The Nordic Liver Transplant Registry

(NLTR)

Annual report 2010

Report prepared by Tom H. Karlsen April 2011

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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 2010

The registry comprises complete data from the liver transplanpation activity at all transplantation centres in Denmark, Sweden, Norway and Finland from 1982-2010. 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 Scandiatransplant in Århus (www.scandiatransplant.org).

Up to the 31st of December 2010, data from a total of 5030 patients had been entered to the NLTR. Of these, 4244 patients had been transplanted one or more times. Of these, 436 (10.3%) had been transplanted more than once, and 79 (1.9%) had been transplanted more than twice. A total of 71 living donor transplantations (8 in 2010) and 68 domino transplantations (7 in 2010) had been performed up to 31st of December 2010. Children below 16 years constituted 479 (11.3%) of the transplanted patients in the registry.

3. Transplantation activity 2010

The total number of patients who underwent first liver transplantation in 2010 was 284 (Figure 1). Of these, 7 were combined liver-kidney transplantations. In addition, 39 re-transplantations were performed. The total number of 323 liver transplantations represents a slight increase from the 316 liver transplantations performed in 2009 (Table 1). The number of re-transplantations is slowly yet constantly now increasing and constituted 12.1% of the overall activity in 2010 (Figure 1).

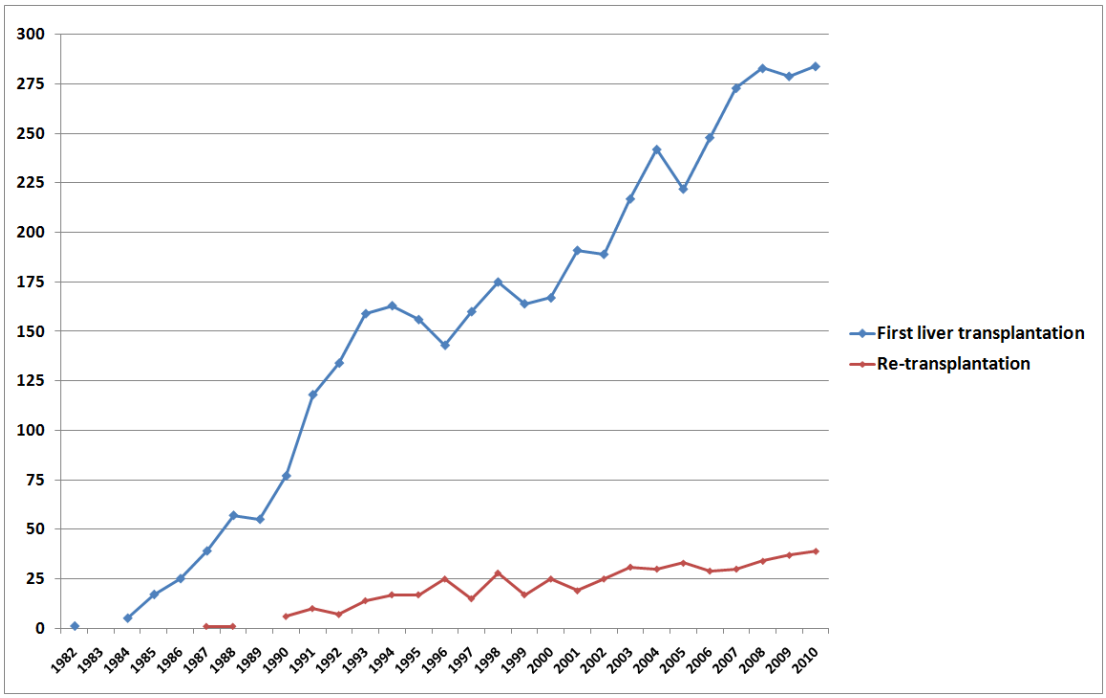

Figure 1. *Number of patients receiving a liver allograft 1982-2010.*

Table 1. *Annual numbers of liver transplantations (TX) since year 2000.*

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**2010**
First TX	166	194	190	217	241	224	249	273	283	279	**284**
Second TX	22	15	22	25	23	29	23	22	30	26	**32**
Third TX	4	2	1	5	7	2	6	7	4	8	**6**
Fourth TX	0	0	1	1	2	0	0	1	0	3	**1**
Fifth TX	0	0	1	0	0	0	0	0	0	0	**0**
Total TX	192	211	215	248	273	255	278	303	317	316	**323**

Table 2. *Liver transplantations performed per center since year 2000.*

	Number of first liver transplantations											***Number of re-transplantations***										
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**2010**	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**2010**
Copenhagen	20	26	32	36	37	36	32	37	43	37	**43**	4	6	8	3	6	4	4	5	1	3	**4**
Gothenburg	39	52	41	62	59	53	52	64	66	78	**61**	10	4	12	7	11	14	8	11	10	11	**19**
Helsinki	28	37	44	40	46	39	49	50	42	42	**47**	3	1	3	3	4	3	4	3	5	6	**3**
Oslo	25	32	25	31	43	32	52	64	69	69	**77**	5	5	0	8	4	7	10	8	10	13	**12**
Stockholm	54	46	44	41	45	56	56	50	52	43	**53**	4	1	1	9	7	4	3	2	6	3	**1**
Uppsala	0	1	4	7	11	7	8	8	11	10	**3**	0	0	0	1	0	0	0	1	2	1	**0**
Total number	166	194	190	217	241	223	249	273	283	279	**284**	26	17	24	31	32	32	29	30	34	37	**39**

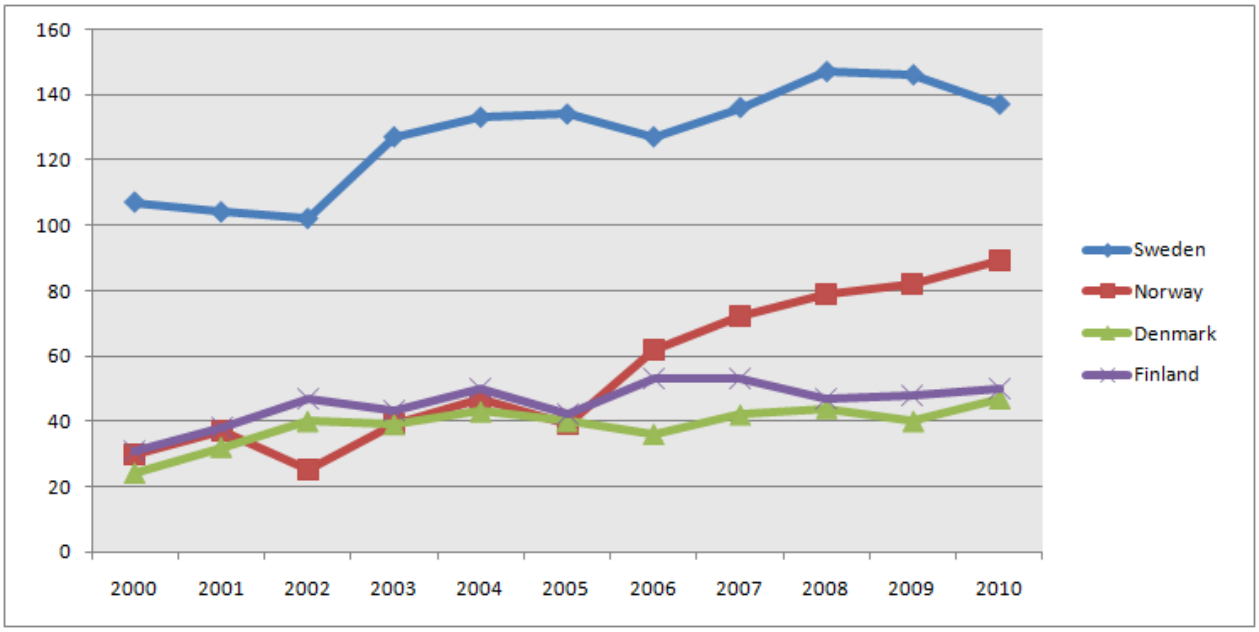

Figure 3. *Total number of liver transplantations per country 2000-2010. Adjusted for population size, annual transplantation rates in 2010 were 14.8 per million for Sweden, 18.0 per million Norway, 9.3 per million for Finland and 8.5 per million for Denmark.*

4. The waiting list 2010

In 2010, a total of 395 entries were made to the liver transplantation waiting list. Thirty two listings were made as 'highly urgent'. A total of 380 withdrawals were made from the waiting list (Table 3). The number of deaths on the waiting list was 21 (Denmark 5, Sweden 12, Finland 0, Norway 4).

Deceased donor	*Living donor*	*Domino*	*Dead*	*Permanent withdrawal*
308	8	7	21*	36

Table 3. *Patients withdrawn from the waiting list in 2010 classified by outcome. *Number of deaths on the waiting list in 2009 was 19, 14 in 2008, 10 in 2007, 17 in 2006 and 16 in 2005.*

There is now a slight increase in waiting times for all blood groups (Table 4). The patients listed as "highly urgent" were transplanted after a median waiting time of 2.0 days.

Table 4. *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*
All blood types	**43**	**39**	**52**	**38**	**40**	**41**	**41**	**51**	**58**	**44**	**64**
Blood type A	39	32	26	27	29	38	26	33	56	24	33
Blood type 0	76	56	102	74	71	60	105	62	76	80	119
Blood type AB	22	61	16	43	10	23	42	52	44	24	36
Blood type B	35	49	75	33	44	44	28	63	84	83	90

There are marked differences in waiting times between the different centres (Table 5), with several trends notable for each country (Figure 4).

Table 5. *Median time on waiting list (days) for patients receiving first liver allograft in 2010 (patients listed as highly urgent are excluded from the calculations).*

	Copenhagen	*Gothenburg*	*Helsinki*	*Oslo*	*Stockholm*
Blood type A	166	65	8	15	49
Blood type 0	328	282	15	53	219
Blood type AB	-	106	13	23	29
Blood type B	190	74	77	15	257

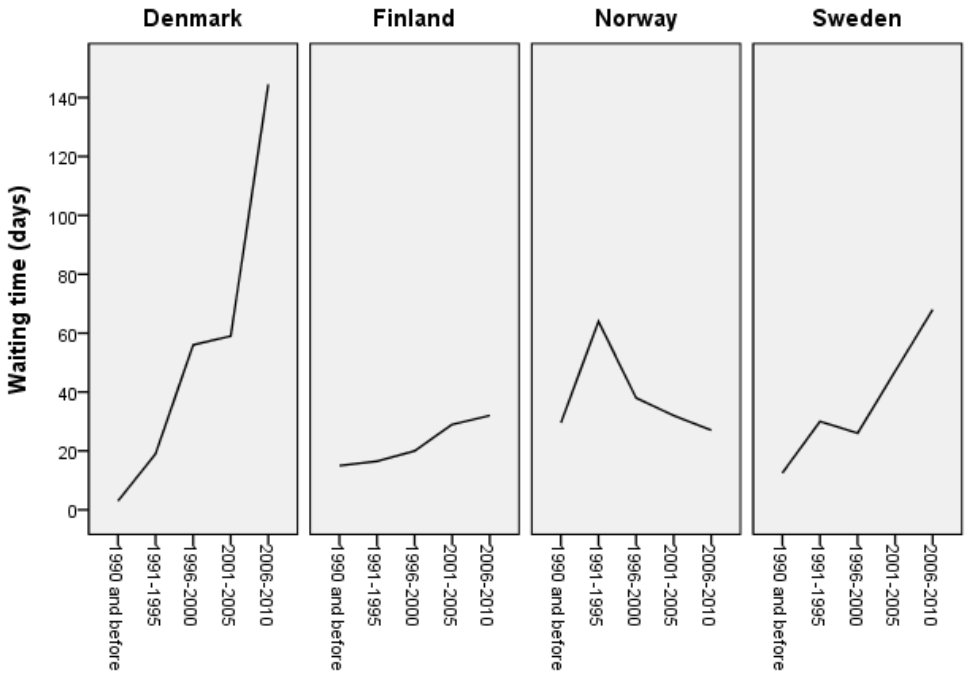

Figure 4. *Median waiting time for first liver transplantation per 5-year period for each country (patients listed as highly urgent are excluded from the analysis).*

5. Age of recipients and donors

Looking at 5 years intervals, both recipient and donor age have increased throughout the period 1982-2010 (Figure 5 and Table 6). Median age of adult liver recipients (≥16 years, first liver transplantation) in 2010 was 54.7 years. Median age of children (<16 years, first liver transplantation) in 2010 was 3.5 years.

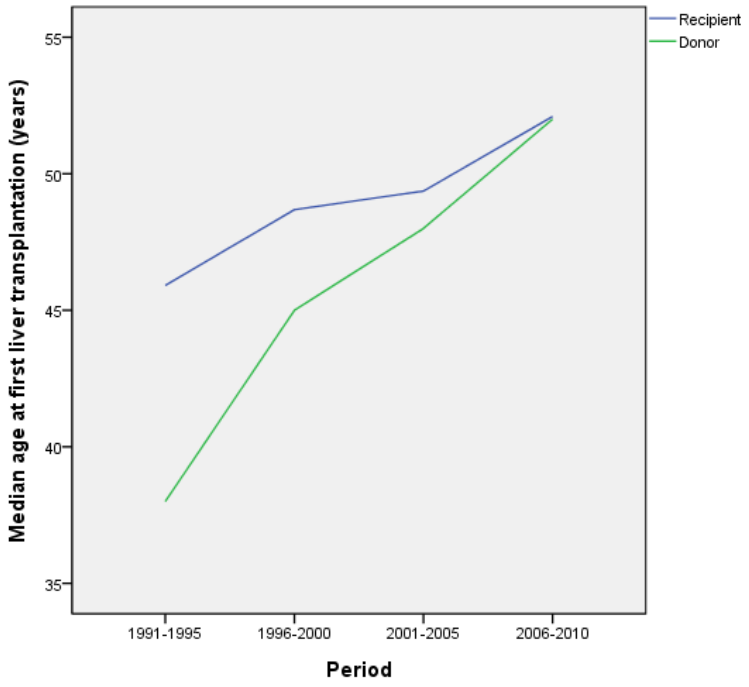

Figure 5. *Median recipient and donor age (years) at first liver transplantation.*

The fraction of first allograft recipients above 60 years was 26.7% in 2010. The fraction of first allograft recipients below 5 years was 4.9% in 2010.

6. Diagnoses

For the first time in many years, primary sclerosing cholangitis (PSC) is no longer the leading indication for liver transplantation in the Nordic countries in 2010 (Table 6). Of the 47 patients transplanted with a primary diagnosis of hepatocellular carcinoma (HCC) in 2010, approximately 50% (n=23) were registered with a positive history of hepatitis C infection (yet note missing data on HCV serology for 7 patients). Altogether, hepatitis C related disease accounted for a total of 16.5% (counting also 49% of hepatocellular carcinoma, 6% alcohol, and 8% of acute liver failures with positive hepatitis C serology), but only 6.7% of these were listed with HCV as the primary diagnosis (Table 6). Hence, HCV related disease and HCC were this year the main indications for liver transplantation in the Nordic countries. After these diagnoses, PSC is still a major indication along with acute liver failure and alcoholic liver disease.

Table 6. *Diagnoses of patients receiving the first liver allograft in 2010 compared with the remainder of the last decade and previous years.*

Diagnosis	*1982-1999 (n)*	*1982-1999 (%)*	*2000-2009 (n)*	*2000-2009 (%)*	*2010 (n)*	*2010(%)*
Acute liver failure	210	12.7	234	10.1	36	12.7
Alcoholic liver cirrhosis	144	8.7	257	11.1	33	11.6
Autoimmune cirrhosis	60	3.6	100	4.3	11	3.9
Biliary atresia	84	5.1	87	3.8	7	2.5
Budd-Chiari	35	2.1	27	1.2	1	0.4
Cryptogenic cirrhosis	69	4.2	83	3.6	0	0.0
Hepatocellular carcinoma	92	5.6	172	7.4	47	16.5
Metabolic liver disease	140	8.5	150	6.5	24	8.5
Other liver diseases (grouped)	157	9.5	228	9.9	29	10.2
Other malignancies	52	3.2	78	3.4	17	6.0
PBC	253	15.3	170	7.4	12	4.2
Polycystic liver disease	19	1.2	33	1.4	2	0.7
Post-hepatitis B cirrhosis	43	2.6	56	2.4	1	0.4
Post-hepatitis C cirrhosis	72	4.4	247	10.7	19	6.7
PSC	219	13.3	389	16.8	45	15.8

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), and there is a slight similar trend also for re-transplantations (Figures 8 and 9). To what extent the 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.

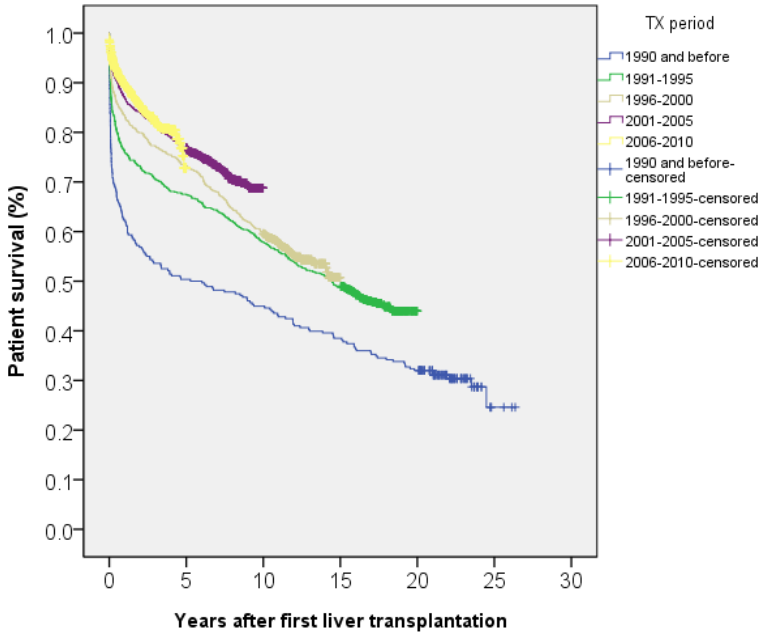

Figure 6. *Kaplan-Meier patient survival curves per 5-years period (first liver transplantation).*

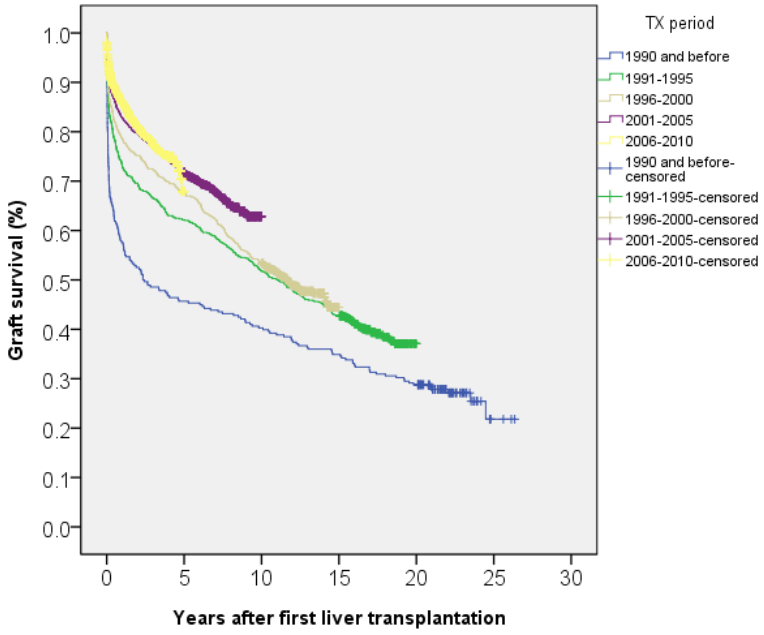

Figure 7. *Kaplan-Meier graftsurvival curves per 5-years period (first liver transplantation).*

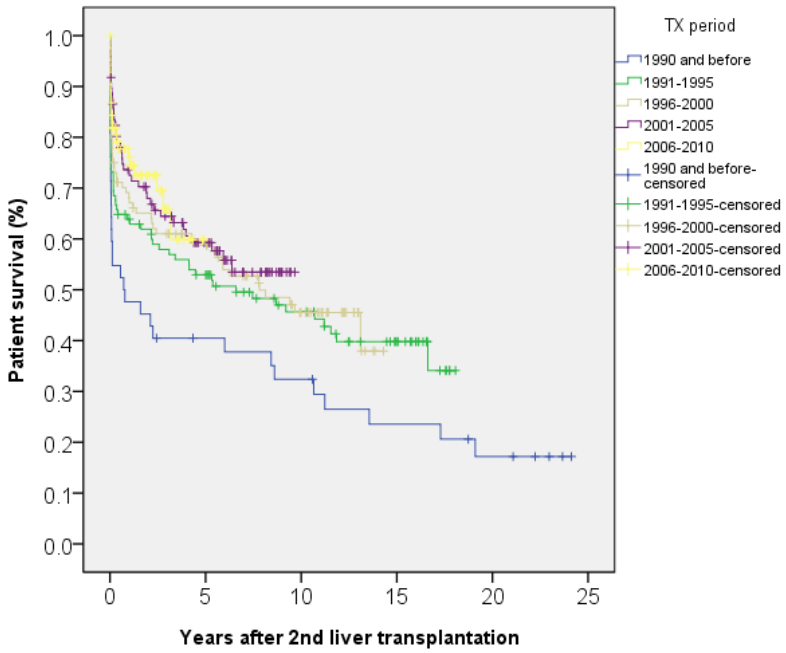

Figure 8. *Kaplan-Meier patient survival curves per 5-years period (second liver transplantation).*

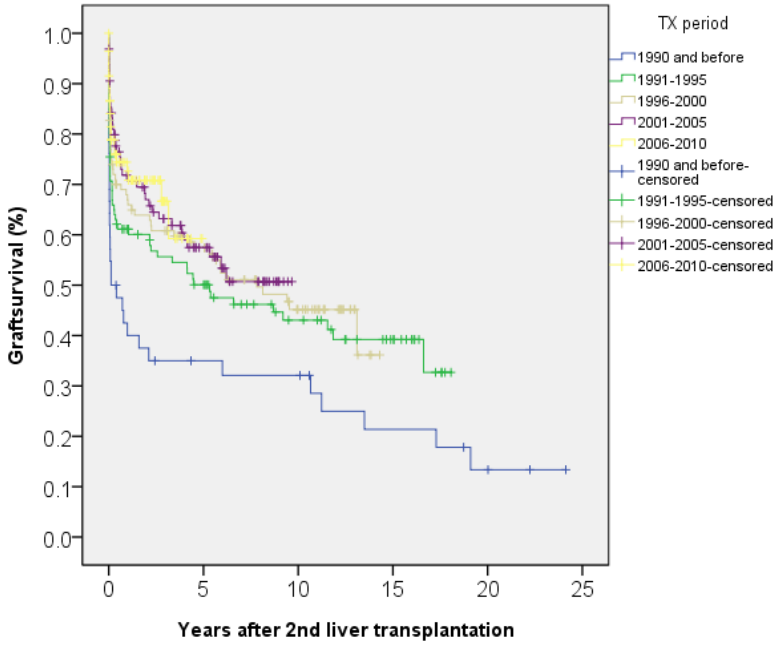

Figure 9. *Kaplan-Meier graft survival curves per 5-years period (second liver transplantation).*

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 or malignant disease (Table 7).

Table 7. *Patient survival rates (1 year and 5 years) according to diagnosis for patients transplanted during the period 2003-2010. Age at first liver transplantation as well as re-transplantation rates for the same period is given for each diagnosis.*

	2003-2010		2003-2010	2003-2010	1982-2010
	% (1 year survival)	% (5 years survival)	Median age (years)	Re-TX	% alive
Acute liver failure	83.5%	76.4%	44	11.6%	58.4%
Alcoholic liver cirrhosis	92.3%	80.0%	57	4.6%	58.3%
Autoimmune cirrhosis	87.5%	87.5%	41	7.7%	67.7%
Biliary atresia	80.7%	75.2%	1	8.6%	63.0%
Budd-Chiari	94.7%	78.7%	34	15.8%	66.7%
Hepatocellular carcinoma	81.9%	60.5%	58	4.7%	49.5%
Metabolic liver disease	92.9%	84.6%	51	2.1%	71.6%
PBC	93.6%	83.1%	57	6.9%	62.7%
Post-hepatitis B cirrhosis	89.6%	83.7%	53	5.1%	61.5%
Post-hepatitis C cirrhosis	87.8%	66.5%	54	6.4%	54.5%
PSC	94.7%	83.7%	43	7.4%	71.4%

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 2010. 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. I also want to thank Ina Marie Andersen for all her help in entering Oslo A and C forms into the NLTR. Quality control of the content of NLTR is a continuous priority, and I have put a particular emphasis onto ensuring integrity of the survival data, including cause of death. Based on the many requests for output and analyses of these data, it seems that these efforts are useful even outside the context of this annual report and various

scientific projects.

Definition of "Event" parameters in Form D were discussed at the NLTG meetings in Stockholm (October 6th 2008) and Gothenburg (March 30th 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 D 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 D is filled out by coordinators). An important initiative settled at the recent NLTG meeting in Uppsala (March 3rd 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).

10. Acknowledgements - financial support

The NLTR received no financial support in 2010. The maintenance of the Oracle system has been performed by Scandiatransplant. We are extremely grateful for the help and support from Frank Pedersen, Christian Mondrup, Bo Hedemark Pedersen 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.

11. Organisation and data ownership

The registry (software) is the property of Scandiatransplant. 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. 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 1990-2010:

1. Keiding S, Ericzon BG, Eriksson S, Flatmark A, Hockerstedt K, Isoniemi H, Karlberg I, Keiding N, Olsson R, Samela K, Schrumpf E, Söderman C. 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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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.
13. Brandsaeter B, Friman S, Broome U, Isoniemi H, Olausson M, Backman L, Hansen B, Schrumpf E, Oksanen A, Ericzon BG, Hockerstedt K, Makisalo H, Kirkegaard P, Bjoro K.Outcome following liver transplantation for primary sclerosing cholangitis in the Nordic countries. Scand J Gastroenterol. 2003;38:1176-83.
14. Brandsaeter B, Isoniemi H, Broome U, Olausson M, Backman L, Hansen B, Schrumpf E, Oksanen A, Ericzon BG, Hockerstedt K, Makisalo H, Kirkegaard P, Friman S, Bjoro K. Liver transplantation for primary sclerosing cholangitis; predictors and consequences of hepatobiliary malignancy. J Hepatol. 2004;40:815-822.
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17. Melum E, Schrumpf E, Bjøro K. Liver TX for hepatitis C cirrhosis in a low prevalence population: risk factors and status at evaluation. Scand J Gastroenterol. 2006;41:592-6.
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Abstracts 1997-2010:

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2. 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
3. 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
4. Höckerstedt K, Ericzon BG, Bjøro K, Friman S, Hjortrup A, Keiding S, Schrumpf E, Duraj F, Olausson M, Mäkisalo H, Bergan A, Kirkegaard P. Liver transplantation in

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8. 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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10. Bjøro K, Höckerstedt K, Friman S, Kirkegaard BG, Ericzon BG. Outcome after listing for highly urgent liver transplantation – impact of AB0 blood type. Joint Meeting of International Liver Transplantation Society and European Liver Transplantation Association. Berlin 2001, abstract no 91
11. Ericzon BG, Bjøro K, Höckerstedt K, Hansen B, Olausson M, Isoniemi H, Kirkegaard P, Söderdaghl 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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