International Journal of Technology Assessment in Health Care, 33:6 (2017), 620–628.

doi:10.1017/S026646231700071X

COMPARISON OF METHODS FOR ESTIMATING CONTEMPORARY COSTS: AN APPLICATION TO LIVER TRANSPLANTATION IN THE UNITED KINGDOM

Jeshika Singh
Health Economics Research Group, Brunel University London
PHMR Limited
jeshikasingh@phmr.com

Louise Longworth
PHMR Limited

Objectives: Our study addresses the important issue of estimating treatment costs from historical data. It is a problem frequently faced by health technology assessment analysts. We compared four approaches used to estimate current costs when good quality contemporary data are not available using liver transplantation as an example.
Methods: First, the total cost estimates extracted for patients from a cohort study, conducted in the 1990s, were inflated using a published inflation multiplier. Second, resource use estimates from the cohort study were extracted for hepatitis C patients and updated using current unit costs. Third, expert elicitation was carried out to identify changes in clinical practice over time and quantify current resource use. Fourth, routine data on resource use were obtained from National Health Service Blood and Transplant (NHSBT).
Results: The first two methods did not account for changes in clinical practice. Also the first was not specific to hepatitis patients. The use of experts confirmed significant changes in clinical practice. However, the quantification of resource use using experts is challenging as clinical specialists may not have a complete overview of clinical pathway. The NHSBT data are the most accurate reflection of transplantation and posttransplantation phase; however, data were not available for the whole pathway of care. The best estimate of total cost, combining NHSBT data and expert elicitation, is £121,211.
Discussion: Observational data from routine care are potentially the most reliable reflection of current resource use. Efforts should be made to make such data readily available and accessible to researchers. Expert elicitation provided reasonable estimates.

Keywords: Hepatitis C, Cost, Liver transplantation, Expert elicitation

Estimating resource use to inform health technology assessments (HTA) often poses a challenge for analysts due to a lack of good quality contemporary data. Significant improvements have been made in the accessibility of routinely collected data; however, such data are not always available, complete, or presented in a level of detail required for an HTA. In the United Kingdom, National Health Service (NHS) providers collect and record data based on Healthcare Resource Groups (HRGs), designed as grouping of treatments with similar clinical characteristics and resource use (1). However, not all procedures have HRG codes, and the codes may not be sufficiently disaggregated by specific population of interest to be useful in economic evaluation.

Alternatively, resource use may be estimated from published data or primary data collection in clinical trials and observational studies. When using previously published data, simply inflating prices using inflation scale (and foreign exchange rate where applicable) is an approach often taken, but this ignores possible changes in clinical practice. Expert opinion is often used to fill in data gaps and/or supplement the trial and observational data (2). In an expert elicitation study, experts are asked to formulate a quantitative judgment based on their own beliefs (independently of the quality of such knowledge) for an uncertain quantity by augmenting existing knowledge or by formulating a probabilistic judgement over the quantity (3;4). Undertaking such exercises requires time and resource, and the added benefit of this compared with a simple inflation adjustment is not currently clear.

Using an example of liver transplantation, we compared alternative methods for estimating contemporary resource use costs. In the European Region, there are an estimated 15 million people with hepatitis C virus (HCV), 2.0 percent of adults and a significant number of those who are chronically infected will develop liver cirrhosis or liver cancer and may require transplantation (1). Liver transplantation is an effective treatment option for end-stage liver disease and acute liver failure and has been available in the United Kingdom NHS since 1983. In the United Kingdom, alcohol and chronic HCV are the leading causes of liver transplantation (2;3). A total of 775 liver transplants were carried out in the NHS in 2013 (4).

Contemporary data on the costs of treating patients undergoing liver transplantation are lacking. Recent HTAs of treatments for HCV and liver disease have frequently used data from

The authors thank the clinical experts for their participation in the study.

the Cost-Effectiveness of Liver Transplant (CELT) study (5–8). CELT was a large cohort study commissioned by the Department of Health to assess all patients considered for liver transplantation in England and Wales in 1995–96, and included the collection of detailed healthcare resource-use information for all patients (9). Researchers using these data have applied simple inflation adjustments to reflect changes in costs in the 20 years since the study was conducted (5–8); however, this will be inaccurate if changes in significant clinical practice have occurred in the interim. If efficiencies were made in delivery of care over that period, simple inflation of total cost or updating unit prices only would overestimate the cost of care. Systematic bias would enter any economic analysis based on it and subsequent policy decision.

This study aims to compare alternative approaches to updating resource cost estimates using liver transplantation for patients with chronic HCV as an example.

METHODS

The potential impact on resource costs and savings of a health technology or procedure is estimated in HTAs by first ascertaining resource use: this is done by identifying the resource item first and then measuring it in terms of frequency (e.g., number of visits to general practitioner), intensity (e.g., daily dosage of medication) and duration of the healthcare activity (e.g., length of stay in the general ward) used by the patient. The total amount of resource use is then multiplied by corresponding unit cost to generate the total resource cost for each item. National estimates of unit prices, for example NHS Reference Costs, are applied to resource use amount to increase generalizability.

Resource use data were identified from the CELT study and updated using four different methods: (i) simple inflation; (ii) updating unit cost estimates; (iii) updating key resource use estimates based on expert opinion and updating unit costs; (iv) updating key resource use estimates based on registry data and updating unit costs. Please note that the first two methods implicitly assume that resource use amongst liver transplant patients has not changed since CELT was conducted over 15 years ago.

CELT included 755 patients assessed for a liver transplant from the six transplant units in England; 477 of whom received a transplant. Detailed resource use data were collected from the assessment of patients for transplant suitability to 2 years posttransplantation on discharge from transplant centers (9). Most unit costs were obtained from the transplant centers and based on 1998/9 £ GBP prices. Drug costs were sourced from the 1999 edition of the British National Formulary (BNF) (10). Of the patients who were assessed in the CELT study, ninety-eight had a primary diagnosis of HCV. A total of sixty-seven patients with HCV underwent liver transplantation, of which sixty-six were followed up in the 2 years posttransplant. This study has been reported in greater detail elsewhere (9).

Resource use data were collected in the CELT study over four phases reflecting key stages in the transplantation procedure. The assessment phase started from date of admission for assessment of suitability of liver transplantation to date of listing for transplantation. For those patients who were not listed for transplantation, the date of discharge was used as the end date. The candidacy phase started from the date of being added to the transplant waiting list to the date the patient was admitted for their transplant operation. The transplant phase was from admission for the transplant operation to discharge following the operation. Finally, the posttransplant phase was defined as date of discharge following the operation for 2 years. The main cost drivers in the CELT study for patients with HCV were length of inpatient stay and duration of transplant operation. In addition, cost of outpatient visits, dietician and physiotherapy sessions, and some key drugs (e.g., immunosuppressant), tests, and treatments also impacted upon the total cost of liver transplantation.

Method 1: Simple Inflation

For simple inflation, the total cost of liver transplantation was updated using inflation indices. An intention to treat approach was taken for completeness. All patients assessed for liver transplantation were included in the cost study regardless of whether they made it to the subsequent phases of candidacy, transplant operation, and follow-up. The mean total cost of liver transplantation for HCV patients in the CELT study was £43,283 and the value ranged from £405 to £302,470 in 1998 prices. The low estimate at the bottom of the range reflects the costs of a patient who was placed on the transplant waiting list but did not receive a transplant because they were too ill to be operated on or died pretransplantation. The cost was updated using a multiplier calculated from the pay and price indices for Hospital & Community Health Services (HCHS) for the years 1998 and 2013 (8).

Method 2: Updating Unit Cost Estimates

This approach comprised extraction of resource use data from the CELT study and applying unit cost data from routinely available national sources. Unit costs of inpatient stay were taken from NHS Reference Costs 2012–13 (1). The prices and recommended doses of immunosuppressant drugs were sourced from the BNF (11). The unit costs of key tests and treatments were sourced from NHS Reference Costs 2012–13 where available, except for biopsy, which was sourced from a recent HTA report from the United Kingdom (1;12). The costs of remaining resource use items were inflated using a HCHS multiplier (13). The unit cost data were applied to resource use data to estimate total cost for HCV patients.

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press

Method 3: Expert Elicitation and Updated Costs

The third approach used expert elicitation to ascertain the key changes in clinical practice of HCV patients undergoing liver transplantation since the mid-1990s and to obtain estimates of some key items of resource use. Expert elicitation comprised of face-to-face interviews with clinical experts in liver transplantation. The aim was to obtain views from professionals with differing expertise from a range of transplant centers and to recruit professionals involved directly in liver transplantation. Brunel Research Ethics Committee provided ethical clearance to conduct the expert elicitation study. Invitation letters and information sheets were sent to consultant hepatologists, surgeons, and transplant co-ordinators identified from seven transplant centers in the United Kingdom. Invitations were sent by a combination of post and email.

The first part of the interview took a semi-structured format and included open-ended questions about how the clinical management of patients with HCV undergoing liver transplantation has changed since mid-1990s. The questions were related to changes in four main areas: clinical practice, patient case-mix, outcomes, and organ retrieval. The experts were also asked questions regarding changes in specific tests and treatments in the clinical management of chronic HCV patients undergoing liver transplantation. A short list of high cost/high volume tests and treatments were identified from the CELT dataset and presented to the experts for their views on their current use. The procedures that were chosen from CELT were: paracentesis, ascitic tape, endoscopic retrograde cholangiopancreatography, endoscopy, continuous veno-venous hemofiltration (CVVH), laparotomy, angiography-hepatic, echocardiogram, multigated acquisition scan (MUGA), magnetic resonance imaging of the abdomen, and electroencephalogram. Additional questions were asked relating to practices that have been discontinued in the past 15 years and new ones that have been introduced.

In the second part of the interview, the experts were asked to estimate some specific healthcare resources used in the management of these patients based on key drivers of costs identified from the CELT study. The questions focused on length of operation and inpatient stay in ward or intensive treatment unit (ITU) by phase, across three phases: pretransplant, transplant, and posttransplant. The assessment and candidacy phases were combined into a pretransplant phase as distinguishing between these was found to be difficult during the CELT study. The posttransplantation phase was further split into first year posttransplant and subsequent years.

An expert elicitation tool adapted from Leal at al. was used to elicit these resource use estimates (14). The tool allowed for variability around the resource use estimates to be captured using probability distributions. The main reason being that focusing only on the "typical" or "average" patient may misrepresent resource use and some patients require more resource-intensive treatment, while others require less (12;13). Resource use estimates were sought for a "typical" or average patient with HCV (M), followed by lower (L) and higher (H) estimates to represent the variance around the resource use estimate. Four complementary intervals were calculated using the estimates M, L, and H as shown in Eq. [1].

$$\left[L, \frac{L+M}{2}\right]; \left[\frac{L+M}{2}, M\right]; \left[M, \frac{M+H}{2}\right]; \left[\frac{M+H}{2}, H\right]. \quad (1)$$

The experts were asked to approximate the proportion of patients likely to receive the amount of care for each interval and a histogram displaying estimates and probabilities provided by the expert was produced in real time. The histogram was shown back to the expert to check whether it represented his or her beliefs. An interactive user-interface was developed in Microsoft Excel 2010 for this exercise, an example screen of which is illustrated in Figure 1. If the histogram failed in representing the expert's opinion, an option was given to repeat the exercise. Depending on their clinical specialty and role in each phase of transplant care, some respondents found it difficult to respond to questions about the frequency of specific procedures and were allowed to omit specific questions if outside their expertise.

A summary of the elicited estimates was compiled and shared with the participating experts by email. The probability distributions elicited from experts were summarized using the vincentization method reported by Leal et al. (14). A simple linear opinion pool method was used to aggregate the results across 0–1 interval space. The probability density function (PDF) for each expert was allocated over small dimensions of that interval space. The PDFs of the experts for each interval was summed and was divided by the number of experts to get an aggregated probability distribution. The qualitative data were analyzed using a framework analysis method reflecting the semi-structured nature of the interview. New unit costs obtained from national sources were applied to expert elicitation data to re-estimate cost of transplantation.

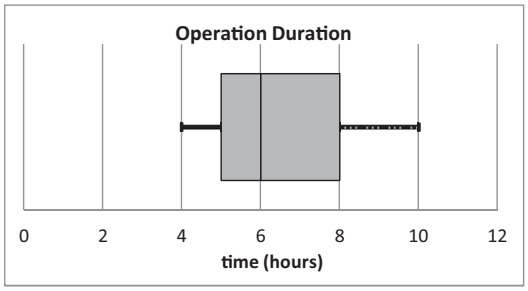
Method 4: Use of Routine Data and Inflation

The fourth approach to estimate costs included observational data on resource-use from the NHS. There are limited observational data in the public domain regarding resources use in liver transplantation in the United Kingdom. NHS Blood and Transplant (NHSBT) is a Special Health Authority to promote and manage blood, tissue, and organ donation and routinely collects resource use information on liver transplantation. We contacted NHSBT for access to routine use data, and in May 2014 they provided us with observational data for all hepatitis patients, HCV and hepatitis B (HBV), who received liver transplantation in the United Kingdom between 2008 and 2013. It included transplant details such as date of transplant, cold ischemia time, veno-venous bypass time, operative reperfusion time (liver out of ice to reperfusion with blood), inpatient stay

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press

1. Duration of liver transplantation operation

What would be typical transplant operation time?	4	hours
What would be the shortest operation time?	6	hours
What would be the longest operation time?	10	hours



1.1 How likely do you think it is that the duration of operation will be between each of the following intervals

Note: all intervals below must have a probability above 0% and sum up to 100%

Between	4	and	5	hours	10 %
Between	5	and	6	hours	20 %
Between	6	and	8	hours	50 %
Between	8	and	10	hours	20 %

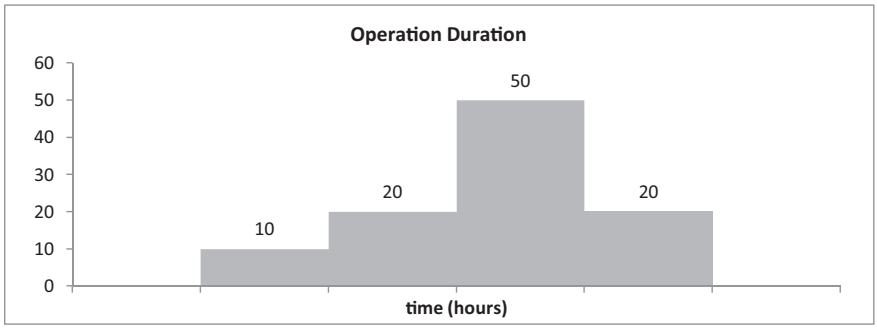


Figure 1. An example of expert elicitation tool used.

in transplantation ITU (ward, ITU, and ventilation), and post-transplantation inpatient stay (ward and ITU). Information on pretransplantation was not available from NHSBT. Current unit costs were applied to new resource use data to re-estimate cost of transplantation.

RESULTS

In this section, we present the cost estimates and resource use identified using the four approaches followed by our re-estimation of total cost of liver transplantation and comparison of methods.

Simple Inflation

The total cost of liver transplantation for patients with HCV simply updated to current prices was £87,432. However, this method does not take into account breakdown of cost by resource use of phase of transplantation.

Updating Unit Cost Estimates

Most unit costs had increased since the CELT study. A summary of updated unit costs are in Tables A and B of the online Supplementary File. Key exceptions were the unit costs of immunosuppressant therapy, which have decreased since the CELT study was conducted. The new total cost of transplantation using this method was £116,009.

Expert Elicitation

Letters of invitation were initially sent to fourteen experts by means of post in mid-December 2013. A total of three or four contact attempts were made to recruit the experts following the initial letter. To increase the sample size, a further twenty-one clinical practitioners were contacted. In total, six full interviews were conducted. An additional expert was identified during one of the interviews and responded to the open-ended question section of the survey, but it was not possible to complete the quantitative elicitation exercise. The interviews

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press

took place between December 2013 and early March 2014, and comprised of two hepatologists, three surgeons, and one transplant co-ordinator from four different liver transplant units in the United Kingdom. The six interviews were recorded and transcribed and lasted 30–60 minutes.

The recurrent themes in each topic area were identified and summarized according to three different phases: pretransplant, transplant, and posttransplant. All the participants in the study stated that clinical practice differed between the liver transplant units and treatment protocols varied. In addition, it was stated that the number of patients treated, severity of liver disease, and number of comorbidities varied across transplant units. After the six interviews, few new themes were raised by the experts, indicating that saturation was achieved.

Some participants noted that the number of patients on the waiting list for liver transplant has increased and the reason being twofold: an increase in number of people being referred for transplant and the supply of donor organs not matching demand. They stated that, while the number of organs from donors after cardiac death (DCD) had increased rapidly, organs from donors after brain death (DBD) had only marginally increased, if at all. Few experts also commented that recurrence of HCV is very common (compared with transplantation due to other indications) and may have increased due to the use of sub-optimal organs. Some of the experts reported an increase in referral to other providers for monitoring, such as local care providers.

Regarding tests and procedures carried out on liver transplant patients, more than one expert said that use of angiography and MUGA have decreased with increased use of echocardiogram, laparotomy and CVVH, and surgeons mentioned that bone-scan procedures during the transplant operation have discontinued. One expert referred to new clinical practices and support that are routinely provided and were introduced since the CELT study, such as cardio-pulmonary exercise testing, detailed cardiovascular disease scanning, and rifaxamin to treat hepatic encephalopathy. Two specific changes in standard drug therapy were highlighted by several experts: tacrolimus replacing cyclosporine as the immunosuppressant of choice, and azathioprine being substituted by mycophenolate mofetil (MMF) for maintenance treatment.

The second part of the interview focused on eliciting resource use estimates from the experts, specifically inpatient stay and operation duration. The variation in resource use data among patients was very large and reflected differences in comorbidities and prognosis of patients. The combined probability distribution of resource use parameters are presented in Figure 2.

Registry Data

Observational data from routine care of patients admitted for liver transplantation were provided by NHSBT in May 2014 for all patients with HCV and HBV who received liver transplantation in the United Kingdom over a 5-year period. The mean age of liver transplant recipients was 52 years, which is comparable to the national profile of all liver transplant recipients as well as CELT study. One-third of patients had had more than one liver graft. Almost all patients received whole liver transplants apart from a case each of reduced and split liver transplant. A little over one-third of the HCV and HBV patients who were transplanted died in the 5-year period.

DBD liver was used in almost 90 percent of the patients transplanted between 2008 and 2013, and only three patients received a DCD liver. In the CELT study, all patients only received DBD liver, with other types of liver transplant introduced in the NHS only recently. A comparison of resource use estimates from the CELT study only, expert elicitation study, and NHSBT dataset is presented in Table 1.

Re-estimating Total Cost of Liver Transplantation

The updated total costs of liver transplantation using different data sources are presented in Table 2 for comparison. Two key changes were made: the length of inpatient stay from CELT study was replaced with mean estimate aggregated from the expert elicitation and NHSBT. And the changes to main drug treatments were incorporated to reflect tacrolimus being replaced by cyclosporine as the standard immunosuppressant for patients (assumed 95 percent tacrolimus and 5 percent cyclosporine based on the expert elicitation). The costs were also adjusted to reflect azathioprine being substituted by MMF for maintenance treatment.

The NHSBT resource use estimates were not available for the pretransplantation phase. The resource use data from NHSBT for transplant and posttransplant were for both HCV and HBV patients. The mean total cost of liver transplantation, excluding pretransplantation, was estimated at £89,598, £93,510, and £103,156 per patient using updating unit prices, expert elicitation, and NHSBT information on resource use. Including pretransplantation the total cost was £87,321, £116,009, and £111,565 using simple inflation, updating unit cost estimates, and expert elicitation, respectively. The NHSBT data are the most accurate reflection of cost estimates for transplantation and posttransplantation phase; however, given lack of NHSBT data for pretransplant phase and given the changes in clinical practice, expert elicitation for pretransplant was added to give a total cost of £121,211.

Comparison of Methods

The first and second methods did not account for changes in clinical practice and yielded similar cost estimates for the pretransplantation phase; however, the results were different for transplantation and follow-up. The changes in unit cost of the key items were mixed, for example, the cost of immunosuppressant drugs had reduced but the cost of tests had increased over

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press

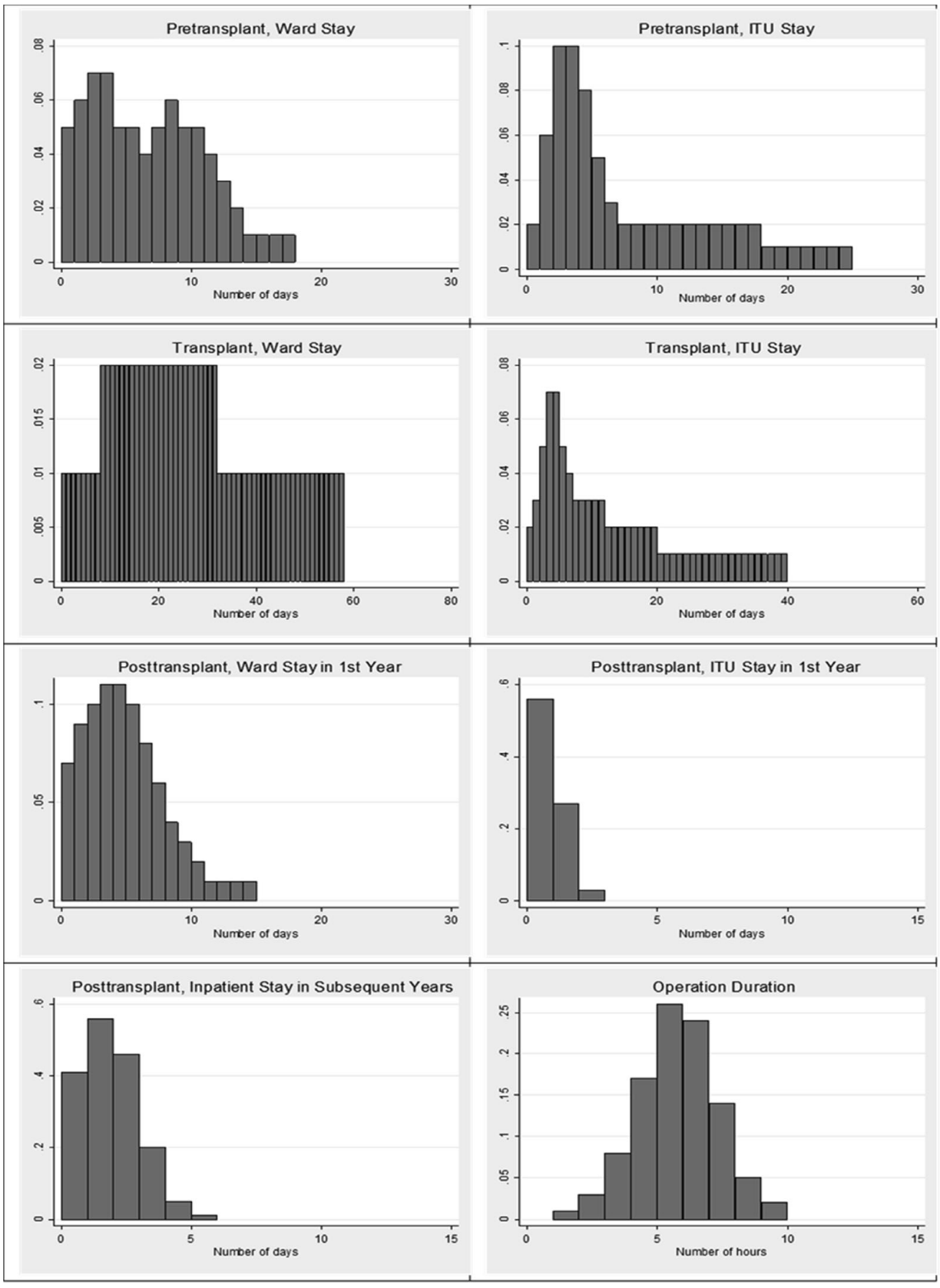


Figure 2. Summary of resource use estimates from expert elicitation.

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press

Table 1. Resource Use Data from Different Sources

Phase	Inpatient stay in days: mean (SD); min-max	
	Ward	ITU
Pretransplant		
CELT study (HCV)	19.04 (17.63); 1–91	0.5 (2.41); 0–16
Expert elicitation (HCV)	4.04 (3.46); 0–180	2.87 (6.51); 0–60
NHSBT (HCV and HBV)	NA	
Transplant		
CELT Study (HCV)	25.76 (49.94); 0–375	7.12 (16.63); 0–131
Expert Elicitation (HCV only)	26.84 (28.00); 4–240	11.38 (17.70); 1–180
NHSBT (HCV and HBV)	20.07 (9.01); 9–48	7.68 (11.74); 2–51
Posttransplant, first year		
CELT Study (HCV)	9.56 (13.62); 0–61	0.46 (1.78); 0–8
Expert elicitation (HCV only)	3.47 (3.82); 0–30	0.25 (1.34); 0–14
NHSBT (HCV and HBV)	12.60 (27.62); 0–62	
Posttransplant, subsequent years		
CELT Study (HCV)	3.77 (10.60); 0–56	0.05 (0.30); 0–2
Expert elicitation (HCV only)	1.02 (1.99); 0–15	
NHSBT (HCV and HBV)	10.45 (21.44);0-107	

HCV, hepatitis C virus; HBV, hepatitis B virus; SD, standard deviation; ITU, intensive treatment unit; CELT study, Cost-Effectiveness of Liver Transplant study; NHSBT, National Health Service Blood and Transplant.

Table 2. Updated Costs of Treating Patients with HCV

Method	Total cost in £s: mean value (SD); min-max
Pretransplant	
Simple inflation (HCV)	23,387 (25,508); 818-138,254
Updating unit costs (HCV)	26,411 (25,590); 838-136,383
Expert elicitation and inflation (HCV)	18,055 (16,642); 6,674-97,155
NHSBT and inflation (HCV and HBV)	NA
Transplant	
Simple inflation (HCV)	44,617 (62,834); 0- 481,784
Updating unit costs (HCV)	57,968 (47,408); 0–281,271
Expert elicitation and inflation (HCV)	64,452 (16,283); 45,240-124,549
NHSBT and inflation (HCV and HBV)	59,150 (18,504); 35,543-130,623
Posttransplant (2 years)	
Simple inflation (HCV)	19,460 (40,798); 0 - 273,450
Updating unit costs (HCV)	31,630 (43,404); 0 -273,627
Expert elicitation and inflation (HCV)	29,058 (35,186); 9,171-250,106
NHSBT and inflation (HCV and HBV)	44,016 (39,183); 21,628-263,042

HCV, hepatitis C virus; HBV, hepatitis B virus; SD, standard deviation; NHSBT, National Health Service Blood and Transplant.

time. The primary reason in difference is the sample used. The first method focused on patients with primary biliary cirrhosis, alcoholic liver disease, and primary sclerosing cholangitis, while the second method is specific to hepatitis patients.

The use of experts to confirm current clinical practice was very useful; however, the quantification of resource use using experts is less clear. The experts suggested that there have been reductions in length of stay for patients in pretransplantation phase. This is likely to be due to more streamlined assessment processes, but is also likely to be in part due to differences in methods of estimation between the CELT study and the elicitation study. The elicitation exercise focused on the resources associated with preparation for transplantation only whereas the CELT study also captured some resource use corresponding to the ongoing treatment of end-stage liver disease and associated complications. Second, in the transplantation phase expert elicitation assumed all patients had transplantation, while the CELT study captured intention to treat patient group and perhaps other complications as well based on the range captured.

The posttransplantation cost estimated from the NHSBT data is much higher than the cost estimated using other methods. The reason could be that patients are often treated by local healthcare providers after discharge, which may be captured by NHSBT but not by the expert elicitation and CELT focused on resource use within the transplant units.

NHSBT data are the preferred dataset, which reflect current practice and capture resources incurred by all NHS providers, but they do not provide a breakdown on resource use for all four phases. Liver transplantation is, however, an exception and central registry data are not available in most disease areas.

DISCUSSION

Our study has provided current estimates of liver transplantation cost to transplant centers in England, in total and for three key phases of treatment: pretransplantation, transplantation, and posttransplantation. The study compared various methods to update cost estimate. The mean total cost of liver transplantation was estimated at £87,432, £116,009, and £111,565 per patient using simple inflation, updating unit cost estimates, and expert elicitation, and total cost of £121,211 was estimated when combining expert elicitation and NHSBT. Nevertheless, the variation in cost is less than 10 percent when using the four approaches.

In the first method, we simply inflated total resource cost using an estimate from the literature and applying inflation over time. The method is quick and easy but does not contain a breakdown of cost by actual disease or resource use, and does not take into account any changes in practice. In the second approach, the resource use data for HCV and HBV patients were extracted from a robust observational study from over 15 years ago was used and only unit costs were inflated to reflect change in prices. This method of simply inflating unit prices is

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press

inaccurate when there have been changes in clinical practice as was identified from the expert elicitation exercise. There have been some significant changes in how HCV patients are treated since the original cohort study was conducted 15 years ago. Experts suggested decreased resource use in the pretransplantation phase compared with CELT because of more streamlined assessment processes in place and some of the assessments being done outside the unit. Regarding the transplant phase, costs calculated using simple inflation of CELT and NHSBT were similar but experts indicated slightly higher estimates.

As our third method, we used expert elicitation to identify key changes in clinical practice and estimated key resource use items, before applying inflated unit costs. Expert elicitation is "appropriately viewed as being second best and a potential source of parameter un-certainty" (2). The main reasons cited are that the experts have limited experience and perspective and that the methods used to identify the experts and elicit their opinion is not robust. However, in this study, several steps were taken to obtain the best estimates possible from expert elicitation exercise. All of the experts were highly experienced in the treatment of patients with HCV and liver transplantation. As each expert may be involved at different stages of patients' care, they were selected to reflect different perspectives from range of clinical professions and a range of transplant centers in the United Kingdom.

The experts indicated a higher mean estimate of days in ward and ITU. They argued that patients with greater number of comorbidities are now being considered for transplantation and to meet increase in demand, sub-optimal (DCD) organs are being used more frequently, both of which have resulted in increased inpatient stay. In the posttransplant phase, the resource use suggested by experts and CELT was similar; however, NHSBT data revealed much higher resource use following discharge after transplant operation. The latter is likely to be correct, because some experts had admitted to not knowing about follow-up as it is usually provided outside the transplant unit and also stated recurrence of HCV as common.

Finally, registry data of patients undergoing liver transplantation were obtained and inflated unit costs were applied to re-estimate the cost of liver transplantation. Observation data of routine care collected by NHSBT are potentially the most reliable reflection of current resource use in the United Kingdom. However, such data are rarely available and accessible. Another potential limitation is that information covering entire patient pathway may not be available; for example, it was not possible to estimate total cost of liver transplantation using NHSBT data as it did not have any data on resource use before transplantation, or it is not aggregated by disease group of interest. Our preferred estimate is using NHSBT estimates for liver transplantation combined with expert elicitation for pretransplantation phases, which gives a total cost of £121,211.

It should be noted that it is rare to have registry data so readily available. Routine collection of resource use data is costly and poses an administrative burden; nevertheless, it is very useful and should be encouraged in other disease areas as well. Also use of electronic record keeping of resource use of patients will perhaps improve transfer of information to those working on HTA.

Liver transplantation remains a costly health intervention for patients with HCV. Also note that our estimates do not include the costs of harvesting donor organs as it was not possible to identify a robust estimate from experts or through literature review.

CONCLUSION

We have estimated the resource use to NHS transplant units of liver transplantation for patients with chronic HCV, using high-quality historical data, expert elicitation, and observational data on routine care where available. Each approach had its limitation. Simple inflation and updating unit cost estimates of resource use is a quick way of updating cost data, but one has to be mindful of changes in clinical practice when using historical data. Using routine data is preferable; however, it may not be available for all items of resource use or in the level of detail or format required. When no routine data are available and simply inflating historical data is inadequate, expert elicitation (conducted robustly) provides a reasonable estimate of resource use.

The mean total cost of liver transplantation was estimated at £87,432, £116,009, and £111,565 per patient using simple inflation, updating unit cost estimates, and expert elicitation. In the case of liver transplantation, the simple inflation method underestimated total costs. There have been significant changes in how HCV patients are treated since the original cohort study was conducted 15 years ago, and this is reflected in the breakdown of costs at different phases (pretransplant, operation, and posttransplant). Our preferred estimate is using NHSBT estimates with expert elicitation for pretransplantation, which gives a total cost of £121,211.

SUPPLEMENTARY MATERIAL

Supplementary Table 1:
https://doi.org/10.1017/S026646231700071X
Supplementary Table 2:
https://doi.org/10.1017/S026646231700071X

CONFLICTS OF INTEREST

The authors have nothing to disclose.

REFERENCES

1. DH. NHS Reference Costs 2012–2013. UK: Department of Health, 2013. https://www.gov.uk/government/publications/nhs-reference-costs-2012-to-2013 (accessed July 21, 2017).

2. Sullivan W, Payne K. The appropriate elicitation of expert opinion in economic models. *Pharmacoeconomics*. 2011;29:455.
3. O'Hagan A, Buck EC, Daneshkhah A. *Uncertain judgements: Eliciting experts' probabilities*. New York: John Wiley & Sons; 2006.
4. Soares MO, Bojke L, Dumville J, et al. Methods to elicit experts' beliefs over uncertain quantities: Application to a cost effectiveness transition model of negative pressure wound therapy for severe pressure ulceration. *Stat Med*. 2011;30:2363-2380.
5. Grieve R, Roberts J, Wright M, et al. Cost effectiveness of interferon alpha or peginterferon alpha with raibavarin for histologically mild chronic hepatitis C. *Gut*. 2006;55:1332-1338.
6. Dakin H, Bentley A, Dusheiko G. Cost-utility analysis of tenofovir disoproxil fumarate in the treatment of chronic hepatitis B. *Value Health*. 2010;13:922-933.
7. Warren E, Wright A, Jones B. Cost-effectiveness of telaprevir in patients with genotype 1 hepatitis C in Australia. *Value Health*. 2014;17:792-800.
8. Crossan C, Tsochatzis EA, Longworth L, et al. Cost-effectiveness of non-invasive methods for assessment and monitoring of liver fibrosis and cirrhosis in patients with chronic liver disease: Systematic review and economic evaluation. *Health Technol Assess*. 2015;19:1-409.
9. Longworth L, Young T, Buxton MJ, et al. Midterm Cost-effectiveness of the liver transplantation program of England and Wales for three disease groups. *Liver Transpl*. 2003;9:1295-1307.
10. BNF. *British National Formulary: Number 38, September 1999*. London: British Medical Association. Royal Pharmaceutical Society of Great Britain; 1999.
11. BNF. *British National Formulary. 2014*. https://bnf.nice.org.uk/.
12. Stevenson M, Lloyd-Jones M, Morgan MY, Wong R. Non-invasive diagnostic assessment tools for the detection of liver fibrosis in patients with suspected alcohol-related liver disease: A systematic review and economic evaluation. *Health Technol Assess*. 2012;16:1-174.
13. PSSRU. Unit costs of health & social care 2013. http://www.pssru.ac.uk/project-pages/unit-costs/2013/ (accessed July 21, 2017).
14. Leal J, Wordsworth S, Legood R, Blair E. Eliciting expert opinion for economic models: An applied example. *Value Health*. 2007;10:195-203.

https://doi.org/10.1017/S026646231700071X Published online by Cambridge University Press