

Methods for the Collection of Resource Use Data within Clinical Trials: A Systematic Review of Studies Funded by the UK Health Technology Assessment Program

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ABSTRACT

Background: The UK Health Technology Assessment (HTA) program funds trials that address issues of clinical and cost-effectiveness to meet the needs of the National Health Service (NHS). The objective of this review was to systematically assess the methods of resource use data collection and costing; and to produce a best practice guide for data capture within economic analyses alongside clinical trials.

Methods: All 100 HTA-funded primary research papers published to June 2009 were reviewed for the health economic methods employed. Data were extracted and summarized by: health technology assessed, costing perspective adopted, evidence of planning and piloting, data collection method, frequency of data collection, and sources of unit cost data.

Results: Ninety-five studies were identified as having conducted an economic analysis, of which 85 recorded patient-level resource use. The review identified important differences in how data are collected. These

included: a priori evidence of analysts having identified important cost drivers; the piloting and validation of patient-completed resource use questionnaires; choice of costing perspective; and frequency of data collection. Areas of commonality included: the extensive use of routine medical records and reliance on patient recall; and the use of standard sources of unit costs.

Conclusion: Economic data collection is variable, even among a homogeneous selection of trials designed to meet the needs of a common organization (NHS). Areas for improvement have been identified, and based on our findings and related reviews and guidelines, a checklist is proposed for good practice relating to economic data collection within clinical trials.

Keywords: clinical trials, cost analysis, economic evaluation, health technology assessment.

Background

Economic evaluations have become increasingly integral to late-phase clinical trials. Data generated from such trials can provide unbiased estimates for the calculation of cost-effectiveness to inform decisions on the effective and efficient use of health care resources. In the UK, the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) program funds research, including clinical trials, to investigate the clinical and cost-effectiveness of a range of health technologies (e.g., medicines, devices, procedures, and screening) used to promote health, prevent and treat disease, and improve rehabilitation and long-term care [1]. The program is “needs-led” in that it prioritizes research projects for commissioning based on: the anticipated benefits of reducing uncertainty (specifically in relation to health outcomes, cost-effectiveness, and targeting of services), the timescale for realizing benefits, the importance of early assessment (specifically in relation to the costs associated with not doing the research), and other factors such as national priorities and prevalence of the disease. Research findings, which are published in the HTA’s own peer-reviewed journal, *Health Technology Assessment* [2], have a bearing on clinical practice within the National Health Service (NHS) directly, and indirectly, via guidance issued by the National Institute of Health and Clinical Excellence (NICE), as well as internationally.

Essential to any trial-based economic evaluation is a robust method for collecting data on resource use. Nevertheless, there are no universally recognized methods for economic data collec-

tion in HTA-funded trials, although a wide variety of techniques are recognized and used. These methods include: patient self-report (by questionnaire, interview, diary cards); use of routinely available data (e.g., medical records and general practitioner (GP) records); and use of expert panels. Each method has its advantages and disadvantages. Reliance on patients, for instance, is the most common approach, but is limited by biases in recall, nonresponse, and evasiveness [3]. The use of routinely collected data depends on accurate recording and information technology infrastructure. Eliciting expert opinion is convenient, but is not generally considered as a reliable or unbiased method of resource use estimation.

There are several published reviews and good practice guidelines of economic evaluations within clinical trials [4–6]; however, the variability in the methods for resource use data collection suggests a need for a standardized approach. Such a guideline should also extend to the piloting and validation of data collection instruments.

The aim of this review was to systematically assess the methods of resource use data collection and costing of published HTA-funded primary research studies, and to produce a best practice guide for future studies.

Methods

All 100 studies published to June 2009 and classed as “primary research” were identified from the *Health Technology Assessment* journal [2]. The original articles containing a health economic assessment (95 of 100) were obtained and reviewed by CHR, with particular attention being paid to chapters, sections, and appendices on economic analysis and data collection methodology. Each article was also searched electronically for the key words “perspective,” “viewpoint,” “questionnaire,” “forms,” “resource,” “notes,” “interview,” “diary,” “cost,” “Netten,”

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“BNF,” “schedule,” “pilot,” “resource,” “valida,” “consult,” “baseline,” “horizon,” and “economic.” Appendices were examined for copies of questionnaires and reference to relevant sections of case report forms. For each article reviewed, data relating to the following fields were extracted:

1. Health technology being assessed;
2. Perspective adopted;
3. Methods for identifying items for costing;
4. Methods for piloting and validation of resource use data collection instrument;
5. Resource use data collection methods;
6. Timing of data collection in relation to the trial duration;
7. Sources of unit costs.

A sample of data extractions was reviewed for accuracy by DAH. Extracted data are summarized and a descriptive analysis is presented.

Results

Ninety-five of the published HTA studies reported an economic evaluation. The majority (75) was experimental in nature; 18 were observational and comprised of cohort, cross-sectional, and case studies; and the remainder were nontrial-based economic analyses. Randomized controlled trials made up the bulk of the experimental group (73 of 75), whereas the other two were randomized crossover trials. All of the five categories of health technologies were assessed: procedures (37 of 95); devices (14); drugs (13); screening (8); setting of care (1); and combinations of the five (22). Studies included in the review are listed in the Appendix (http://www.ispor.org/Publications/value/ViHsupplementary/ViH13i8_Hughes.asp). A summary of the data extracted from each study is presented in Table 1.

Perspective

The choice of the perspective of an economic evaluation dictates the resource items that are to be costed. There were no fixed protocols adhered to when defining the perspective, although nine studies referred to various guidelines [7–9] to support their choice. As expected, all 95 studies included an NHS perspective; 21 also included Personal Social Service (PSS) costs, and 26 included costs to the NHS and patients. Seven studies were identified that assessed costs to each group. The term “societal perspective” was used frequently, but did not seem to be well defined. For example, some studies which reported a societal perspective would in fact have been better described as having adopted an NHS and patient perspective [10–12].

Planning and Piloting

Less than a quarter of studies (22 of 95) demonstrated any evidence that a systematic approach had been followed for resource identification at the planning stage. Where evidence was presented, this was usually done by consulting with health-care professionals or conducting a review of published economic literature. The majority of the studies (85 of 95) captured patient-level health-care resource use. Nevertheless, only 28 (of the 85) studies reported validating their health-care resource use data collection methods; and in only 21 of the 57 studies which used patient- or carer-completed questionnaires or diaries was there evidence of piloting. Methods for piloting varied widely—from adopting formats that had been piloted in previous similar [13], or even dissimilar [14] studies, to asking two carers to test a resource use diary [15]. Health-care resource use data collection

methods were validated usually by comparing resource use data questionnaire content with routinely collected data sources such as GP notes [16,17] and hospital records [18,19].

Methods for Data Collection

For the purpose of the review, the methods used to capture patient-level data have been categorized as follows:

1. Medical records taken from routine primary and secondary care sources (e.g., patient notes, databases);
2. Prospective forms completed by trial researchers or health-care professional (not based on patient recall or abstracted from routine sources);
3. Prospective forms completed by trial researchers or health-care professional (based on patient recall);
4. Patient or carer-completed diaries (carer in this context meaning nonhealth-care professional);
5. Patient-completed or carer-completed forms.

A majority of the studies (61 of the 85) used at least two methods, typically involving patient- or carer-completed form and medical records. Fifty-nine studies relied on medical records, and 48 used patient- or carer-completed forms. Prospective methods based on patient recall were reported in 23 of the 85 studies. A similar number (22) was found for prospective methods that were not associated with patient recall or based on data abstracted from medical records. Patient- or carer-completed diaries were used in 20 studies. Taking into account the overlap of methodologies, 63 studies used nondiary-based patient recall (involving one or more of: patient-completed forms, carer-completed forms, or prospective methods such as face-to-face interview). Forty-three of these 63 trials supplemented methods based on patient recall, with data from other routine sources such as GP records, hospital notes, and hospital databases. Only 14 of these, however, used routine data to capture the same data as recorded by questionnaire.

Frequency of Data Collection

Trial durations (patient study period, as opposed to overall length of trial) within the 85 HTA studies that include a patient-level economic evaluation, ranged from a few days to 15 years, reflecting the nature of the health technology being assessed. The timing of resource use data collection in relation to the trial duration could not be determined in 6 of the 85 studies. Baseline economic data were measured in 51 studies. This usually involved either administering a baseline questionnaire to measure resource use prior to or at the index procedure, or a retrospective data extraction from patient records.

Between baseline and end of study, the favored time for resource use data collection fell in the last quarter of the trial duration (50 of 79 cases) and the least favored fell in the third quarter (17). First and second quarter data collections occurred at similar frequencies (37 and 35, respectively).

Unless otherwise specified, we defined the recall periods in the 63 studies that involved patient-, carer-, and researcher-completed forms (not diaries) as the time since the previous recall questionnaire where one existed, or otherwise, defined as the time between randomization and the first questionnaire. Using this definition, 55 studies in which recall periods could be estimated (of the 63), yielded a total of 121 recall periods. Median recall period was 4.5 months (interquartile range, 2 to 6 months). The median number of recall-based questionnaires deployed per patient in each of the 55 studies was 2 (interquartile range, 2 to 3).

Table 1 A summary of methods of resource use data collection and costing

Characteristic	Health technology				
	Drug	Devices	Procedure	Screening	Mixed, including setting of care
Number of studies	13	14	37	8	23
Type of Study	1 observational and 12 experimental	10 experimental and 4 observational	32 experimental and 5 observational	4 observational, 3 experimental and 1 cost analysis	18 experimental, 4 observational, and 1 cost analysis
Trial duration (months)	Range from 0.16 to 48 months	Range from 3 to 42 months	Range from 6 to 60 months	Range from 2 to 180 months	Range from 0.25 to 36 months
Which perspective was adopted?	All NHS with 5 including patient perspective and 5 including a PSS perspective. Three adopted NHS/PSS/Patient perspective	All NHS with 3 including patient perspective and 2 including a PSS perspective	All NHS with 10 including patient perspective and 6 including a PSS perspective. Two adopted NHS/PSS/Patient perspective	All NHS with 2 including patient perspective	All NHS with 6 including patient perspective and 8 including a PSS perspective. Two adopted NHS/PSS/Patient perspective
Evidence of how resource items for costing were identified/selected	2 (15%)	2 (14%)	8 (22%)	3 (38%)	7 (30%)
Data on patient-level resource use captured as part of the study	13 (100%)	11 (79%)	36 (97%)	4 (50%)	21 (91%)
Patient (or carer/guardian)-completed forms	6 (46%)	6 (43%)	24 (65%)	3 (38%)	9 (39%)
Patient (or carer/guardian)-completed diary	5 (38%)	0 (0%)	10 (27%)	0 (0%)	5 (22%)
Researcher/health-care practitioner-completed forms based on patient/carer recall	5 (38%)	2 (14%)	10 (27%)	0 (0%)	6 (26%)
Researcher/health-care practitioner-completed. Not routinely collected data; not based on patient recall	2 (15%)	5 (36%)	11 (30%)	0 (0%)	4 (17%)
Routinely collected medical or other records	6 (46%)	7 (50%)	30 (81%)	2 (25%)	14 (61%)
Baseline economic data taken and used in analysis	9 (69%)	4 (29%)	22 (59%)	3 (38%)	13 (57%)
Evidence of piloting of questionnaires for completion by patient (or carer/guardian)	3 (23%)	2 (14%)	10 (27%)	3 (38%)	3 (13%)
Evidence of validation of health-care resource use data collection methods	3 (23%)	3 (21%)	15 (41%)	0 (0%)	7 (30%)
Were costs modeled beyond the time horizon of the trial?	2 (15%)	2 (14%)	4 (11%)	2 (25%)	2 (9%)

Sources of Unit Cost Data

Studies were reliant on a limited number of primary sources of unit costs. The annual compendium of Unit Costs of Health and Social Care by Netten & Curtis [20] was used extensively (72 of 95 economic studies). Drug costs were included in 57 of the 95 economic studies. They were for the most part taken from the British National Formulary [21], a biannual publication that reports prices that are calculated from the net cost used in pricing NHS prescriptions dispensed in the previous year. Two studies referred to the Monthly Index of Medical Specialties [22], which sources generic drug costs from the Drug Tariff [23] (a monthly publication compiled on behalf of the Department of Health by the NHS Prescription Pricing Division) and branded medicines from manufacturers. Seven studies referred to the Drug Tariff directly.

Fifty-two economic evaluations used unit costs that had been sourced locally. These were mostly provided by NHS Trusts, although local councils were sometimes used [24] as were other miscellaneous local sources such as acupuncturists [14,25] and medical herbalists [14]. Thirty-six of the 95 evaluations used health-care resource groups (HRGs). These are a secondary health-care classification of groups of procedures and treatments that are clinically meaningful and are expected to use similar amounts of resource. They are generated from the content of the patient record and use a combination of administration, procedure, and diagnoses primary classifications to describe the care received by a patient [26]. A large number of secondary sources of unit costs were also used by analysts to value resources. These included national pay scales, prices provided by vendors, costs published by the Chartered Institute of Public Finance & Accountancy, and estimates derived from published studies.

Discussion

Published guidelines and reviews on the conduct of economic evaluations alongside clinical trials outline the available methods for estimating health-care resource use, and sources of unit costs [4,5,27]. Nevertheless, they offer no standard methodology, and as a consequence, this introduces important differences in how such data are collected [28]. This is evident even among the homogeneous selection of trials (i.e., UK NIHR HTA-funded) that address the needs of a common organization (NHS) included in the present review. In line with HTA's remit of generating high-quality research on the effectiveness, costs, and broader impact of health technologies, almost all (95%) clinical trials contain an economic analysis. An important consideration in any trial-based economic evaluation, however, is the external validity of the results. Not all trials are suitable as a vehicle for economic analyses, and not all economic questions can be addressed adequately through trial-based evaluation. Trials are often limited by, for instance, being insufficient in duration of follow-up, not including all relevant comparators, and being selective in terms of inclusion and exclusion criteria. Consequently, results may not always be generalizable, and trial-based assessments are increasingly being viewed as one component of a broader framework of evidence synthesis and decision analysis [29]. Although HTA-funded trials are generally pragmatic in design—to address issues of effectiveness as opposed to efficacy—the appropriateness (or otherwise) of conducting an economic evaluation for all the health technologies evaluated was not assessed in our review. We considered this unlikely to have an impact on the *methods* employed for the collection of resource use data although acknowledge the potential impact on the interpretation of the *results* of the analyses.

Our review has revealed some areas of commonality in the methods used. These include: the extensive use of routine medical records, reliance on patient recall, and the use of standard sources of unit costs. Nevertheless, there were also important differences in health economists' approaches to resource costing. Analysts' choice of perspective was without full explanation in many instances, although this might be expected given that all studies address areas of priority for the NHS. Nevertheless, this might still have a significant impact on the estimation of cost-effectiveness, and relevance to decision makers. Theoretically, the correct perspective should be the one that takes into account the costs and benefits of the intervention, no matter on whomsoever they should fall [30]—such a holistic perspective is by definition a societal one. In practice, societal perspectives will usually be relevant when a patient has complex needs that extend beyond the scope of primary or secondary health-care providers and PSS to include, for instance, social security and housing benefit; criminal justice; education; patient and their families; and lost production. Despite this, HTA studies usually adopt an NHS perspective. Some studies also included PSS, patient, and/or a poorly-defined "societal" perspective, which might have consequences if costs and benefits were to accrue outside of the chosen area [30,31]. This is in line with the NICE guideline on the methods of technology appraisal [8], which recommends that costs should be taken from the perspective of the NHS and PSS but also accept—in exceptional circumstances—analyses where some costs (or cost savings) fall outside of this perspective. The choice of appropriate perspective is still a matter of ongoing debate for health economic analysis [32]. Within the United Kingdom, further consideration should also be given to regional variations—whereas the NHS and PSS are financed separately in England and Scotland, they are within the same government departments in Wales and Northern Ireland.

Evidence that a systematic approach had been followed for resource identification at the planning stage (e.g., pilot study, systematic review of relevant literature, expert opinion) was present in a minority of studies. It is important to conduct these exercises not just to identify the main cost-driving events associated with a health technology, but also to assess which baseline cost data are required, and what data are needed to maximize external validity.

Piloting of data collection instruments is fundamental to ensuring their reliability [6], although there is little in the way of standard methodology with respect to the collection of resource data, and widespread practice is not evident. Validation of data collection instruments is an important procedure for accurate data capture. Studies identified in the present review that reported methods for validation used the following techniques:

1. Questionnaire responses compared to routinely collected data such as hospital notes. One study, for instance, validated through triangulation by comparison of GP notes, patients' responses to questionnaire, and hospital notes [33].
2. Prevalidation from previous literature or pilot studies (e.g., Client Service Receipt Inventory [34]).
3. Validation using combined data from electronic systems (e.g., condition-specific databases checked against GP records and hospital admissions database [35]).

The use of questionnaires based on patient recall was found to be the most variable aspect of the HTA trials studied. Fifty-nine of 121 recall periods covered time spans of 6 months or greater. This is one potential source of bias in methods of patient/carer self-reported health-care resource use. Richards et al. [36] reported that older patients tend to underestimate resource use

Table 2 Good practice checklist for resource use data capture alongside HTA clinical trials

Practice	Recommendation
Perspective	Should be aligned with that of the decision maker (e.g., NHS and /or Personal Social Services, multi-agency public sector; societal). Avoid inappropriate use of the phrase "societal perspective."
Identify resources for measurement	Items for costing should be identified a priori from consultation with health-care professionals, pilot studies, or literature searches. It is important to identify the expected main cost-driving events and to justify the range of resource items that are to be valued. Issues for consideration: (i) What are the consequences of not collecting these data?; (ii) What information is available on the key events within the study?; (iii) Which baseline data are needed?; (iv) What data are needed to maximize external validity?; (v) Protocol-driven resource use should be identified, and adjusted for, accordingly.
Data collection/analysis plan	A plan detailing how cost and resource use data will be obtained is essential—paying particular attention to: (i) the frequency of resource data collection; (ii) identifying if data collection needs to be resource-, effects- or schedule-driven [6]; (iii) considering whether the methods of resource use data collection will impact on the trial outcome (e.g., diaries may improve adherence to intervention); (iv) single-site or multi-site sources; (v) the time horizon within which resource use data are needed; (vi) statistical analysis.
Resource use data collection	The choice depends on the balance between factors that include: (i) reliability of patient recall; (ii) burden on the researcher/health-care practitioner; (iii) completeness and appropriateness of routinely collected data; (iv) information technology systems; and (v) the cost of research (i.e., acquiring the data). The method selected, and frequency of data capture, should be informed by previous studies or pilot studies [4].
Baseline cost data	Should be collected as an important predictor of future costs. In studies with a small sample size, baseline characteristics need to be balanced [44]. Costs can be adjusted for baseline differences for example by use of appropriate regression-based modelling.
Piloting	Patient-/carer-completed forms should be piloted to test clarity, ease of use and completion rates [11]. Piloting is also useful in determining the main cost-driving events related to the health technology.
Validation	Where possible, alternative methods of resource use data collection should be employed to test for validity [28,37].
Non-trial estimates of resource use	If nontrial resource use estimates are used to supplement trial-based data, there needs to be a documented and systematic approach to their selection. Resources used as a result of the trial protocol should be excluded.
Method of costing	Top-down microcosting, applying national costs to patient-level units of resource use where they exist. This increases generalizability.
Unit costs	Valued using national costs for the most recently available year [7]. If national costs do not exist for items of resource use, apply unit costs sourced locally.
Standardized reporting format	A common reporting format for economic evaluations would improve transparency and enhance benchmarking between similar studies [45].

compared with health providers even within relatively short time frames. A second source of bias relates to completeness. Mistry et al. [37] reported that missing items from patient-completed questionnaires tended to force reliance on GP records. Other methods of acquiring resource use data are not without their limitations either. Byford et al. [38], for instance, showed that GP records are unreliable for gathering nonpractice-based health service data (e.g., hospital and community health services).

There is a range of conceptual approaches to costing. In addition to gross-costing and microcosting methodologies, bottom-up microcosting and top-down microcosting have been described [39]. The bottom-up microcosting method is characterized by the identification of patient-specific resource use and hospital-specific unit costs. It has been proposed as the gold standard in hospital service costing methodology but is considered very time-consuming and best suited to the main cost drivers. Top-down microcosting is characterized by the identification of patient-specific resource use and national tariffs as unit costs. This is the favored methodology in the HTA trials as national tariffs are more readily available than local unit costs and are more generalizable across the NHS.

The use of routinely collected data has been made increasingly possible with advances in information technology. Hospital electronic database systems, for instance, when used in tandem with routine electronic patient administration systems, may go some way toward making hospital-specific unit costs more accessible. A further NHS development in England (but not elsewhere in the United Kingdom) has been Payment by Results (PbR), a means of paying health-care providers a fixed price for each individual case treated [40]. The currency of patient resource use associated with PbR is the HRG. Patient-specific HRGs are available as extracts from the NHS Information Centre [41] and routine data will be made available to health economists using multiple-linked databases through the development of a Health Research Support Service [42]. Another ongoing development in

England is the NHS Care Records Service [43] which will comprise of detailed records containing patient-level information on both primary and secondary care. The availability of such routine data for research purposes should be exploited but because of the uncertainty as to which data collection method is the most accurate, we recommended that more than one technique be used to measure those resources that contribute the most to the overall cost.

Conclusion

The review indicates variable practice in economic data collection in published HTA-funded trials. Areas for improvement have been identified and, based on our findings and related reviews and guidelines, we propose a checklist for good practice relating to economic data collection within clinical trials (Table 2).

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