資料２

インタビューシート

相手の方の言葉＆ものがたりを
ゆっくり聴いて
この時間をぜひ楽しんでください！

＜インタビューのはじめに：以下をインタビューを受ける方に読んであげてください。＞

＊＊＊

◆これからインタビューを始めさせていただきますので、よろしくお願いします。

・インタビュー時間は、これから約４０分（２人で８０分）です。

・もしかすると、ちょっと気恥ずかしい感じがするかもしれませんが、ゆっくりと思い出しながら、話をしてください。

・ゆったり考える時間も大切です。沈黙や“間”を恐れず、その沈黙の時間も大切にしたいと思います。また、その時々で、浮かんできた言葉、気持ち、感覚などを大切にしてください。

・もっと知りたいことがあったら、「それはどういうことですか？」などと質問をするかもしれませんが、話したくないことは話さなくて大丈夫です。

・これからお話していただくお話の詳細は、今日のこのセッション中を含め、他の人と共有することはありません。全てこの場限りです。

・ただし、キーワードなど、後ほど全体で紹介し合う機会があります。ですのでメモを取ることがあります。

・インタビューを受けている間は、お手もとのシートをみないでお答え下さいね！

◆それでは、質問に入ります。

＊＊＊

＜　次のページから問いが始まります。＞

1．地域での医療やがん対策について、今のあなたの関わりや取り組みについてお聞きします。４つおたずねしますので、順番にお話し下さい。

① 地域での医療やがん対策について、あなたが今関わっている、取り組んでいることは何ですか？

② その関わりや取り組みについて、あなたはどういう想いをもっていますか？

③ その関わりや取り組みを始めることになったきっかけ、理由、動機はなんですか？

④ そこにあなたを導いてくれたひととの出逢いや出来事は何ですか？

2．今まであなたが生きてきた中で、最も印象に残っていることについてお聞きします。４つおたずねしますので、順番にお話し下さい。

① 今まであなたが生きてきた中で、最も印象に残っていること、例えば、自分に関係のある出来事やひととの出会いなど、はどんなものですか？嬉しかったこと、楽しかったこと、悲しかったこと、悔しかったこと、成功体験、失敗体験など、何でも結構です。

② 特に印象に残っているのは、どういうところですか？

③ その中で、同僚、家族、地域の人など、「ひととのつながり」を感じた場面、あるいは「ひととのつながり」が欲しいと感じた場面は、どういうところですか？

④ その最も印象に残っていることの中で、あなたが大切にしていることは何ですか？

4．ある朝、目が覚めると、あなたが理想としてきた世界が目の前に広がっていました。あまりにも理想的なので、夢ではないかと疑っているほどです。
そんな理想の世界について、３つおたずねしますので、順番にお話し下さい。

① あなたは、どのように過ごしているでしょうか？どんな人、誰と関わり、どのような日常を送っているでしょうか？

② あなたが仕事をしている職場や、あなたが属している組織、地域は、どのようになっていますか？

③ そのとき、あなたは、周りの人々にとってどんな存在でしょうか？どのような『価値』を誰に与えているのでしょうか？

＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊（以上です）

資料３

○当日の概要

・開会後、案内文と同趣旨の 2005 年からの流れと島根県との関係の説明、そして、それらと企画者（吉見）との個人的な関係のストーリーテリング（物語）、を行った。
・しかし、メンバー紹介、自己紹介、など、先に参加者から要望があがるなど、「この会は何で誰がやっているのか」というような疑問の提示もあり、自己紹介、チェックインをしっかり実施することとし、当初は一言で巡回する予定だったところを十分お話いただいて一周した。そのため時間はお昼前までとなった。
・そのまま予定のワールドカフェののちお昼にすることを提案したが、服薬等のこともあり、食事が早い方がよいことが判明したこと、そして昼で退出される方もあるので、自己紹介がしっかりできたところで一旦区切ることができること、にて参加者の方々の合意を得た。
・お昼の間にスタッフでミーティングし、予定を見直し、午後はしっかりワールドカフェを行ったうえでそのハーベスト、という方向性とした。
・ 13 時からワールドカフェ。20 分 x 3 ラウンド、そののち一旦もとの席に戻り振り返りとした。

※ワールドカフェの問い
「地域でくらしてきて ／もっとも印象に／残っていることは／何ですか？」
「あなたが、暮らし、／生きていく上で／とても大事にしていること／大事にしたいことは／何ですか？」
「あなたがとても／大事にしていることを／誰と、どのように、／わかちあいますか？」
の 3 問。

・振り返りシェアとフリーディスカッションをサークル形式で行うこととした。フリーディスカッションは強制発言でなく自発発言なので、全員の発言ではなかったが、豊かな言葉がたくさんでてきた：つながり、出会いなおし、場の力、など、企画意図としていたものや期待していた言葉が参加者から投げかけられた。
・終了・解散ののち、お時間がある方で小さいサークルをつくり対話した。うちの地域や施設でも実施したい、ほか対話の場をいろいろやりたい、という発言もあった。場や対話の力というのは現場に近いほど活きてくる可能性がある。

（以上）　文責・吉見

Ⅷ. 研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
Fukuda H, Imai H	Cost Effectiveness Analysis of Liver Transplantation. In Liver Cancer, Causes, Diagnosis and Treatment	Benjamin J.Valverde	Liver Cancer:Causes,Diagnosis and Treatment	Nova Science Publisher,Inc.	アメリカ	2011 印刷中	

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Fukuda H, Imai H	Cost Effectiveness Analysis of Liver Transplantation. In Liver Cancer, Causes, Diagnosis and Treatment	Progress in Economics Research	24		2011 印刷中

In: Liver Cancer: Causes, Diagnosis and Treatment
Editors: Benjamin J. Valverde
ISBN: 978-1-61209-115-0

Chapter 7

COST EFFECTIVENESS ANALYSIS OF LIVER TRANSPLANTATION

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For patients with end-stage liver disease (ESLD), liver transplantation is an established therapy. The efficacy of deceased donor liver transplantation (DDLT) has been verified in various studies, and the procedure is a socially acceptable medical technique. On the other hand, one current challenge is the increase in the number of DDLT cases, causing longer waiting periods for available organs, a situation that has been recognized as a social issue. Living donor liver transplantation (LDLT) is performed as an alternative.

However, liver transplantation is a costly medical procedure. Thus, it is difficult to determine whether a novel technique should be covered by health insurance solely from the perspective of its effectiveness, given the intense pressure to reduce medical costs. Health economics assessment (HEA) takes into account both economics and effectiveness. Therefore, such assessment should be carried out and the results should be presented and understood by the public before a new technique is accepted.

This chapter summarizes past findings regarding cost, effectiveness, and cost-effectiveness, and offers points to consider when conducting an adequate HEA. After reading this chapter, readers will be able to perform cost-effectiveness analyses adequately not only for liver transplantation but also for other health technologies.

This chapter consists of the following 7 sections. Section 1 shows trends in the number of liver transplantation cases and current survival data. Costs associated with liver transplantation are discussed in Section 2. We conduct a systematic review and present the cost estimates of liver transplantation. Additionally, we examine the quality of cost studies and discuss the costing and reporting methods that enable the readers to make appropriate decisions. Furthermore, from the viewpoint of international comparisons, we compare a breakdown of the costs of liver transplantation. With regard to effectiveness, we provide an introduction to the methods used to assess utility. We also list past publications that have estimated utility scores. Section 4 provides a systematic review of the cost-effectiveness of

liver transplantation and examines whether liver transplantation is cost-effective. Section 5 examines cost-utility analyses for LDLT conducted in Japan. There are very few reports of such studies. In Section 6, we discuss practical aspects of undertaking cost-effectiveness analyses: which cost items should be included in a cost analysis and how cost-effectiveness should be judged are the major issues addressed in this section. We also examine ethical issues in resource allocation that a cost-effectiveness analysis alone is unable to deal with. Finally, in Section 7, we conclude the chapter with some further recommendations on how to conduct cost-effectiveness analyses.

1. CURRENT STATUS OF LIVER TRANSPLANTATION

1.1. Number of Liver Transplantations Cases

The first human liver transplantation was performed at the University of Colorado by Starzl in 1963. The number of liver transplantation cases increased from the 1980s to the 1990s, and over 5000 patients per year received liver transplants after 2001. Liver transplantation has been widely performed in advanced countries, with the cumulative number of cases totaling approximately 103,000 in the US as of August 23, 2010 [1] and approximately 88,000 in the EU as of June 2009 [2]. Liver transplantation has been accepted as an established therapy for ESLD patients. By the end of 2008, there were approximately 5,300 cases of liver transplantation reported in Japan.

However, there are significant differences in the number ratio of LDLT cases to DDLT cases in Western countries versus that in Japan. DDLT is the major liver transplantation performed in the US and Europe. For a period of time however, the US has steered toward an increase in the number of LDLT cases. The lack of deceased donors owing to an increase in the number of DDLT cases is expected to be solved with the use of living donors. The proportion of LDLT cases was 10.1% (524 cases) of all liver transplantation cases (5195) (Table 1) in 2001. However, once a dead case is reported, the number of LDLT cases has decreased rapidly to ensure donor safety. As a result, LDLT accounted for fewer than 4% of all cases in 2009 [1]. Also in Europe, deceased donors are commonly used in liver transplantation and the proportion of LDLT cases was only 3.9% [2]. In contrast, 400-500 liver transplantations per year are performed in Japan, and most of them are LDLT [3]. This represents a large difference between Western countries and Japan.

Table 1. Trends of number of liver transplantation cases

		Total	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
USA	Total	103,427	2,634	6,320	6,319	6,494	6,651	6,444	6,171	5,673	5,332	5,196	5,000
	CDLT	99,301	2,510	6,101	6,070	6,228	6,363	6,121	5,848	5,351	4,969	4,672	4,595
	CDLT, %	96.0%	95.3%	96.5%	96.1%	95.9%	95.7%	95.0%	94.8%	94.3%	93.2%	89.9%	91.9%
Europe	Total	87,964	-	4,646	5,638	5,490	5,481	5,422	5,096	5,142	4,948	4,821	4,587
Japan	Total	5,250	-	-	477	443	510	566	554	442	441	423	333
	CDLT	61	-	-	13	10	5	4	3	2	7	6	6
	CDLT, %	1.2%	-	-	2.7%	2.3%	1.0%	0.7%	0.5%	0.5%	1.6%	1.4%	1.8%

1.2. Survival Rates in Liver Transplantation

Table 2 shows survival rates by country. The US and countries in the Europe have similar survival rates for patients who have undergone DDLT. The 1- and 5-year survival rates are 87.3% and 73.4% in the US, [1], and 83% and 71% in the Europe, respectively [2]. On the other hand, the 1-year and 5-year survival rates of LDLT are 83.2% and 76.8% in Japan [3]. They are 91.7% and 77.7% in the US respectively [1], which is not significantly different from those in Japan.

Table 2. Survival rates in liver transplantation

Country	DD or LD	n	Survival rates			
			1 year	3 year	5 year	10 year
US [1]	DD	10,533	87.3	—	73.4	58.7
	LD	592	91.7	—	77.7	70.7
Europe [2]	Total	63,221	83	—	71	61
Japan [3]	DD	61	77.0	75.3	72.1	68.3
	LD	5,189	83.2	79.1	76.8	72.8

DD: deceased donor liver transplantation
LD: living donor liver transplantation

2. COST OF LIVER TRANSPLANTATION

2.1. Systematic Review of Liver Transplantation Costs

Liver transplantation is an established treatment for patients with ESLD. However, liver transplantation involves high medical costs because of multiple diagnostic procedures, a surgery lasting many hours, a long hospital stay with intensive care, and long-term immunosuppressive therapy. Under the current cost-containment policy, it is imperative for both insurers and policy makers to determine how much a liver transplantation costs. Thus, in this section, we aim to conduct a systematic review of published studies in which the costs of liver transplantation that have been estimated.

Using the MEDLINE database, we conducted a literature search up to June 30, 2010. For search keywords we used "Liver Transplantation" [MESH] AND "Costs and Cost Analysis" [MESH], and as a result, we retrieved 310 papers. We identify papers that potentially provide therapeutic cost estimations of liver transplantation through titles and abstracts, and examined the entire texts of the papers. Furthermore, we analyzed the references cited in the studies obtained in the MEDLINE search. When screening was reasonably complete, we selected 38 papers that actually provided cost estimates of liver transplantation for the use in our review [4–41].

Table 3 provides an overview of 89 studies conducted between 1990 and 2009 that assessed the costs of liver transplantation. All reported costs were converted to US dollars for the year 2009. Because of differences in purchasing power parity (PPP) and the year of study between the articles, we adjusted the cost estimates using the PPP for gross domestic product (GDP) between the US and other countries, and the consumer price index (CPI) for the US.

PPP for GDP is reported by OECD and CPI was provided by the US Bureau of Labor Statistics (http://www.bls.gov/cpi/). A major finding from the included studies was the large variation in cost estimates because of the variety of cost scope used in the studies, which prevented meaningful comparison between them. Thus, readers seeking estimates of liver transplantation costs must pay close attention when interpreting such estimates. Although some studies included costs from pretransplantation to post-transplantation, the majority estimated and reported costs only for the liver transplantation operation itself. However, even focusing solely on the liver transplantation itself, to increase comparability between the publications, the reported costs per case ranged from US$59,396 to US$312,665.

Table 3. Costs of liver transplantation

First author	Country	Study duration	n	Cost estimates (US$, 2009)			
				Pre	operataion	Post	Total
Buchanan [4]	**USA**	**2002.3-2007.8**	**990**	**135,155**	**312,665**	**79,257**	**552,204**
Markley [5]	**USA**	**2004.1-2006.2**	**166**	**excl.**	**117,254**	**excl.**	**117,254**
Passarani [6]	**Italy**	**2001.6-2003.11**	**12**	**239,124**		**excl.**	**239,124**
Englesbe [7]	**USA**	**2002.7-2005.6**	**240**	**excl.**	**214,032**	**excl.**	**214,032**
Ishida [8]	**Japan**	**1999.1-2001.12**	**11**	**8,962**	**190,532**		**199,494**
Kogure [9]	**Japan**	**2001.9-2005.1**	**17**	**excl.**	**107,544**		**107,544**
Washburn [10]	**USA**	**2002.2-2004.5**	**222**	**excl.**	**85,542**		**85,542**
Kraus [11]	**Germary**	**2003.6-2003.9**	**38**	**excl.**	**62,234**	**excl.**	**62,234**
Oostenbrink [12]	**Netherlands**	**1995.1-2001.8**	**179**	**189,144**			**189,144**
Reed [13]	**USA**	**Unknown**	**888**	**excl.**	**198,420**	**excl.**	**198,420**
Brand [14]	**USA**	**1996.11-1997.12**	**26**	**90,142**	**207,326**		**297,467**
Cole [15]	**USA**	**1997.1-2002.1**	**47**	**excl.**	**127,906**	**196,667**	**324,572**
Filipponi [16]	**Italy**	**1997.1-2000.12**	**252**	**excl.**	**119,288**		**119,288**
Longworth [17]	**UK**	**1995.12-1996.12**	**208**	**128,236**			**128,236**
Trotter [18]	**USA**	**1997.8-2000.6**	**67**	**9,831**	**127,210**	**43,112**	**180,153**
Azoulay [19]	**France**	**1986.9-1999.9**	**139**	**excl.**	**116,627**		**116,627**
Sagmeister [20]	**Switzerland**	**1995.1-2000.10**	**51**	**excl.**	**81,477**	**12,350**	**93,827**
Taylor [21]	**Canada**	**1991.1-1992.12**	**119**	**676**	**67,861**	**6,046**	**110,307**
Skeike [22]	**Norway**	**1998.1-1998.7**	**8**	**excl.**	**77,783**	**excl.**	**77,783**
Best [23]	**USA**	**1993.1-1999.12**	**1621**	**13,071**	**179,425**	**51,204**	**243,699**
Bucuvalas [24]	**USA**	**1994.3-1999.4**	**83**	**excl.**	**194,684**		**194,684**
Nair [25]	**USA**	**1994.1-1996.12**	**121**	**excl.**	**151,168**	**excl.**	**151,168**
Schnitzler [26]	**USA**	**1990.4-1994.6**	**683**	**excl.**	**269,768**	**excl.**	**269,768**
van Agthoven [27]	**Netherlands**	**1993.1-1997.11**	**100**	**32,828**	**122,727**		**155,554**
Freeman [28]	**USA**	**Unknown**	**37**	**excl.**	**82,378**		**82,378**
Gilbert [29]	**USA**	**1991.1-1996.12**	**144**	**43,467**	**209,673**		**253,139**
Rufat [30]	**France**	**1994.1-1995.12**	**71**	**13,448**	**79,431**		**92,879**
Showstack [31]	**USA**	**1991.1-1994.7**	**711**	**excl.**	**286,379**	**excl.**	**286,379**
Brown [32]	**USA**	**1992.6-1993.6**	**111**	**excl.**	**299,501**	**excl.**	**299,501**
Geevarghese [33]	**USA**	**1991.2-1996.3**	**100**	**excl.**	**153,633**	**excl.**	**153,633**
Russo [34]	**USA**	**1991.9-1996.12**	**130**	**excl.**	**148,230**	**excl.**	**148,230**
Schulak [35]	**USA**	**1984.7-1996.6**	**935**	**excl.**	**123,923**	**excl.**	**123,923**
Brown [36]	**USA**	**1992.7-1993.6**	**111**	**excl.**	**299,501**	**excl.**	**299,501**
Smith [37]	**USA**	**1990.1-1992.12**	**91**	**excl.**	**309,530**		**309,530**
Pageaux [38]	**France**	**1989.3-1991.12**	**39**	**excl.**	**120,084**		**120,084**
Evans [39]	**USA**	**1988.1-1988.12**	**unknown**	**excl.**	**216,460**	**excl.**	**216,460**
Burroughs [40]	**UK**	**1988.10-1989.10**	**23**	**excl.**	**59,396**	**5,281**	**64,677**
Bonsel [41]	**Netherlands**	**1979.3-1987.9**	**76**	**39,781**	**137,002**	**88,027**	**264,810**

excl.: excluded

n.r.: cost included but not reported

2.2. International Comparison of Cost Estimates

The US carried out the majority of studies on liver transplantation cost analysis, accounting for 57.9% (22 of 38 papers). Studies were also conducted in the Netherlands (3) France (3), the UK (2), Italy (2), Japan (2), Germany (1), Norway (1), Switzerland (1), and Canada (1). An analysis of the number of papers published by continent showed 25 in North America, 13 in Europe, and 2 in Asia (both in Japan).

A comparison of the reported cost estimates (2009 US$) showed that the cost of liver transplantation in the US was higher than that in other countries. (Figure 1). As for the costs of pretransplantation, there seems to be no significant difference in median cost between the US and Europe (US: US$43,467 versus Europe: US$32,828). However, the cost studies conducted inthe US showed large variations in cost estimates (min: US$43,467 versus max: US$135,155). Although liver transplantation itself performed in the US would cost in an estimated ranged from US$117,254 to US$312,665, the costs of liver transplantation reported from Europe ranged from US$59,396 to US$137,002. The median cost estimate from the US is about 2.5 times that from Europe (US: US$198,420 versus Europe: US$79,630). Regarding post-transplantation costs, there is also a large difference between the US and European values, namely US$65,231 (median) and US$12,350 (median), respectively. When the total costs of liver transplantation, including pretransplantation, transplantation itself, and post-transplantation, were compared, the highest cost estimates are from the US, followed by Japan and Europe. For Japan, however, there is only one reported study in which cost estimates for LDLT were investigated.

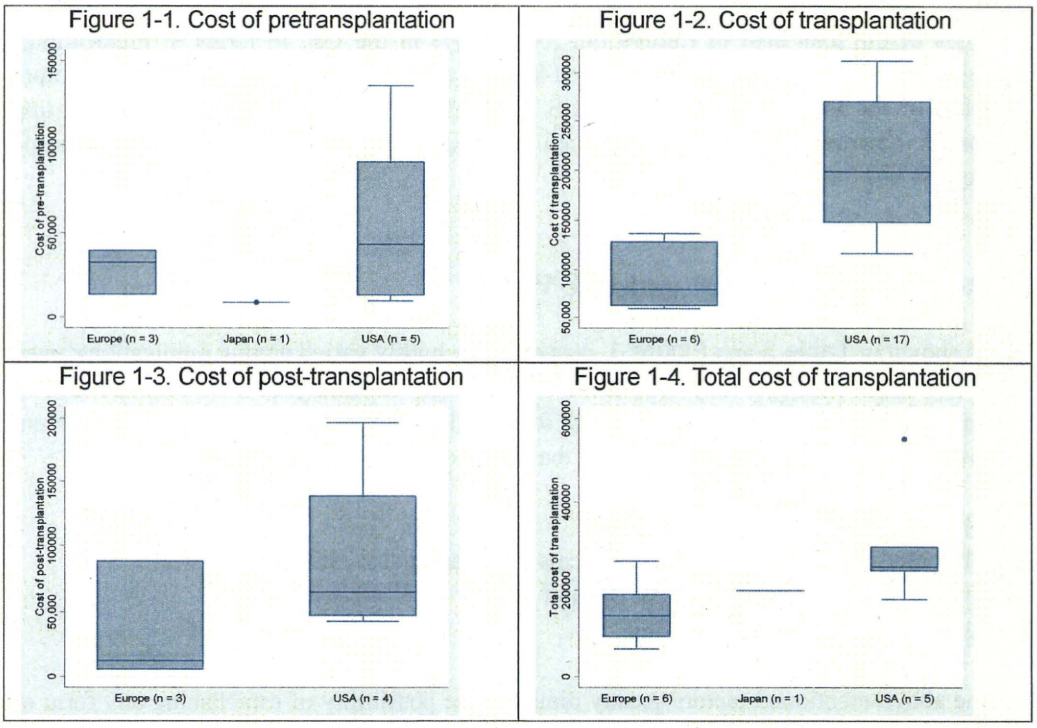


Figure 1. International comparison of liver transplantation costs

We examined whether the breakdown of costs for liver transplantation differed between the US and Europe. Table 4 shows the results by publication and area. Of the 38 publications that estimated costs of liver transplantation, we identified seven studies that included professional fees in the cost estimates and reported the breakdown of those costs; there were five studies from Europe and two from the US. Although the study conducted by Gilvert *et al.* [29] did not report professional fees in their cost estimates, they may have been included in other cost components.

Table 4. Comparison of breakdown of costs of liver transplantation: Europe vs. US

Region	Europe					USA	
First author	Oostenbrink [12]	van Aghoven [27]	Burroughs [40]	Filipponi [16]	Rufat [30]	Gilbert [29]	Evans [39]
Country	Netherlands	Netherlands	UK	Italy	France	USA	USA
Professional fees	**13.6%**	**38.8%**	**32.5%**	**18.9%**	**29.4%**	—	**16.7%**
Hospitalization	**36.5%**	**16.8%**	—	**18.7%**	**18.9%**	**34.9%**	**9.4%**
Transplantation	**7.6%**	**6.6%**	**6.0%**	**1.3%**	**2.9%**	**14.8%**	**20.3%**
Medication	**8.8%**	**10.9%**	**8.5%**	**15.1%**	**16.5%**	**5.9%**	**6.5%**
Diagnostic	**20.4%**	**2.6%**	**37.0%**	**27.9%**	**16.6%**	**18.4%**	**29.2%**
Blood	—	**2.9%**	**3.5%**	—	**9.1%**	**26.0%**	**3.9%**
Others	**13.1%**	**21.4%**	**12.5%**	**18.1%**	**6.6%**	**0.0%**	**14.0%**

7 studies that included professional fees in the costs estimates and reported the breakdown of costs.

There was a large difference in the proportion of total cost due to the liver transplantation itself between the US and Europe. The costs of transplantation accounted, on average, for less than 10% of the total cost in Europe but for 15-20% in the US. In terms of medications, although some studies from Europe reported that the costs of medications accounted for more than 10% of the total, studies from the US reported proportions of only 5-6%. Regarding diagnostics, however, the proportions ranged from 20% to 30% in studies from both Europe and the US.

2.3. Reasons Why the Cost Estimate Varies

As shown in Table 3 and Figure 1, cost estimate highly varied among publications, even within the same country. Why was there such a high variability in cost estimate among publications? The following factors account for such large differences in the cost of treatment and operations for the same disease within the same country among studies [42-44]:

[1] Severity of the disease
[2] Including scope and expense of items included in cost estimation
[3] Individual medical treatment per unit
[4] Cost estimation methodology

The above-mentioned factors greatly diminish the possibility of establishing any form of generalizability. Thus, reported cost estimates should not be directly applied to another researcher's findings, but instead as Cronbach advised, these estimates should be treated as

"working assumptions" and applied indirectly [45]. That is, the working assumptions used in cost estimation should be considered in the context of where and how the estimates were intended to be used. In particular, regarding cost data, researchers should report the factors mentioned above.

2.4. Evaluation of the Quality of Cost Studies

Researchers must increase the transferability of their cost estimates for readers to be able to meaningfully extrapolate these estimates to studies in their own institutions or countries. Although past studies showed detailed information on disease severity, insufficient attention has been paid to the following three perspectives:

[1] Reporting the scope of costing explicitly
[2] Reporting unit costs explicitly
[3] Reporting costing methods explicitly

Table 5 shows the evaluation criteria for the transferability of cost studies

Table 5. Evaluation criteria for transferability of cost studies

Axis	Criteria
(1) Reporting the scope of costing explicitly	(A) All components of costs were described and data on costs in each component were reported
	(B) All components of costs were described but data on costs in each component were not reported
	(C) Only scope of costing was described but components of costs were not described
(2) Reporting unit costs explicitly	Unit costs were reported
	Unit costs were not reported
(3) Reporting costing methods explicitly	Microcosting
	Costs extracted from the hospital accounting system
	Costs calculated using cost-to-charge ratio
	Medicare Fee
	Charge

As the first perspective, we assess whether estimates have clarified the scopes of costing, and we have established a hierarchy of three levels of transparency as follows:

A. All components of costs were described and data on costs in each component were reported.
B. All components of costs were described, but data on costs in each component were not reported.
C. Only the scope of costing was described, and components of costs were not described.

Cost studies that provide a clear description of the scope of costing and data on costs in each component (Level A) are the most valuable. Such studies enable readers to determine whether the estimates include cost items without exaggeration or omission (internal validity).

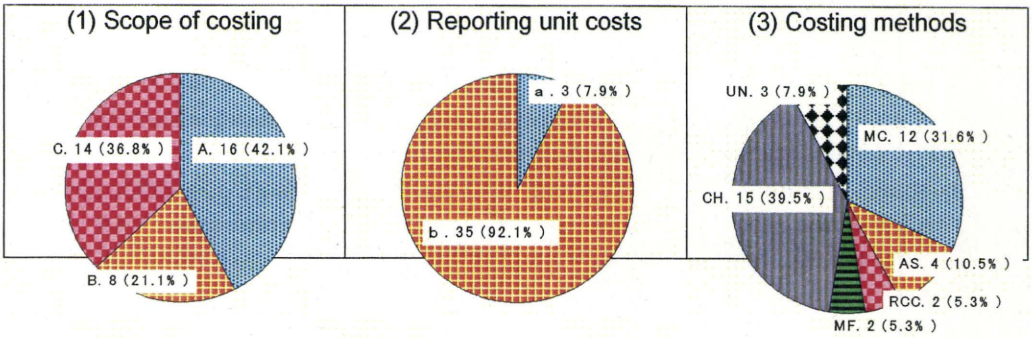
Furthermore, because there is detailed information regarding costs in each component, the reader can comparatively evaluate the cost component in his or her own institution versus the institution where the original evaluation was conducted. It is thus possible to adjust for intrinsic differences and to allow the reader to apply these to his or her own institution (external validity). Cost studies that report all components of costs alone (Level B) enable readers to assess the internal validity of the cost estimates. However, readers would be unable to determine the potential applicability to their own settings. Cost studies that provide limited descriptions of the scope of costing (Level C) have little value, because readers would be unable to determine either internal or external validity.

As variations in unit costs are affected by country or hospital, it is desirable that cost estimates provide data on unit costs (as the second axis) explicitly. Because providing exact data on unit costs for all items used would be unnecessarily expensive, a cost study should provide unit costs for high-cost items. For readers, such data on unit costs contribute to being able to assess extrapolation of a cost study.

To report costing methods (the third axis) has two meanings. First, readers should be able to understand the viewpoint of the analysis reported. This is essential, because an item may be a cost from one viewpoint, but not from another. Second, readers should be able to understand the types of costs included in the analysis. Resource uses and their costs can be divided into resource use directly attributable to the patient, such as professional fees for intervention and medications, and resource use indirectly attributable to the patient, such as overhead costs. According to such information on costing methods, readers will be able to determine which cost components the cost study included and the degree of accuracy of the cost estimates.

Methods for estimating costs can be broadly categorized into five types: charges, costs calculated using the cost-to-charge ratio (RCC), Medicare fees, costs extracted from a hospital accounting system, and microcosting. Because the costing method used in a cost study likely depends on the study aim, there is no one answer as to which costing method is best for estimating costs. Moreover, some charges are determined politically and therefore have high usability only for other researchers in the same country subject to the same insurance/reimbursement payment systems. The ability to extrapolate such information to different countries is greatly reduced. Furthermore, because cost estimates using RCC include the influence of charge data, it is not desirable to extrapolate such information to different countries.

Results of the evaluation of transferability of cost studies are shown in Figure 2. The transferability of the scope of costing was graded from Levels A to C. There were 16 (42.1%) studies graded Level A, eight (21.1%) studies graded Level B, and 14 (36.8%) studies graded Level C. There were only three (7.9%) studies that showed unit cost data.



(1) A: All components of costs were described and data for costs in each component were reported, B: All components of costs were described but data for costs in each component were not reported,C: Only scope of costing was described but components of costs were not described

(2) a: Unit costs were reported, b: Unit costs were not reported

(3) MC: Microcosting, AS: Costs extracted from the hospital accounting system, RCC: Costs calculated using cost-to-charge ratio, MF: Medicare Fee, CH: Charge, UN: Unknown

Regarding costing methods, in 15 (40%) studies, cost estimates were calculated using charges. This was followed by 12 (31.6%) publications with cost estimates calculated using microcosting methods, four (10.5%) publications using hospital accounting systems, two (5.3%) studies that used RCC, and two (5.3%) studies using Medicare fee information. There were also three (7.9%) studies with an unknown method of costing. When there is no information regarding costing methods in a cost study, readers are unable to determine the study viewpoint or costing scope, and thus the study loses its value.

3. Effectiveness of Liver Transplantation

Although several indicators can be used to assess the effectiveness of liver transplantation for ESLD, one of the most important indicators is survival rate. Given advances in medical technology, 1-year survival rates for liver transplantation now exceed 80% in developed countries and exceed 70% at 5 years. Now, improvement in health-related quality of life is an essential component to assess.

3.1. Methods to Assess Utility of Liver Transplantation

Methods to assess health-related quality of life can be categorized into two types: "health status assessment," which assesses the state of health and its influence on function and disability, and "utility assessment," which evaluates the value or desirability of a particular health state. In this section, we focus only on utility assessment. The most simple and straightforward instrument is the visual analog scale (VAS) method. Although VAS is strictly a rating rather than a utility measure, it is often used in utility assessment. A method fully consistent with expected utility theory is that of the standard gamble (SG). However, the SG approach involves respondents' understanding of the concept of probabilities, which is difficult for some people. Instead, the time trade-off approach was developed to avoid the concept of probabilities. These evaluation methods, however, are relatively time-consuming

for assessments and involve cognitive effort by respondents. To minimize these problems, indirect measurement methods have been developed. Three instruments in common use today are the EuroQol (EQ-5D), Short Form Six Dimensions (SF-6D) and Health Utilities Index (HUI). For each instrument, patients are asked to complete a simple questionnaire that defines their generic state of health, and the appropriate utility is determined from a scoring algorithm. In many studies, the utility scores of patients who underwent liver transplantation since the late 1990s have been examined and assessed using the following instruments: VAS [46,50], TTO [46], SG [46,50], SG-transformed VAS [51], EQ-5D [47-50,52,53], HUI [50], and SF-6D [47].

3.2. Utility in Liver Transplantation Patients

Researchers have assessed utility in patients who underwent liver transplantations, both pre- and post-transplantation (Table 6). For example, Sherman *et al.* evaluated utility in patients waiting for liver transplants [46]. They interviewed 10 patients and assessed utility scores using VAS, TTO, and SG instruments. The mean ± SE VAS score was 0.62 ± 0.06. In contrast, the mean ± SE TTO and SG scores were 0.81 ± 0.10 and 0.72 ± 0.10, respectively. These results showed that VAS yielded the lowest score, SG the middle score, and TTO the highest score. Three reported studies have shown the estimated utility scores using the EQ-5D instrument; the scores ranged from 0.462 to 0.53 [47-49]. Regarding the SF-6D instrument, in one reported study, the score was 0.606, which was higher than that using EQ-5D [47].

Table 6. Utility scores for liver transplantation

First author	n	VAS	TTO	SG	SG-transformed VAS	HUI	EQ5D	SF6D
Pre-liver transplantation								
Sherman[a] [46]	**10**	**0.62**	**0.81**	**0.72**	—	—	—	—
Longworth [47]	**183**	—	—	—	—	—	**0.517**	**0.606**
Ratcliffe [48]	**164**	—	—	—	—	—	**0.53**	—
Ratcliffe [49]	**279**	—	—	—	—	—	**0.462**	—
Post-liver transplantation								
Chong[a] [50]	**30**	**0.65**	—	**0.73**	—	**0.7**	**0.69**	—
Siebert[a] [51]	**8**	—	—	—	**0.86**	—	—	—
Longworth [47]	**183**	—	—	—	—	—	**0.608**	**0.615**
Ratcliffe[b] [48]	**164**	—	—	—	—	—	**0.62**	—
Ratcliffe[b] [49]	**279**	—	—	—	—	—	**0.636**	—
Bryan [52]	**121**	—	—	—	—	—	**0.75**	—
Lewis[c] [53]	**12**	—	—	—	—	—	**0.74**	—

a. Patients with hepatitis C only
b. 3 months post-liver transplantation
c. median

In seven reported studies, post-transplantation was assessed utility scores. The most common method used was EQ-5D. Although the instrument and patient population varied,

reported scores ranged from 0.6 to 0.7 [47-53]. Changes in utility scores of patients pre- and post-transplantation were reported in two studies [47,48]. In the study by Longworth and Bryan [47], the utility score determined by EQ-5D improved significantly from 0.517 to 0.608 ($p < 0.05$), whereas the mean SF-6D score at 12 months post-transplantation was not significantly different from the pretransplant score (0.606 vs. 0.615). In the study by Ratcliffe *et al.* [48], the EQ-5D scores at pre- and post-transplantation showed a statistically significant improvement from 0.53 to 0.62 ($p = 0.003$).

4. COST EFFECTIVENESS OF LIVER TRANSPLANTATION

In Sections 2 and 3, we provided an overview of studies examining cost and effectiveness, respectively. Although liver transplantation is a high-cost intervention benefiting relatively few people, currently, post-liver transplantation survival rates are high and patient utility significantly improves from pre- to post-transplantation. Next, in Section 4, we examine by cost-effectiveness analysis (CEA) whether liver transplantation is worth implementing.

Although liver transplantation is an expensive medical technique, it contributes to the prolongation of life and improvement of utility in patients with ESLD. However, not enough medical resources are available, and the balance between effectiveness and economics should be evaluated to be able to propose a method of resource allocation. Therefore, CEA and cost-utility analysis (CUA) are effective approaches. In Section 4, we analyze whether liver transplantation is a technique that provides a high cost-effectiveness.

The four HEA studies published from 1990 to 2002 were reviewed by Ishida and Imai *et al.*[54]. The studies include those conducted in the US [55], Netherlands [56], Switzerland [20], and Japan [57]. Live-year extension as an outcome index was used in three CEA studies and quality-adjusted life year (QALY) was used in one CUA study. Additionally, of these 4 studies, HEA was performed for DDLT in three studies and for LDLT in two studies.

In this section, we will first summarize the results of the incremental cost effectiveness ratio (ICER) and incremental cost utility ratio (ICUR) of liver transplantation by adding the recent papers to the review reported by Ishida and Imai *et al.*[54]. After that, we will determine whether liver transplantation is appropriate considering its cost. Additionally, to evaluate the HEA results on liver transplantation in each country, we will make an international comparison.

4.1. Systematic Review of Cost-Effectiveness Analyses of Liver Transplantation

Ishida and Imai *et al.* [54] reviewed papers published up to July 2003, and we updated their information by conducting a literature search for publications between August 2003 and June 30, 2010. Using the MEDLINE database, we searched for the keywords "Liver Transplantation" [MESH] AND "Costs and Cost Analysis" [MESH].

As a result, 39 papers were retrieved. We extracted papers that seemed likely to provide HEA studies of liver transplantation through titles and abstracts, and examined the entire texts of the selected papers. Owing to a close examination of the papers, four papers [20, 55-57]

were identified in the publications up to June 30, 2010 in addition to the four papers [8,17,58,59] included in the review by Ishida and Imai *et al.*[54], making a total of eight HEA studies. We assume that more papers are expected to be identified for the review later as we examine the references and citations included in these papers.

Detailed information on the HEA studies on liver transplantation included in our review are shown in Table 7. Of these studies, four were CEA studies using life-year extension as an outcome index, and the remaining four were CUA studies using QALY as an outcome index.

Table 7. Results of cost-effectiveness analysis for liver transplantation patients

First author	Year Country	Number of transplantations	Time	DD or LD	Incremental Cost-Effectiveness Ratio (US$, 2009)	Cost-Effectiveness
Northup [58]	2009 USA	1635	00-09	DD and DD + LD	[DD] 42,903 / QALY [DD + LD] 127,348 / QALY	Superior in cost-effectiveness to DD.
Ishida [8]	2006 Japan	11	99-01	LD	[3 months follow-up] 721,643 / QALY [24 months follow-up] 112,300 / QALY	Superior in cost-effectiveness
Ouwens [59]	2003 Netherlands	81	78-87	DD	39,757 / LYG	Not mentioned
Longworth [17]	2003 UK	208	95-96	DD	[PBC] 56,660 / QALY [PSC] 42,090 / QALY [ALC] 95,410 / QALY	Cost-effectiveness for PBC and PSC. Not superior for ALD.
Sagmeister [20]	2002 Switzerland	51	95-00	DD and DD + LD	[DD] 15,442 / QALY [DD+LD] 16,184 / QALY	Superior in cost-effectiveness
Hisashige [57]	1997 Japan	180	90s	LD	[6 years follow-up] 130,659 / LYG [Follow-up to 80 years] ¥16,352 / LYG	Superior in cost-effectiveness
Bonsel [56]	1990 Netherlands	76	78-87	DD	[1 LYG] 252,764 / LYG [5 LYG] 89,323 / LYG	Superior in cost-effectiveness
Kankaanpaa [55]	1990 USA	32	81-86	DD	[Death within 1 year] 520,683 / LYG [Death after 1 year] 109,617 / LYG	Caution

DD: deceased donor liver transplantation
LD: living donor liver transplantation
LYG: life-year gained
QALY: quality-adjusted life year
PBC: primary biliary cirrhosis, PSC: primary sclerosing cholangitis, ALD: alcoholic liver disease

Northup *et al.* performed a CEA of DDLT and LDLT using a multistage Markov decision analysis with a 10-year time horizon [58]. All direct and indirect outpatient and inpatient costs, including those in the pretransplantation, perioperative, and post-transplantation time periods, were estimated using microcosting algorithms. The utility to the recipient at post-transplantation was derived from past studies. Mean costs per patient who underwent DDLT were estimated at US$180,804 and US$248,225 for a patient who was listed for DDLT with an LDLT available. The DDLT-only strategy cost an average of US$35,976/QALY. The incremental cost-effectiveness ratio of moving from the DDLT-only strategy to LDLT was approximately US$248,225. Given that an ICER of less than US$50,000 (US$59,627, after adjusting for inflation to 2009 US$)/QALY was accepted as cost-effective, then DDLT is a cost-effective treatment.

Ouens *et al.* conducted a CEA of 81 liver transplantation cases in the Netherlands from 1978 to 1987 [59]. The median follow-up after transplantation was approximately 1 year. Although estimates of treatment costs were based on data from the literature, costs included direct medical costs from pretransplantation to the follow-up period after transplantation. In the first 3 years of follow-up, direct medical costs per patient totaled US$145,726. They calculated QALYs using EQ-5D questionnaires. The costs per QALY gained for liver transplantation was US$39,757. Because the authors sought to compare cost-effectiveness between lung, heart, and liver transplantations, the study did not compare the cost-effectiveness of liver transplantation with a cost-effectiveness threshold.

Longworth *et al.* performed a CEA for patients with primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), and alcoholic liver disease (ALD), who were on a waiting list for liver transplantation over 27 months in England and Wales [17]. Costs were estimated over the 27 months from the time of listing using a microcosting approach. Total costs per transplantation ranged from US$103,637 to US$130,322. QALY was assessed using the EQ-5D classification system, administered by a postal questionnaire to participants. The mean costs per QALY gained were US$56,660, US$42,090, and US$94,410 for PBC, PSC, and ALD patients, respectively. Considering that the National Health Service (NHS) has decided that it can afford to pay a maximum of approximately£30,000 (US$59,193, after adjusting for inflation to 2009 US$) for an additional QALY, the authors proposed that liver transplantation was a cost-effectiveness treatment for patients with PBC and PSC, but not for ALD patients.

Sagmeister *et al.* [20] conducted a CEA using the Markov model. They compared the effectiveness, lifetime costs, and cost-effectiveness of DDLT with those of combined DDLT and LDLT for ESLD patients. For patients with DDLT, cost estimates included costs of transplantation, annual costs of decompensated cirrhosis, costs in the first year after transplantation, and costs for the following years after transplantation. For patients with LDLT, cost estimates included costs of transplantation, costs of lobectomy (for the donor), costs for donor evaluation, annual costs of decompensated cirrhosis, costs in the first year after transplantation, and costs for the following years after transplantation. However, the report provided insufficient information regarding costing methods. The cost of DDLT was estimated to be US$81,477. They derived the utility of health states in the model by a time trade-off technique and calculated QALYs. Marginal cost for one additional QALY gained per patient with ESLD treated by DDLT amounted to US$15,442 and that treated by combined DDLT and LDLT amounted to US$16,184. Given that the most frequently used threshold for cost-effectiveness in the US is US$50,000/QALY, both DDLT and combined DDLT and LDLT were cost-effective based on this criterion.

Hisashige *et al.* conducted a CEA of LDLT in 180 patients (mostly 1-2-year-old pediatric patients) with biliary atresia [57]. They evaluated direct medical costs and assessed life years gained as the outcome. While cost per life year gained by liver transplantation was estimated at US$130,659/LYG with a 6-year follow-up, it was US$16,352/LYG with follow-up to 80 years. Compared with the thresholds of cost-effectiveness established by Laupacis *et al.*[60] (See Section 6-2), LDLT was determined to be a cost-effective intervention. Indeed, they concluded that the longer the recipient survived, the more cost-effective it became.

In a study of 76 liver transplantation cases, Bonsel *et al.* analyzed the cost-effectiveness of liver transplantation during the 1978-1987 period [56]. Cost data were abstracted from the hospital administrative system and calculated costs per patient at various treatment stages,

such as screening, waiting time, from the operation to 3 months, 4-12 months after the transplantation, and each post-transplantation year (from the 2nd to the 5th year). Life years gained was assessed as the effectiveness criterion. The total costs per transplantation, including 5 years of follow-up, amounted to US$475,112. Combining cost data and effectiveness data resulted in an ICER from US$252,764/LYG (1-year follow-up) to US$89,323/LYG (5-year follow-up). With the 5-year follow-up results, they concluded that the cost-effectiveness of liver transplantation was acceptable.

Kankaanpaa conducted a CEA examining 32 liver transplant patients from 1981 to 1986 [55]. The cost figures included direct costs (charges for hospital facilities, pretransplantation work-up, and professional fees) and indirect costs (traveling costs, lodging costs, and rehabilitation costs). Direct costs were calculated using charges, and the professional charges included those for the transplantation itself, anesthesia, pretransplant hospitalization and work-up, and post-transplantation follow-up visits. The effectiveness data were obtained using life years gained. The cost study showed the average total cost of the first year to be US$562,635. Whereas the cost per life-year saved in seven patients who died within 1 year was calculated to be US$520,683/LYG, the cost per life-year saved in 25 patients who survived more than 1 year was calculated to be US$109,617/LYG. Kankaanpaa did not make a conclusion about the cost-effectiveness of liver transplantation in the paper.

The cost-utility analysis of LDLT conducted by Ishida *et al.* [8] is shown in Section 5.

4.2. International Comparison of Cost-Effectiveness Analyses

The following counties conducted HEA studies of liver transplantation: US (2) [47,50], Europe (4) [17,20,56,59], and Japan (2) [8,57]. HEA studies were actively conducted in Europe, whereas more than half of the cost analysis studies on liver transplantation were carried out in the US.

In the US, Kankaanpaa [55] and Northup *et al.* [58] carried out cost-effectiveness analyses. Kankaanpaa calculated the costs per actuarial life-year saved as US$520,683/LYG and US$109,617/LYG for patients surviving < 1 year and surviving > 1 year, respectively. Although Kankaanpaa avoided a conclusion as to whether liver transplantation was cost-effective, such treatment resulting in more than 1-year survival seems to be cost-effective, as determined on the basis of thresholds frequently used in the US (however, the use of life-years gained rather than QALY makes this determination difficult). Moreover, Northup *et al.* concluded that DDLT is a cost-effective treatment with an ICER of less than US$50,000 per QALY. However, LDLT in combination with DDLT proved to be modestly more effective, but much more expensive, than the DDLT-only strategy per QALY saved.

Of the studies conducted in Europe, most have concluded that DDLT is a cost-effective technique. However, for patients with ADL, liver transplantation was considered not to be a cost-effective treatment. In contrast, the two reported cost-effectiveness studies conducted in Japan both focused on LDLT. Both studies [8,57] determined that LDLT is a cost-effective treatment. Consequently, liver transplantation is recognized as a therapeutic procedure that provides excellent cost-effectiveness regardless of country.

5. Cost Utility Analysis of LDLT in Japan

5.1. Background

Liver transplantation is the only treatment available for patients with ESLD. LDLT is becoming increasingly common in the face of shortages of deceased donors and concomitant rapid increases in the waiting time for DDLT. However, LDLT has not yet become fully accepted, as issues including donor safety [61-63], medical ethics [64-67], and economics remain somewhat controversial.

Survival rates for LDLT have improved for patients with ESLD [1,3] because of refinements in organ preservation, surgical technique and immunosuppressive therapies. Conversely, little has been done to clarify its cost-effectiveness. The lack of economic assessment of medical costs for LDLT may obstruct its social acceptance due to criticisms of high medical expenses under the current conditions of tight medical financing, and may thus hinder the utilization of precious medical resources. A published economic study of LDLT has shown costs below the suggested upper limit of cost-effectiveness (less than US$50,000) [20], but this study shows limitations regarding the use of hypothetical estimates of medical cost and health-related quality of life (HRQOL).

In Section 5, we examine the cost-utility of LDLT using trial-based cost estimates and utility scores, rather than model-based estimates, for patients with ESLD.

5.2. Methods

The study of Ishida *et al.* [8] comprises of both cost and utility analyses, based on the data from patients with ESLD treated at the Hokkaido University Hospital in Sapporo, Japan. The potential subjects in this study were patients aged 18 to 60 years old who fulfilled LDLT criteria (physical and mental examinations, written informed consent both patients and their families, etc.) and treated in the First Department of Surgery at the hospital between January 1999 and December 2001. All the participants in this study received written information about the goals and research methods of the study and they provided their written consent. The Ethics Committee of the School of Medicine, Hokkaido University, approved the study protocol.

Information regarding medical costs was derived from 11 participants. In cost-utility analysis, medical costs generally differ from medical charges [68]. Because no cost-charge ratio has been reported in Japan or in the hospital, medical charges were substituted for medical costs. These charges were based on the national fee schedule for each participant and the duration of estimation for medical costs was from the first day of preoperative evaluation for LDLT to 24 months post-LDLT. The schedule contained the data under 2 headings: hospitalization and outpatient care. We selected 10 categories for hospitalization (consultation, home care, medication, injection, treatment, surgery, examination, imaging, hospitalization, and others) and 9 items for outpatient care (consultation, home care, medication, injection, treatment, surgery, examination, imaging, and others). The medical costs of medications including immunosuppressants after discharge were extrapolated on the basis of immunosuppressants prescribed at the time of discharge. All medical costs were