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THE IMPORTANCE OF COST CENSORING – THE CASE OF TRANSPLANTATION

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Abstract: An event that commonly arises in clinical studies, particularly those where survival or death are the main outcome measures, is censoring. Censoring occurs when the end point of interest has not been observed for an individual in the study. The technique of censoring is also relevant to economic evaluations of clinical interventions where, in addition to outcomes, information on *costs* may also be censored. Several techniques have been proposed in the literature that aim to adjust for censored cost data when evaluating the total average cost of a medical intervention. Techniques for estimating total average cost range from simply ignoring the issue of censoring altogether to using Kaplan-Meier survival estimates in order to allow for censored observations.

The paper reports the findings of an extensive literature review of the methods used to handle this issue in previous costing studies and economic evaluation studies of solid organ transplantation procedures. It was found that, to date, the majority of studies have addressed the issue of censoring by simply ignoring it altogether. Using interim data from an economic evaluation study of the liver transplantation program in England and Wales, the variety of results that can be obtained from the different estimation methods are illustrated and recommendations are made as to the approach which should be adopted in future costing studies and economic evaluations of solid organ transplantation and other clinical interventions where censored cost information is present.

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Introduction

An event that commonly arises in clinical studies, particularly those in which survival or mortality are the main outcome measures, is censoring. Censoring occurs when the end point of interest e.g. death has not been observed for particular individuals within a study. There are several reasons why censoring may arise, individuals may be lost to follow-up, or withdrawn from the study or have died for reasons unrelated to the cause if interest, or they may not have had the event of interest at the time of data analysis.

The most common type of censoring is known as right censoring, where an individual is censored after their last known survival time. It is right censored data that will be dealt with in this paper.

The technique of censoring is also relevant to economic evaluations of health care interventions where, information on costs may be censored for the same reasons listed above for clinical studies. Several techniques have been proposed in the literature, which aim to adjust for censoring when estimating the total average cost of a health care intervention. The aim of this paper is to review these proposed methods and point out some of their strengths and failings. A literature review of the methods that other researchers have used in costing and economic evaluation studies of solid organ transplant procedures will also be presented. This will be followed by an example, using interim data from an economic evaluation of the liver transplant program in England and Wales, which demonstrate the differences in results obtained by using the alternative methods proposed for handling censored costs data. Finally recommendations are made as to the approach which should be adopted in future costing and economic evaluations of solid organ transplantation and other clinical interventions where censored cost information is present.

2. Kaplan-Meier

Before describing the alternative methods for estimating total average costs for a particular study period a brief summary of the Kaplan-Meier method for estimating survival will be given, a more detailed explanation of the method can be found in numerous articles on survival analysis[1, 2]. This method forms a crucial step in some of the techniques proposed for calculating average costs.

The assumptions that need to be held in order to calculate survival estimates are relatively few. It is not even necessary for the survival times to follow a mathematical distribution, such as the normal distribution. All that is required is simply that the censored survival times are independent of the censoring mechanism and that the survival times for the individuals are independent of each another. For example, if individuals were being withdrawn from a study because of a deterioration in their condition which relates to the outcome/s of interest then the censoring mechanism would be dependent on the survival times, this would mean that the Kaplan-Meier method would not be valid. Alternatively, if individuals are being withdrawn from a study because of a deterioration in a condition which is not related to the outcome/s of interest then the censoring mechanism is not dependant upon the survival times and the Kaplan-Meier method would therefore be valid.

Let t_i denote an individual's survival time, which is represented by either the length of time between entering the study and death (the event of interest) or the length of time between entering the study

and being censored. Time may be measured in any unit of interest, months for example. The data for all individuals are then arranged in ascending order of time (shortest time first) and the times are divided into intervals. The first interval starts at zero and ends immediately prior to the first death time (censored times are ignored for the moment). The second interval begins at the first death time, so this is included in the interval, and ends immediately prior to the second death time. This division continues up to the final death time. It is thus possible to calculate the probability of surviving through each of the intervals by subtracting the number of deaths occurring during the interval from the number of individuals alive at the beginning of the interval and dividing this by number of individuals alive at the beginning of the interval. For the first interval the probability of surviving will be 1.00 as the interval ends before the first death occurs.

Censoring times are considered within the interval that they occur, but are ignored after that time. From these probabilities it is now possible to calculate the Kaplan-Meier survival estimates of the probability of surviving beyond a time point $t_{(k)}$. The probability of surviving beyond time $t_{(3)}$, for example, is the probability of surviving through the interval $t_{(3)}$, calculated above, multiplied by the probability of surviving through $t_{(2)}$ multiplied by the probability of surviving through $t_{(1)}$. The Kaplan-Meier survival estimate for a given study period is thus denoted by the following equation:

$$\hat{S}(t) = \prod_{j=1}^{k} \frac{n_j - d_j}{n_j} \qquad (1)$$

Where, n_j denotes the number of patients alive at time $t_{(k)}$ and d_j denotes the number of deaths at this time point.

A survival plot of the Kaplan-Meier probabilities can then be plotted, as a step function, where the area under the survival curve represents the mean survival time for the study group. It is also possible to calculate the median survival time by determining the time point at which 50% of the study population are still alive.

3. Alternative censoring methods

There are several methods that are used, or proposed, in the literature in order to calculate the total average costs of health care interventions within the context of economic evaluation. These techniques range from ignoring the issue of censoring to more complex methods using survival analysis techniques, such as the Kaplan-Meier method. Each of the methods presented below results in some degree of bias, the degree of which depends upon the method chosen and the data set of interest.

Method 1: *Ignoring the issue of censoring.*

For this method, the total average cost is calculated by ignoring the issue of censoring, thereby effectively treating the censored individuals as if they had died at the point of censoring. The total average cost is then simply represented by the mean cost for the entire group of individuals. This method underestimates the total average costs since any costs incurred beyond the point of censoring are not taken into account. The amount of bias occurring depends upon the proportion of

individuals who are censored, if a high proportion of observations are uncensored then the degree of bias using this method becomes minimal.

Method 2: *Ignoring the censored cases*

As with Method 1 the idea behind this method is as it appears, the total average costs are calculated from the cases where a death time is observed, in other words the censored cases are ignored. Here, average costs are biased towards the costs of the individuals with shorter survival times, as censored cases are more likely to survive for longer. In common with Method 1, overall the degree of bias is likely to depend upon the proportion of censored cases.

Method 3:*Using the Kaplan-Meier estimator on a cost scale.*

Fenn *et al*[3] recognised the potential bias that could arise from the above methods and proposed an alternative method (though used by others in the context of economic evaluations prior to this time[4, 5]) that adjusted for the problem of censoring. Basically, the authors applied the Kaplan-Meier method for estimating survival to the cost scale. In other words the data is ordered by increasing total cost per patient, rather than survival, and the intervals begin at the cost of one dead individual and end immediately before the cost of the next individual who died, with the probabilities of obtaining a certain cost being calculated as described in Section 2. previously. As with the Kaplan-Meier method for estimating survival, the total average cost can then be obtained by calculating the area under the cost 'survival' curve.

However, the authors did not take into account the assumption of independence and hence this method is also likely to be biased, as pointed out by Lin *et al*[6] and Hallstorm *et al*[7]. In order to calculate unbiased Kaplan-Meier estimates it is necessary for the survival times of the individuals to be independent of their censoring mechanism. When applying the method to the cost scale, costs must also be independent of censoring and this is not the case. To illustrate, if two individuals who enter a study simultaneously are censored at the same time point, but the first individual incurs costs that are twice as high as the second individual's costs, this means that, on the censored cost scale, the first individual with the higher costs will be censored at some point beyond the second individual. The censoring mechanism is therefore not independent of costs, which means that this method is likely to result in an overestimation of the total average costs.

Method 4: *Estimated costs adjusted by survival probabilities*

In 1997, Lin *et al*[6] proposed a new method for using the Kaplan-Meier survival estimates to obtain total average costs which also avoided the problem of bias due to dependence between costs and censoring. The method requires that information on costs is available at specific time intervals throughout the entire period of the study, for example monthly costs. The method consists of dividing the total time period for the study into K, smaller intervals of equal length, the smaller the interval the more precise the total average cost estimate. The estimated cost can then be calculated as follows:

$$\hat{C}_{CH} = \sum_{k=1}^{K} \hat{S}_k \hat{C}_k \qquad (2)$$

Where $\hat{S}_k$ is the Kaplan-Meier estimate for the k[th] interval and $\hat{C}_k$ is the expected cost for the k[th] interval that is estimated from the average cost incurred in the k[th] interval by individuals who where alive to incur costs at the start of the interval. If censoring does not occur at the end of an interval but at the beginning or in the middle of an interval then bias occurs, resulting in an underestimation of cost. However as the cause of bias is also true of the Kaplan-Meier survival method, the resulting estimate is still likely to be more accurate than that obtained from any of the above mentioned methods.

Method 5: *Estimated costs adjusted by death probabilities*

In some situations it is possible that only the total aggregated cost for each individual is known, rather than disaggregated costs for each individual over the whole study period. An alternative method to method 4 is offered by Lin *et al*[6] if this situation were to arise.

As with method 4 the study period is divided into K time intervals of equal length, and as before, the Kaplan-Meier estimate is derived for each interval. The total average cost can then be obtained as follows:

$$\hat{C}_{NH} = \sum_{k=1}^{K+1} \hat{A}_k (\hat{S}_k - \hat{S}_{k+1}) \qquad (3)$$

Where $\hat{S}_k$ and $\hat{S}_{k+1}$ are the Kaplan-Meier estimates for the k[th] and (k+1)[th] intervals respectively, so $\hat{S}_k - \hat{S}_{k+1}$ is the probability of dying in the k[th] interval and $\hat{A}_k$ is the mean total cost for individuals who die in the k[th] interval. The mean total cost for the K+1th interval is the average cost of individuals who survived to the end of the study period. The total individual costs for the cases that are censored before the end of the study are not included in the calculation in this method. The authors admit, "some loss of efficiency may result from disregarding the costs of the censored cases" and suggest that 5 or more deaths should occur in each interval to obtain an accurate estimation of the total average cost.

4. Literature review of costing studies and economic evaluations of solid organ transplants

A literature review of costing studies and economic evaluations of solid organ transplants was performed in order to establish the techniques used by other researchers to overcome the problem of censored costs data. MEDLINE and BIDS electronic database searches were carried out in order to find relevant articles. The time period of interest was 1970-1999. Where other potentially relevant references were quoted within the papers identified by the database search, these were also obtained. Papers (including conference abstracts) were deemed suitable for inclusion into the review if they were not a review paper of other authors' work and represented original costing or economic evaluation studies of solid organ transplant procedures.

A total of 25 articles, 58.1% of those reviewed in total, from 20 different studies, were considered as suitable for inclusion. A summary of the studies identified, their methods and findings, are given in Table 1 at the end of the paper. If no method of censoring was stated anywhere in the study then it was assumed that the issue of censoring was ignored (method 1). This was found for 60% of the studies identified, indicating that the average total cost of transplantation was underestimated. In three studies the issue of censoring was not applicable as only the cost of the transplant operation and the time spent in hospital after the operation was considered. The remaining studies (25%) did use some form of censoring by dividing the post transplant period into smaller lengths and calculating average costs for each period. Van Enckevort *et al*[13-15] weighted the average total cost per patient by the probability of survival or death, this is the nearest any study came to using Method 4, potentially the most accurate predictor of average total costs.

In comparing the methods used in previous costing and economic evaluation studies of solid organ transplant procedures, it is clear that aside from how these studies have handled the censored costs issues, there remain marked differences in the approaches used. Studies have tended to vary widely in the stages of the transplant procedure which have been included in the exercise, with some studies including assessment for suitable transplant candidates to a period after transplantation,[8,13-15] others have evaluated the transplant hospital stay only.[11,17,25] Studies have also differed as to whether or not they have included the cost of procuring the donor organ. The types of costs collected were also found to vary widely with some studies including direct costs only[17,26,29] and others including additional cost categories (direct non-medical and/or indirect costs).[13-15,21,22] Some studies, particularly those emanating from the US have tended to use charges or fees data rather than unit cost data in informing average total cost estimates.

5. Empirical example of comparison of methods

The variation in average total costs that can be obtained from using the various methods described is illustrated within this section. The data presented here represents interim data from an economic evaluation of the liver transplantation programme in England and Wales. Information on patient based resource use during the transplant and follow up phase (to two years post-transplant) was collected from each centre. Unit costs for resource use information were also collected from the finance department at each centre.

The analysis considers the total average cost of transplantation, beginning when an individual is hospitalised for a first study transplantation and ending either at death or at a maximum of 2-years post-transplantation. Resource items included the transplant operation, ITU and ward stay both prior to and after the operation, post-transplant admissions, treatments, tests, drugs, blood products, nutrition, physiotherapy and dietician sessions. Costs are presented in 1999 UK pounds and are undiscounted at this stage.

A total of 199 liver transplants were undertaken at the two centres during the study period. No significant differences in demographic characteristics occurred between the patient's transplanted at the two centres (see Table 2). The table also shows that there was no difference in post-transplant

survival after liver transplantation at either centre. Over 80% of the transplant patients survived the operation, of these 111 (68.9%) patients were censored at the end of the study period. The remaining 50 (31.1%) patients were censored before the end of the study and have incomplete 2-year costs. The median survival time for patients who died before the end of the study was 4 months.

Table 2: Demographic characteristics and survival information for each centre and overall.

	Centre 1 (n = 116)	**Centre 2 (n = 83)**	**Overall (n = 199)**	**P-value***
Males (%)	62 (53.4)	40 (48.2)	102 (51.3)	0.465
Median age (IQR)†	52 (41 to 59)	53 (44 to 58)	53 (42 to 58)	0.597
Primary liver disease:				
Alcoholic cirrhosis (%)	16 (13.8)	9 (10.8)	25 (12.6)	0.500
Post hepatitic C cirrhosis	22 (19.0)	14 (16.9)	36 (18.1)	
Primary biliary cirrhosis	14 (12.1)	14 (16.9)	28 (14.1)	
Acute hepatic failure	7 (6.0)	4 (4.8)	11 (5.5)	
Post hepatitic C cirrhosis	9 (7.8)	3 (3.6)	12 (6.0)	
Re-transplanted	9 (7.8)	3 (3.6)	12 (6.0)	
Other disease	39 (33.6)	36 (43.4)	75 (37.7)	
Survivors (%)	96 (82.8)	65 (78.3)	161 (80.9)	0.431
Survival length in months:				
Median (IQR)	24 (20 to 24)	24 (21 to 24)	24 (20 to 24)	0.841‡

* P-values represent difference between centres and are for the $?^2$ test for categorical data and Wilcoxon sigh rank test for continuous data. † IQR – Inter quartile range. ‡ Wilcoxon test for differences in survival.

Total costs per patient from admission for transplantation to 2-years post transplantation ranged from £712 to £176,538. Average total costs ranged from £23,535 when using the full cost mean, ignoring the issue of censoring, and £76,687 when using the Kaplan-Meier estimates on a cost rather than survival scale (see Table 3). Patients who died during the study period incurred higher costs than patients who remained alive or who were censored (Mean total cost for those patients who remained alive was £19,420, mean total cost for those patients who died was £40,969).

Table 3: Two-year average total costs for liver transplantation according to the method used to deal with censored data.

	N	**Average total cost**	**Standard error**
Method 1	199	£23, 535	1, 757.70
Method 2	38	£40, 969	2, 860.84
Method 3	199	£80, 567	6, 440.49
Method 4	199	£31, 203	2, 312.61
Method 5	199	£24, 520	1, 863.26

6. Discussion

The empirical example that has been used here illustrates the wide range of results that can be obtained depending upon how the issue of censoring is dealt with when calculating the total average cost of health care interventions within economic evaluations. The most striking results are obtained when calculating costs from the Kaplan-Meier estimator on a cost rather than survival scale (Method 3), the average total cost estimate being almost twice as high as that obtained when the censored cases are ignored using Method 2. The overestimation of total cost from this method is due to the fact that censoring and costs were not independent of each other and as the majority of the patients in this study incur relatively large total costs (in excess of £10,000 per patient), the method can easily overestimate the true average cost per patient by a significant amount.

Lin *et al*[6] demonstrated what we believe to be the most unbiased method for estimating the average total cost with censored cost data from equation 2 (Method 4). Using the results we have obtained in our empirical example by this method relative to other methods used as a benchmark, we estimate that the total average costs estimated by the majority of studies highlighted in our literature review (which ignored the issue of censoring altogether) may have underestimated the 'true' average total costs of transplantation by as much as 25%. Potentially of greater concern within the context of the economic evaluation of health care interventions is the large overestimation that is possible when using the Kaplan-Meier estimate on the cost scale (Method 3). It is true that over 70% of the studies included in our review were published prior to Lin *et al*[6] and Fenn *et al's*[3] work entering the public domain. Hence it is not entirely surprising to find that so many studies from this period effectively ignored the issue of cost censoring altogether. However, it was also found that only 33% of studies published after Lin *et al*[6] and Fenn *et al's*[3] work entered the public domain considered the issue of cost censoring.

Although we consider that, of the methods proposed, method 4 offers the most theoretically unbiased approach, as it allows for the issue of censoring by weighting the costs using Kaplan-Meier *survival* estimates, there are drawbacks to the use of this method in practice. The method requires costs to be stored in a format that makes it possible to calculate the total costs for each patient within each chosen interval. It was found that the manipulation process required to place the data into the necessary format was quite complex and time consuming and could not be achieved without the use of statistical software packages such as STATA[33] and SAS[34] to manage the process (EXCEL was not able to handle the manipulation). However, it is possible that the problems we encountered in manipulating the data were magnified due to the relatively large volume of data within our data set in comparison to that used for economic evaluations in areas other than transplantation.

In our empirical example the majority of patients were censored, though only a quarter were censored prior to the end of the study period. It is important that further work is undertaken to assess the effect of the degree of censoring in the date set on the variation in the results obtained using the five methods described in this paper. If all individuals or the majority of individuals in the study die during the study period then the degree of accuracy of the first two methods will be high.

However, such scenarios are unlikely in practice. It is important to explore further at what degree of censoring these methods become less accurate and how much accuracy is lost. These issues also needs exploring for the other proposed methods, especially method 5 where censored costs are essentially ignored if they occur before the end of the study. Another issue that could be explored further is the choice of the interval lengths for Lin's[6] methods and how a change in the interval length affects the magnitude of the overall results obtained. Lin *et al*[6] recommend that at least five deaths per interval are necessary in order to predict the total average cost accurately when only the total cost per patient is known. If we had followed Lin *et al's* recommendations for our example then the number of intervals would have been only 2 or 3. The accuracy of method 5 over a small number of large intervals is questionable.

Fenn *et al*[35] have also suggested that it is possible to use Cox regression or Weibull models in order to adjust for factors that may affect the average total costs. As with using the Kaplan-Meier estimates on a cost scale, assumptions need to be upheld for this method to produce accurate results. The additional assumption here, is the assumption of proportionality. Proportionality implies that the hazard of death at any given time for an individual in one group is proportional to the hazard at that time for a similar individual in another group.[2] For example, assume that the effect of gender on survival is to be investigated. A Kaplan-Meier survival plot of each sex can then be used to check that proportionality holds. If the two survival curves do not cross then proportionality holds. Caution needs to be taken if applying the Cox or Weibull models to Lin *et al's*[6] methods. Consideration as to whether the factors being adjusted for relate to survival or cost and whether the proportionality assumption needs to hold true for both costs and survival need to be considered. Unfortunately these issues are beyond the scope of this paper, although the authors hope to consider these issues further in future research.

Table 1: Summary of the review of costing studies and economic evaluations of solid organ transplants

Authors	Type of organ	Study population	Comparison group	Cost methods	Type of cost censoring	Survival methods	Results Presented in	Results**
Buxton M, Acheson R *et al* (8)	Heart	1982 to 1984. 2 UK heart Tx.* programmes	Waiting list	Assessment to post Tx. & donor cost.	Sum of average costs survival/death over 6-mths.	KM† (Turnbull et al's method)	1983/4 UK £ Total cost	Harefield = £50, 402 Papworth = £62, 044
Van Hout B.A. (9)	Heart	1984 to 1987. 2 Dutch Tx. centres	Waiting list	Screening, WL‡, Tx., post Tx.	Method 3	KM	Dutch fl. Discount 5%	Per life yr = £16,471 Per QALY= £20,545
Evans R.W. (10)	Heart	2 published papers	None	Pre to post Tx. Donor.	Method 1	Not applicable as costing study only	1980 US $	Tx. (1 yr.) = £111,309
Evans R.W. Manninen D.L. *et al* (11)	Heart-Lung	1988. 42 patients randomly selected from all US Tx. programs	None	Tx. (hospital, professional fees & donor organ acquisition)	Tx. phase only so not applicable	Not applicable as costing study only	1988 US $ Median cost	Tx. = £ 84,503
Abu-Elmagd K.M. Reyes J. *et al* (12)	Intestinal	109 consecutive Tx. patients in US over 8 yrs.	TPN therapy	Not described	Method 1	KM	US $ (TPN 1992)	TPN = £93,975 Intestine = £82,877
Van Enckevort P *et al* (13-15)	Lung	1990 to 1995. Dutch lung Tx. program (N=57)	Waiting list	Assessment to post Tx. Direct medical & non-medical costs & indirect non-medical	3 month cost post Tx. = (%survive * average. cost survive) + (%died * average cost died)	KM & Weibull models for waiting list group	US $	Tx. = £247,048 WL = £49,539 Per life yr. = £45,108 Per QALY = £38,217
Ramsey D. *et al* (16)	Lung	1st 25 patients Tx. in US centre	Waiting list	Waiting list to post Tx.	Method 1	DEALE to estimate life expectancy	1993 US $ Discount 5%	Tx. = £266,170 WL = £98,555 Per QALY =£110,776
Gartner *et al* (17)	Lung	March to Aug. 1994 in US, all lung tx. (N=20)	None	Direct costs. Tx. phase only	Tx. phase only so not applicable	(No. deaths)/N	1994 US $	Mean = £96,432 Median = £59,094
Bonsel G.J. *et al* (18-20)	Liver	1979 to 1987 in Netherlands (N = 145)	Prognostic models	Unit & hospital costs per vol. per patient	Method 1	KM & Cox models for shadow group	1987 Dutch Fl. 5% discount	Tx. = £71,429
Kankaanpaa J. (21-22)	Liver	1981 to 1986 US, 32 adult Tx.	None	Direct & indirect costs pre Tx. to Post Tx.	Two groups. Those survive < 1 yr. & those survive > 1 yr.	(No. deaths)/N	1986 US $ 5% discount.Life yr.	<1yr. = £156,625 > 1 yr. = £35,084

Tx.=Transplant, KM=Kaplan-Meier, WL=Waiting list **All results quoted in UK £, without adjustment for inflation (UK £1= US $0.63, 65.25 Phillipine Pesos, NZ $3.16, 3.50 Dutch Guilders , 2.36 Canadian $)

Table 1: Summary of the review of costing studies and economic evaluations of solid organ transplants (cont.)

Williams J.W. *et al* (23)	Liver	1982 to 1985 US. 55 consecutive Tx. 2 hospitals.	20 patients died before Tx. 1984	Charges to patients' pre Tx. to post Tx.	Method 1	(No. deaths)/N	1984 US $'s	Tx. = £73,619 Shadow = £28,595
Burroughs A.K. *et al* (24)	Liver	Oct. 1988 to Oct 1989 UK, 23 consecutive Tx.	May/June '89 14 cirrhotic's	Per Tx. up to 6 mth post Tx. Cost accounting.	Method 1	(No. deaths)/N	Median	Tx. = £ 17, 242 Cirrhotic = £ 5, 453
Evans R.W *et al* (25)	Liver	1988. 416 random patients from US pop.	None	Tx. only. Hospital cost summary forms.	Tx. phase only so not applicable	Not applicable as costing study only	1988 US $'s Median	Tx. = £91,341
Croxson B.E Ashton T (26)	Kidney	A model based population.	Haemodialysis (HD) in centre and at home	Direct cost to patient. Prospective–Auckland Health Board	Method 1	Data from dialysis units	1988 NZ $'s 10% discount	Tx. = £25,063 HD-home= £253,242 HD-centre=£31,078
Whiting J.F *et al* (27)	Kidney	Not documented	HD patients	Markov decision analytic model	Method 1	Literature review	5% discount 3% inflation	Tx. = £93,348 HD = £25,307
Naidas O.D *et al* (28)	Kidney	1995, 71 Tx. in Philippine's	60 HD & 52 CAPD patients	Patient prospective	Method 1	Cox regression	1995 Philippine pesos	Tx. = £51,592 HD = £60.773 CAPD=£53,422
Karlberg I Nyberg G (29)	Kidney	1988 to 1991, all Tx. in Sweden	CAPD or HD	Direct cost from centre	Method 1	Assumed constant over time	US $'s Yr. cost of program	Tx. = £15,662,500 CAPD=£53,252,500
Hornberger J.C *et al* (30)	Kidney	1995 US from USRDS report & Medicare program 1982 to 1992	1st Tx. v Re-Tx.	Societal prospective. Decision analytic techniques.	Method 1	Published data	Cost per QALY discounted at 5%	1st Tx. = £165,094 Re-Tx. = £164,335 Per QALY = £6049
Tousignant P *et al* (31)	Kidney	1970 to 1978 Canada. 16 case matched Tx. 2 hospitals	16 case matched HD patients	Services & treatments from financial records & questionnaires	7 year costs in yearly intervals	Extrapolation of observed death rates	1977 Canadian $'s No discount.	Difference in costs = -$ 266,692 in favour of Tx.
Eggars P (32)	Kidney	1989. Not stated – looks like all Tx. in US	HD	Medical expenditures & costs.	Method 1	Published data, a linear model fitted	1989 US $'s 3% discount	Tx. = £66,788 HD = £20,549

*** Tx.=Transplant, KM=Kaplan-Meier, WL=Waiting list **All results quoted in UK £, without adjustment for inflation (UK £1= US $0.63, 65.25 Phillipine Pesos, NZ $3.16, 3.50 Dutch Guilders, 2.36 Canadian $)**

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