics.

For an economic evaluation to be reliable, detailed patient characteristics, resource use, cost and quality-of-life data are needed. The ideal collection method for these parameters is a large multicentre RCT that incorporates a wide variety of providers. However, a key theme that emerged from the review and survey concerned a high level of variation in current practice in the NHS. This variation makes it unlikely that a RCT will provide sufficient evidence for a broad economic evaluation. We surmise that, in order to explore this variation and mitigate generalisability issues, broad observational data will be necessary. Information from large observational data sets such as the Systemic Anti-Cancer Therapy and the General Practice Research Database could be linked to provide a clearer portrait of current provision.

**Study registration**

This study is registered as PROSPERO CRD42013004851.

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