

# *The Nordic Liver Transplant Registry*

*(NLTR)*

## *Annual report 2011*

*Report prepared by Tom H. Karlsen July 2012*

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## **1. Source of data**

Numbers and graphs in the present report are based on data extracted from the Nordic Liver Transplant Registry (NLTR) March 2011. Prior to this export, data were subjected to extensive integrity and quality control. Entry of missing data and correction of errors were performed by transplant coordinators at all centers prior to the final data extraction.

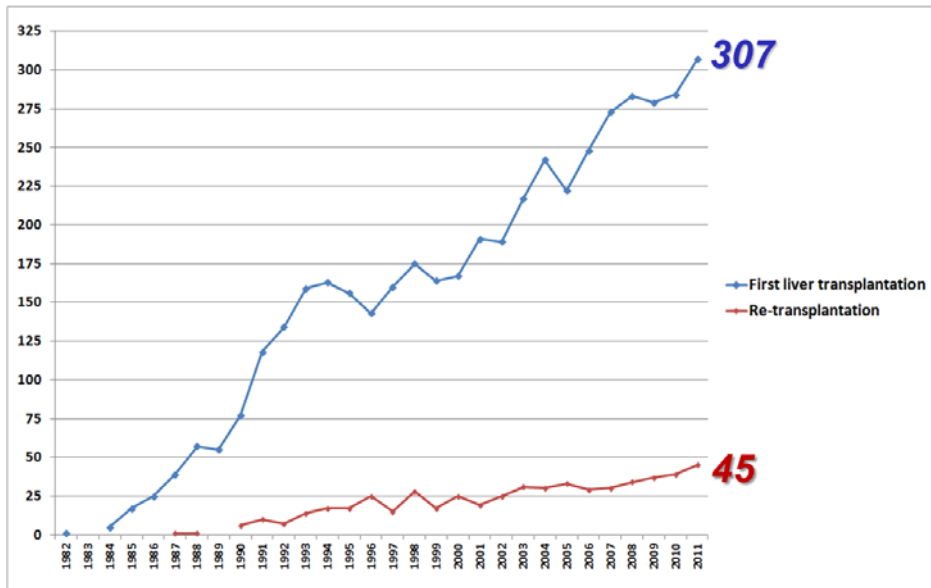
## **2. Data content NLTR 2011**

The registry comprises complete data from the liver transplantation activity at all transplantation centres in Denmark, Sweden, Norway and Finland from 1982 and to time of writing. However, before 1990, only transplanted patients are registered. After 1990, the registry covers all patients entered to the liver transplantation waiting list, regardless of transplantation status. From September 1994, complete waiting list data are available from all patients in addition to the transplantation details. Data are stored at ScandiTransplant in Århus ([www.scandiTransplant.org](http://www.scandiTransplant.org)).

Up to the 31<sup>st</sup> of December 2011, data from a total of 5341 patients had been entered to the NLTR. Of these, 4550 patients had been transplanted. Of these, 473 (10.4%) had been transplanted more than once, and 74 (1.6%) had been transplanted more than twice. A total of 75 living donor transplantations (4 in 2011) and 71 domino transplantations (3 in 2011) had been performed up to 31<sup>st</sup> of December 2011. Children below 16 years constituted 509 (11.1%) of the transplanted patients in the registry.

## **3. Transplantation activity 2011**

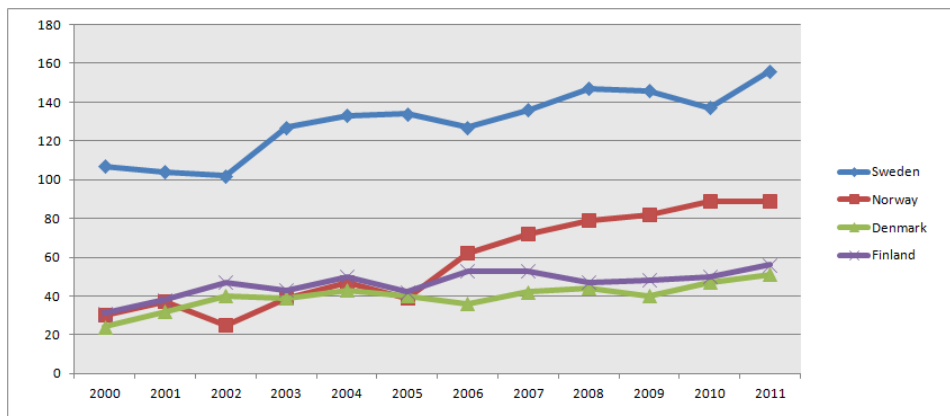
The total number of patients who underwent first liver transplantation in 2011 was 307 (Figure 1). Of these, 8 were combined liver-kidney transplantations. In addition, 45 re-transplantations were performed. The total number of 352 liver transplantations represents a substantial increase from the 323 liver transplantations performed in 2010 (Table 1, Figure 2).



**Figure 1.** Number of patients receiving a liver allograft 1982-2011.

**Table 1.** Liver transplantations performed per center since year 2000.

	Number of first transplantations											Number of re-transplantations												
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Copenhagen	20	26	32	36	37	36	32	37	43	37	43	42	4	6	6	3	6	4	4	5	1	3	4	9
Göteborg	39	52	41	62	59	55	52	64	66	76	61	67	10	4	12	7	11	14	8	11	10	11	19	16
Helsinki	28	37	44	40	48	39	49	50	42	42	47	52	3	1	3	3	4	3	4	3	5	6	3	4
Cela	26	32	26	31	43	32	52	64	69	69	77	81	5	5	0	6	4	7	10	8	10	13	12	8
Stockholm	54	46	44	41	45	56	58	50	52	43	53	65	4	1	1	9	7	4	3	2	6	3	1	8
Uppsala	0	1	4	7	11	7	8	8	11	10	3	8	0	0	0	1	0	0	0	1	2	1	0	6
Total number	166	194	190	217	241	223	249	273	283	279	284	307	26	17	24	31	32	32	29	30	34	37	39	45



**Figure 2.** Total number of liver transplantations per country 2000-2011. Adjusted for population size, annual transplantation rates in 2011 were 17.1 per million for Sweden, 17.9 per million Norway, 10.7 per million for Finland and 9.8 per million for Denmark.

#### 4. The waiting list 2011

In 2011, a total of 368 entries were made to the liver transplantation waiting list. Thirty four listings were made as ‘highly urgent’ (32 in 2010 in comparison). A total of 385 withdrawals were made from the waiting list (Table 2). The number of deaths on the waiting list is low in 2011 and was 10 (Denmark 4, Sweden 3, Finland 1, Norway 2).

**Table 2.** Patients withdrawn from the waiting list in 2011 classified by outcome. \*Number of deaths on the waiting list in 2010 was 21, in 2009 it was 19, 14 in 2008, 10 in 2007, 17 in 2006 and 16 in 2005.

<b>Deceased donor</b>	<b>Living donor</b>	<b>Domino</b>	<b>Dead</b>	<b>Permanent withdrawal</b>
345	4	3	10*	23

There is no consistent increase in waiting times for any blood group (Table 3).

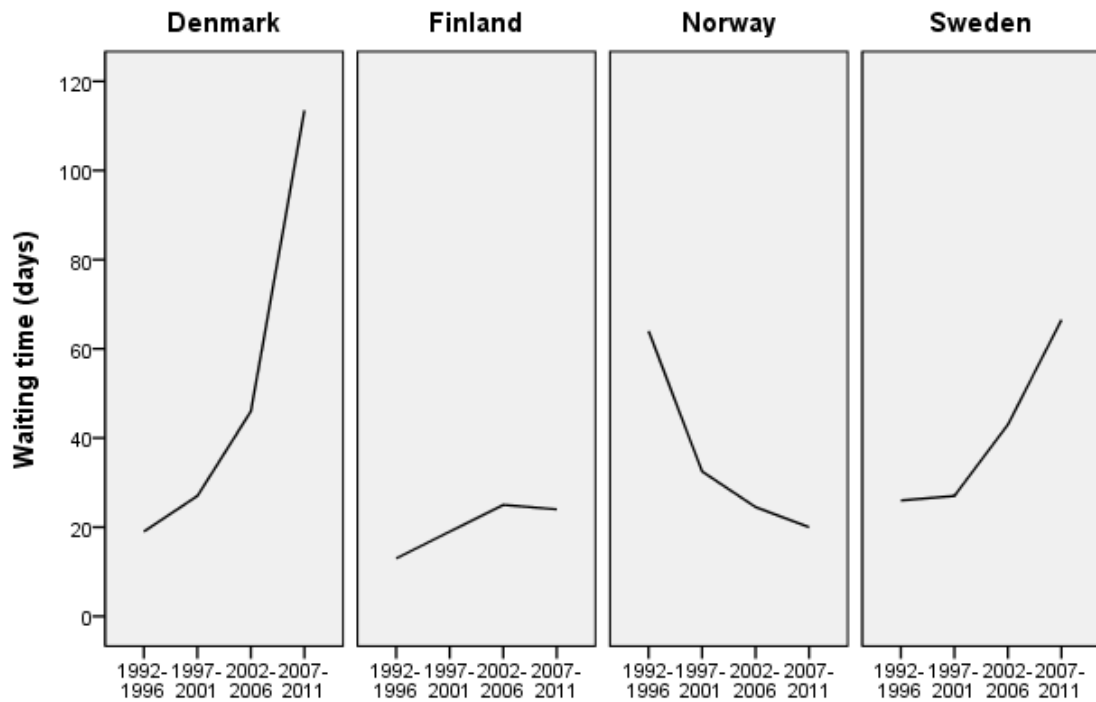
**Table 3.** Median time on waiting list (days) for patients receiving first liver allograft since year 2000 (patients listed as highly urgent are excluded from the calculations).

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
<b>All blood types</b>	<b>43</b>	<b>39</b>	<b>52</b>	<b>38</b>	<b>40</b>	<b>41</b>	<b>41</b>	<b>51</b>	<b>58</b>	<b>44</b>	<b>64</b>	<b>46</b>
Blood type A	39	32	26	27	29	38	26	33	56	24	33	27
Blood type O	76	56	102	74	71	60	105	62	76	80	119	98
Blood type AB	22	61	16	43	10	23	42	52	44	24	36	14
Blood type B	35	49	75	33	44	44	28	63	84	83	90	67

There are marked differences in waiting times between the different centres (Table 4), with several trends notable for each country (Figure 4).

**Table 4.** Median time on waiting list (days) for patients receiving first liver allograft in 2011 (patients listed as highly urgent are excluded from the calculations, numbers in brackets are 2010 numbers for comparison).

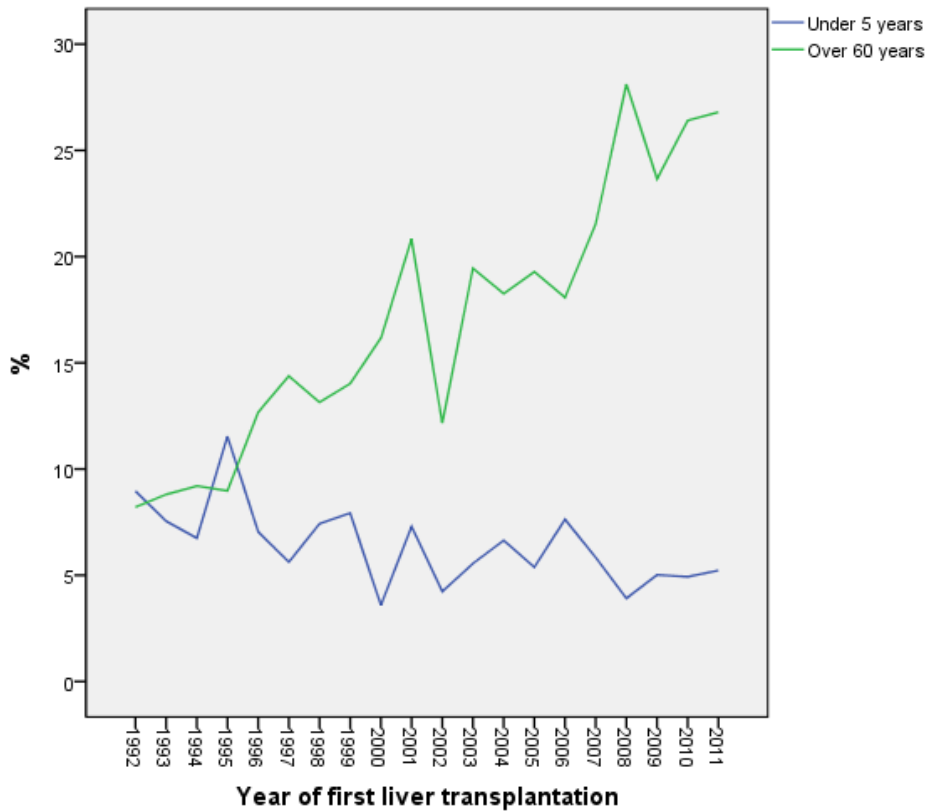
	<b>Copenhagen</b>	<b>Gothenburg</b>	<b>Helsinki</b>	<b>Oslo</b>	<b>Stockholm</b>
Blood type A	55 (166)	33 (65)	30 (8)	7 (15)	66 (49)
Blood type O	272 (328)	174 (282)	30 (15)	23 (53)	171 (219)
Blood type AB	84 (-)	17 (106)	31 (13)	1 (23)	18 (29)
Blood type B	265 (190)	49 (74)	107 (77)	17 (15)	118 (257)



**Figure 4.** Median waiting time for first liver transplantation per 5-year period for each country (patients listed as highly urgent are excluded from the analysis).

## 5. Age of recipients and donors

Both recipient and donor age have increased throughout the period 1982-2011 (Figure 5), but are now reasonably stable over the recent years. Median age of adult liver recipients ( $\geq 16$  years, first liver transplantation) in 2011 was 54.3 years. Median age of children ( $< 16$  years, first liver transplantation) in 2011 was 3.8 years.



**Figure 5.** Median recipient and donor age (years) at first liver transplantation.

## 6. Diagnoses

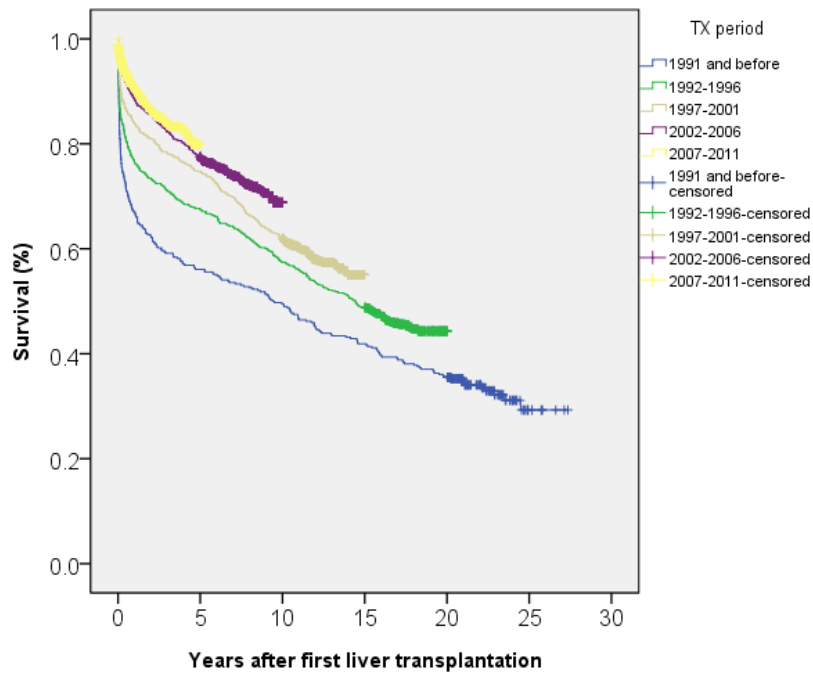
In 2011, primary sclerosing cholangitis (PSC) was again the leading indication for liver transplantation in the Nordic countries (Table 5). Of the 49 patients transplanted with a primary diagnosis of hepatocellular carcinoma (HCC) in 2011, approximately 50% (n=22) were registered with a positive history of hepatitis C infection (yet note missing data on HCV serology for 9 patients). Hepatitis C related disease accounted for a total of 14.1% (counting also hepatocellular carcinoma and 2 patients with alcoholic cirrhosis for whom a positive HCV serology was registered).

**Table 5.** Diagnoses of patients receiving the first liver allograft in 2011 compared with 2010 and the remainder of the last decade and previous years. Top indications were PSC, HCC, HCV and alcoholic cirrhosis. \* HCC: 22 pos. HCV, 9 ND (18 neg. HCV), Alcohol: 2 pos. HCV, 14 ND (23 neg. HCV); i.e. 43 (14.1%) HCV related

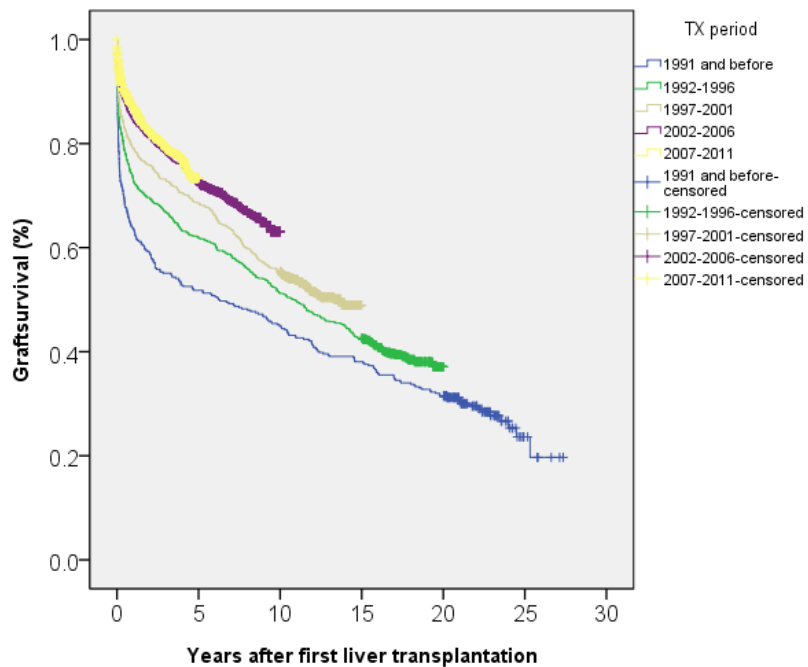
Diagnosis	1982-1999 (n)	1982-1999 (%)	2000-2009 (n)	2000-2009 (%)	2010 (n)	2010 (%)	2011 (n)	2011 (%)
Acute liver failure	210	12,7	234	10,1	36	12,6	21	6,8
<b>Alcoholic liver cirrhosis</b>	<b>144</b>	<b>8,7</b>	<b>257</b>	<b>11,1</b>	<b>33</b>	<b>11,6</b>	<b>39</b>	<b>12,7</b>
Autoimmune cirrhosis	60	3,6	100	4,3	11	3,9	13	4,2
Biliary atresia	84	5,1	87	3,8	7	2,5	6	2,0
Budd-Chiari	35	2,1	27	1,2	1	0,4	3	1,0
<b>Hepatocellular carcinoma</b>	<b>92</b>	<b>5,6</b>	<b>172</b>	<b>7,4</b>	<b>47</b>	<b>16,5</b>	<b>49</b>	<b>16,0*</b>
Metabolic liver disease	141	8,6	146	6,3	24	8,4	18	5,9
Other liver diseases (grouped)	175	10,6	276	12	25	8,8	28	9,1
Other malignancies	54	3,2	78	3,4	17	6,0	15	5,0
PBC	253	15,4	170	7,4	12	4,2	14	4,6
Polycystic liver disease	19	1,2	33	1,4	2	0,7	6	2,0
Post-hepatitis B cirrhosis	43	2,6	56	2,4	1	0,4	6	2,0
<b>Post-hepatitis C cirrhosis</b>	<b>72</b>	<b>4,4</b>	<b>247</b>	<b>7,4</b>	<b>19</b>	<b>6,7</b>	<b>24</b>	<b>7,8</b>
<b>PSC</b>	<b>219</b>	<b>13,3</b>	<b>389</b>	<b>16,8</b>	<b>45</b>	<b>15,8</b>	<b>64</b>	<b>20,9</b>

## 7. Patient and liver graft survival

When looking at 5-years intervals, patient survival (defined as time from the first liver transplantation until death) and graft survival (defined as time from the first liver transplantation until death or re-transplantation) were dramatically improving over the first years of the Nordic liver transplantation programs (Figures 6 and 7). This trend towards a continuous increase in survival now seems to be less pronounced (Figure 6). There are considerable differences in long term survival rates according to diagnosis category (Figure 8), also for re-transplantations (Figure 9). To what extent the apparent lack of a further improvement in overall results is due to change in age and diagnoses of patients or lack of improvement as such warrants further investigations. There is also a need to assess factors that influence long term survival.

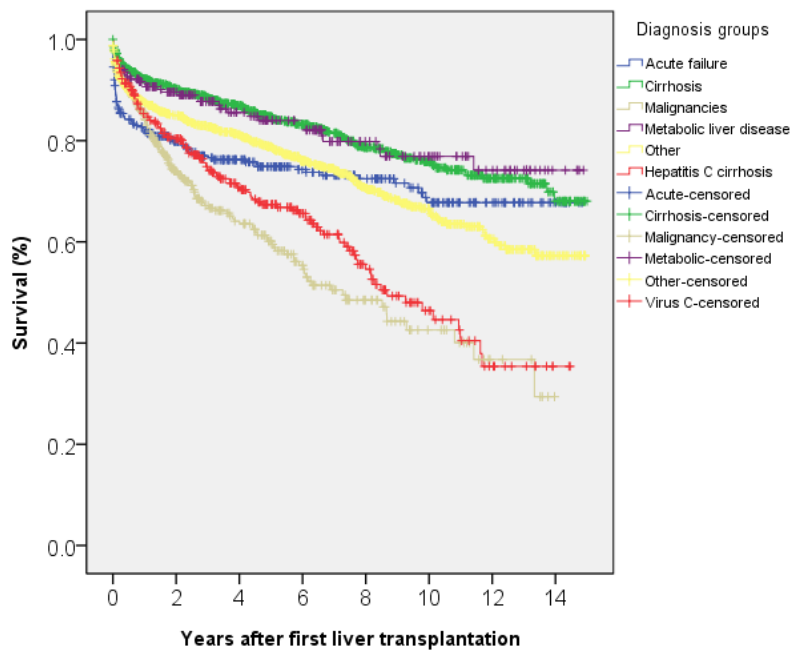


**Figure 6.** Kaplan-Meier patient survival curves per 5-years period (first liver transplantation).

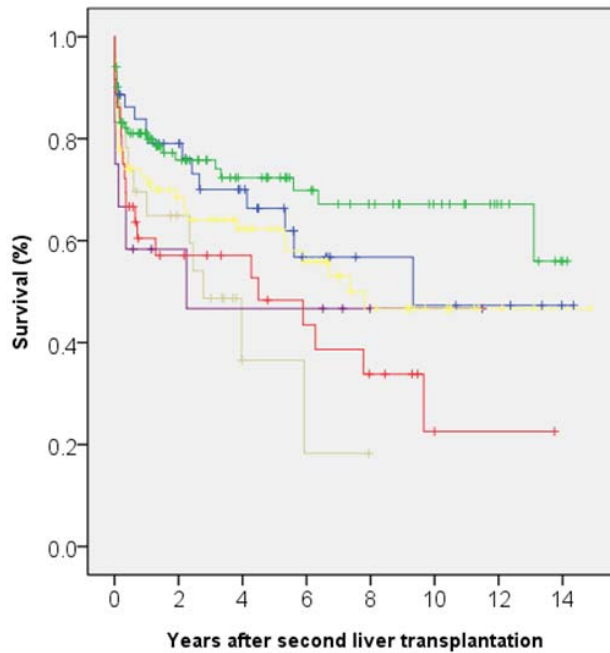


**Figure 7.** Kaplan-Meier graftsurvival curves per 5-years period (first liver transplantation).





**Figure 8.** Kaplan-Meier patient survival curves per diagnosis category (first liver TX).



**Figure 9.** Kaplan-Meier graft survival curves per diagnosis category (second liver TX), legend categories as in Figure 8.

As apparent from Figures 8 and 9, there are distinct differences in patient survival rates according to diagnosis. Inferior long term survival is notable for patients receiving a liver allograft on the basis of HCV cirrhosis and malignant disease (Table 7).

**Table 7.** Patient survival rates (1 year and 5 years) according to diagnosis for patients transplanted during the period 2002-2011 (after the introduction of the piggy-back technique). Age at first liver transplantation as well as re-transplantation rates for the same period are given for each diagnosis.

	2002-2011		2002-2011	2002-2011	2002-2011	1982-2011
	% (1 year survival)	% (5 years survival)	Median age (years)	% above 60 years	Re-TX	% alive
Acute liver failure	84.3%	76.7%	44	12.9 %	12.0 %	59.4 %
Alcoholic liver cirrhosis	91.3%	80.8%	57	28.8 %	4.5 %	59.7 %
Autoimmune cirrhosis	88.0%	84.2%	41	19.6 %	8.0 %	66.8 %
Biliary atresia	83.6%	77.6%	0.8	0.0 %	9.9 %	61.8 %
Budd-Chiari	91.8%	77.7%	37	7.7 %	15.4 %	64.3 %
Hepatocellular carcinoma	85.8%	64.3%	58	40.7 %	5.7 %	54.4 %
Metabolic liver disease	93.3%	85.7%	50	29.2 %	3.6 %	71.1 %
PBC	93.8%	85.9%	57	35.9 %	7.2 %	62.2 %
Post-hepatitis B cirrhosis	92.5%	83.5%	50	20.0 %	5.5 %	61.5 %
Post-hepatitis C cirrhosis	85.9%	67.8%	54	19.3 %	7.2 %	54.7 %
PSC	95.4%	85.7%	44	22.0 %	8.8 %	72.4 %

## 8. Maintenance of the registry

There are notable differences between each centre in terms of how extensively data are entered into the NLTR. Most importantly, diagnosis information, waiting list/transplantation status and survival data for all patients are now complete for 2011. I am extremely grateful for the meticulous follow-up provided by the transplant coordinators upon my neverending requests of enquiry into possible errors and missing data. In Oslo, I particularly want to thank Stein Foss, in Gothenburg Christina Wibeck, in Stockholm Susanne Klang and Kerstin Larsson, in Copenhagen Inger Palfelt, in Uppsala Catharina Gelin, and in Helsinki it is always Helena Isoniemi who answers my requests. Quality control of the content of NLTR is a continuous priority, and a particular emphasis is put into ensuring integrity of the survival data, including cause of death.

Definition of “Event” parameters in Form C were discussed at the NLTG meetings in Stockholm (October 6<sup>th</sup> 2008) and Gothenburg (March 30<sup>th</sup> 2009) and will be repeated

here for the convenience of the reader. An important basis of a consensus on these parameters was that the intention of “Events” in Form C is *not* exhaustive registration of details, but for this section to serve as a rough tool to identify particular patient groups (e.g. with evidence for recurrent disease) for further enquiries based on interviews or in-depth review of medical records.

- “New onset renal failure”: GFR<60
- “Recurrent PSC”: Histology + cholangiography required
- “Recurrent PBC”: Histology required
- “Recurrent AIH”: Histology + serology required
- “Recurrent HCV”: Infection (HCV RNA) + histologically verified liver injury

In general, a physician should be consulted before entering any “Y” for “Recurrent disease” (re. transplant centres where Form C is filled out by coordinators). An important initiative settled at the NLTG meeting in Uppsala (March 3<sup>rd</sup> 2010) was that all Nordic countries now onward will perform protocol liver biopsies following liver transplantation (timing details not settled, most likely 1, 3, 5,10,15 and 20 years). There are marked differences in the utilization of the Form C between the centers.

## **10. Acknowledgements - financial support**

The NLTR received no financial support in 2011. The maintenance of the Oracle system has been performed by Scandiarttransplant. We are extremely grateful for the help and support from Frank Pedersen, Christian Mondrup and Ilse Duus in Aarhus. Without their assistance it would very simply not have been possible to maintain the registry and I sincerely hope their efforts are recognized by the NLTG and Scandiarttransplant.

## **11. Organisation and data ownership**

The registry (software) is the property of Scandiarttransplant. The data in the registry are the property of the hospitals represented in the Nordic Liver Transplantation Group. Utilisation of data in research projects should be censored by the latter and need to comply with national guidelines for research ethics and data handling. Co-authorships for publications from research projects should be allocated according to the Vancouver guidelines, this includes presentations of data at conferences. The quality statistics of the

transplantation activity presented in this report must not be used in other contexts without permission from the Nordic Liver Transplantation Group.

## 12. Publications based on the NLTR

### *Full length articles 1990-2011:*

1. Keiding S, Ericzon BG, Eriksson S, Flatmark A, Hockerstedt K, Isoniemi H, Karlberg I, Keiding N, Olsson R, Samela K, Schrumpf E. Survival after liver transplantation of patients with primary biliary cirrhosis in the Nordic countries. Comparison with expected survival in another series of transplantations and in an international trial of medical treatment. *Scand J Gastroenterol* 1990; 25:11-8
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3. Hockerstedt K, Isoniemi H, Ericzon BG, Broome U, Friman S, Persson H, Bergan A, Schrumpf E, Kirkegaard P, Hjortrup A. Is a 3-day waiting list appropriate for patients with acute liver failure? *Transpl Proc* 1994;26:1786-7
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10. Brandsæter B, Höckerstedt K, Ericzon BG, Friman S, Kirkegaard P, Isoniemi H, Foss A, Olausson M, Hansen B, Bjøro K. Outcome following listing for liver transplantation due to fulminant hepatic failure in the Nordic countries. *Liver Transplantation* 2002;8:1055-62
11. Bjøro K, Ericzon BG, Kirkegaard P, Höckerstedt K, Söderdahl G, Olausson M, Foss A, Schmidt LE, Brandsæter B, Friman S. Liver transplantation for fulminant hepatic failure: impact of donor-recipient ABO-matching on the outcome. *Transplantation* 2003; 75:347-53

12. Brandsæter Bjørn, Broomé Ulrika, Isoniemi Helena, Friman Styrbjörn, Hansen Bent, Schrumpf Erik, Oksanen Antti, Ericzon Bo-Göran, Höckerstedt Krister, Mäkisalo Heikki, Olsson Rolf, Olausson Michael, Kirkegaard Preben, Bjøro Kristian. Liver transplantation for primary sclerosing cholangitis in the Nordic countries: outcome after acceptance to the waiting list. *Liver Transpl.* 2003;9:961-9.
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### **Abstracts 1997-2011:**

16. Bjøro K, Keiding S, Ericzon BG, Friman S, Olausson M, Kirkegaard P, Hjortrup A, Höckerstedt K, Isoniemi H, Bergan A, Schrumpf E. The Nordic liver transplant registry. Organisation and outcome of 1160 patients accepted for liver transplantation 1990-1996. *Scandinavian Congress for Organ transplantation, Oslo 1997, abstract*
17. Bjøro K, Keiding S, Ericzon BG, Friman S, Olausson M, Kirkegaard P, Hjortrup A, Höckerstedt K, Isoniemi H, Bergan A, Schrumpf E. Indication for liver transplantation in the Nordic countries during 1982-1996. *Scandinavian Congress for Organ transplantation, Oslo 1997, abstract*
18. Bjøro K, Olsson R, Broome U, Höckerstedt K, Schrumpf E, Kirkegaard P, Isoniemi H, Ericzon BG, Olausson M, Hansen B, Bergan A, Friman S. Liver transplantation for primary sclerosing cholangitis (PSC). *9th Congress of the European Society for Organ transplantation, Oslo 1999, abstract no 52*

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23. Foss A, Höckerstedt K, Ericzon BG, Friman S, Kirkegaard P, Bergan A, Mäkisalo H, Söderdahl G, Olausson M, Hansen B, Bjøro K. Improved outcome after liver transplantation for fulminant hepatic failure during 1990 to 1999. Scandinavian Congress for organ transplantation, Helsinki 2000, abstract
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26. Ericzon BG, Bjøro K, Höckerstedt K, Hansen B, Olausson M, Isoniemi H, Kirkegaard P, Söderdahl G, Foss A, Friman S. Time to request AB0-identity when transplanting for fulminant hepatic failure? Transpl Odysse, Istanbul, August 2001
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