

The Nordic Liver Transplant Registry

(NLTR)

Annual report 2009

Report prepared by Tom H. Karlsen March 2010

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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 2010. 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 2009

The registry comprises complete data from the liver transplantation activity at all transplantation centres in Denmark, Sweden, Norway and Finland from 1982-2009. 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).

Up to the 31st of December 2009, data from a total of 4681 patients had been entered to the NLTR. Of these, 3960 patients had been transplanted. Of these, 381 (9.6%) had been transplanted more than one time, and 62 (1.6%) had been transplanted more than two times. Sixty two percent of all transplant recipients were alive as of 31.12.09. Highly urgent calls had been performed in 354 (9.5%) of the 3735 listings for first liver transplantation in the period from 1st of September 1994 to 31st of December 2009 and 264 (74.6%) of these patients received a liver graft. A total of 63 living donor transplantations (2 in 2009) and 61 domino transplantations (8 in 2009) had been performed up to 31st of December 2009. Children below 16 years constituted 456 (11.5%) of the transplanted patients in the registry.

3. Transplantation activity 2009

The total number of patients who underwent first liver transplantation in 2009 was 279 (Figure 1). Of these, 5 were combined liver-kidney transplantations, 1 was combined liver-pancreas and 1 was combined heart-liver. In addition, 37 re-transplantations were performed. The total number of 316 liver transplantations is approximately the same as in

2008 (Table 1). The number of re-transplantations is relatively stable and constituted 11.7% of the overall activity in 2009 (Figure 1).

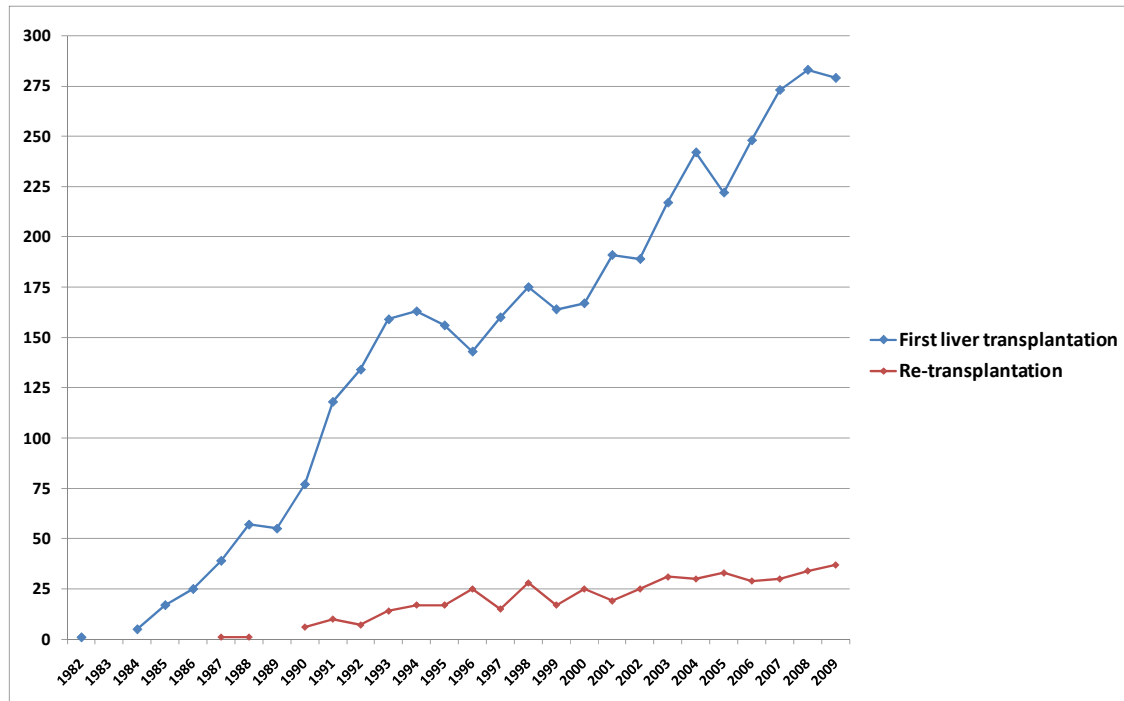


Figure 1. Number of patients receiving a liver allograft 1982-2009.

Table 1. Annual numbers of liver transplantations (TX) over the last ten years.

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

Table 2. Liver transplantations performed per center over the last ten years.

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

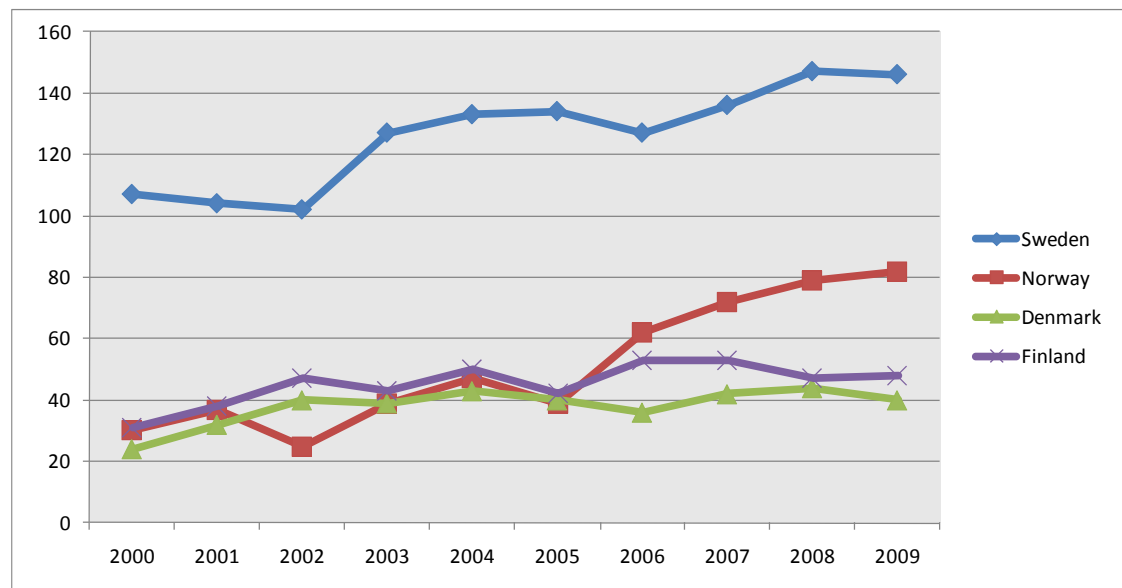


Figure 3. Total number of liver transplantations per country 2000-2009. Adjusted for population size, annual transplantation rates in 2009 were 16.1 per million for Sweden, 16.9 per million Norway, 9.1 per million for Finland and 7.3 per million for Denmark.

4. The waiting list 2009

In 2009, a total of 404 entries were made to the liver transplantation waiting list. Twenty four listings were made as ‘highly urgent’. A total of 364 withdrawals were made from the waiting list (Table 3). The number of deaths on the waiting list was 19 (Denmark 4, Sweden 5, Finland 4, Norway 6); two of these were children below the age of 16 years.

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

<i>Deceased donor</i>	<i>Living donor</i>	<i>Domino</i>	<i>Dead</i>	<i>Permanent withdrawal</i>
306	2	8	19	29

Patients who received their first liver allograft in 2009 had waited a median of 44 days (excluding patients listed as “highly urgent”). Importantly, this means that during the last ten years of increasing activity, the waiting times have remained stable (Table 4). The patients listed as “highly urgent” were transplanted after a median waiting time of 3.0 days.

Table 4. Median time on waiting list (days) for patients receiving first liver allograft over the last ten years (patients listed as highly urgent are excluded from the calculations).

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

There are, however, 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 2009 (patients listed as highly urgent are excluded from the calculations).

	<i>Copenhagen</i>	<i>Gothenburg</i>	<i>Helsinki</i>	<i>Oslo</i>	<i>Stockholm</i>	<i>Uppsala</i>
Blood type A	150	19	9	13	83	17
Blood type O	129	84	109	54	204	185
Blood type AB	-	7	3	19	74	-
Blood type B	266	45	48	53	193	29

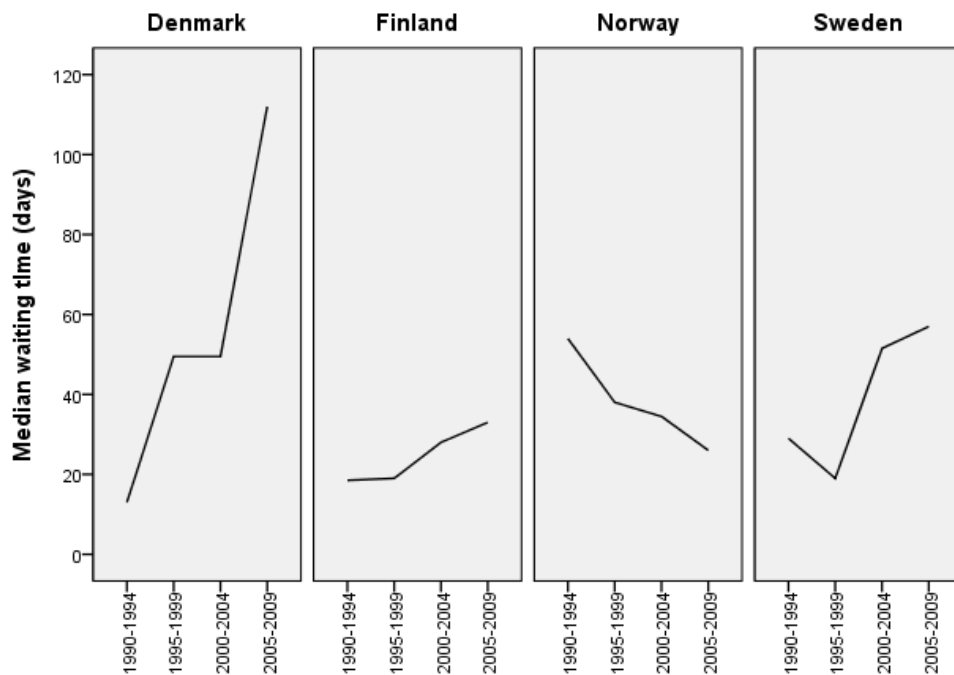


Figure 4. Median waiting time for first liver transplantation per 5-year period for each country (patients listed as highly urgent are excluded from the analysis).

5. Age of recipients and donors

Looking at 5 years intervals, both recipient and donor age have increased throughout the period 1982-2009 (Figure 5 and Table 6). Median age of adult liver recipients (≥ 16 years, first liver transplantation) in 2009 was 53 years (oldest patient 73.2 years). Median age of children (< 16 years, first liver transplantation) in 2009 was 3.0 years (youngest patient 24 days).

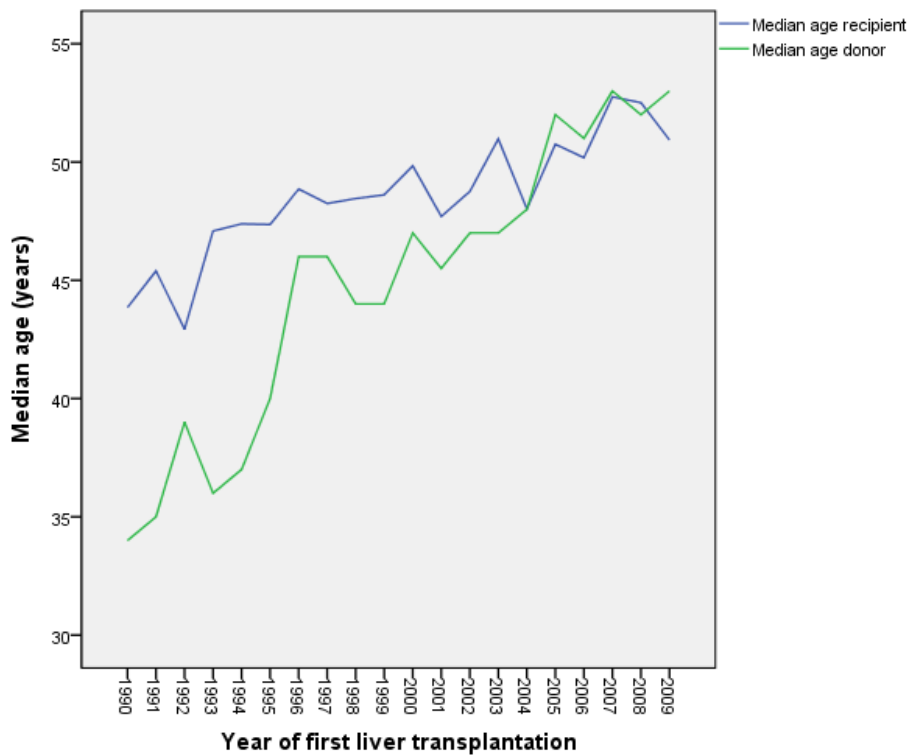


Figure 5. Recipient and donor age at first liver transplantation over the last 20 years.

Table 6. Recipient age (range) per 5-year period.

TX period	Median age (years)	Range (years)
Before 1990	40	0.4 - 64
1990-1994	46	0.5 - 71
1995-1999	48	0.3 - 73
2000-2004	49	0.3 - 74
2005-2009	51	0.1 - 74

The fraction of first allograft recipients above 60 years was 23.7% in 2009. The fraction of first allograft recipients below 5 years was 5.0% in 2009.

6. Diagnoses

Primary sclerosing cholangitis (PSC) was the leading diagnosis for liver transplantation in the Nordic countries in 2009 (Table 7). Other important diagnoses were alcoholic liver cirrhosis, post-hepatitis C cirrhosis and metabolic liver disease. Of the 23 patients transplanted on the basis of hepatocellular carcinoma in 2009, approximately 1/4 (n=5)

were registered with a positive history of hepatitis C infection (missing data for 6 patients).

Table 7. Diagnoses of patients receiving the first liver allograft in 2009 compared with the remainder of the last decade and previous years (one missing diagnosis in 2009).

Diagnosis	1982-1999 (n)	1982-1999 (%)	2000-2008 (n)	2000-2008 (%)	2009 (n)	2009 (%)
Acute liver failure	210	12.7	209	10.5	24	8.6
Alcoholic liver cirrhosis	144	8.7	226	11.3	31	11.1
Autoimmune cirrhosis	60	3.6	89	4.5	10	3.6
Biliary atresia	84	5.1	79	4.0	8	2.9
Budd-Chiari	35	2.1	23	1.2	4	1.4
Hepatocellular carcinoma	92	5.6	149	7.5	22	7.9
Metabolic liver disease	141	8.6	121	6.1	29	10.4
Other liver diseases (grouped)	175	10.9	242	12.1	30	10.8
Other malignancies	54	3.2	64	3.2	15	5.4
PBC	253	15.4	149	7.5	21	7.5
Polycystic liver disease	19	1.2	30	1.5	4	1.4
Post-hepatitis B cirrhosis	43	2.6	51	2.6	4	1.4
Post-hepatitis C cirrhosis	72	4.4	214	10.7	32	11.5
PSC	219	13.3	347	17.4	44	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 graftsurvival (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 only a slight similar trend for re-transplantations (Figures 8 and 9).

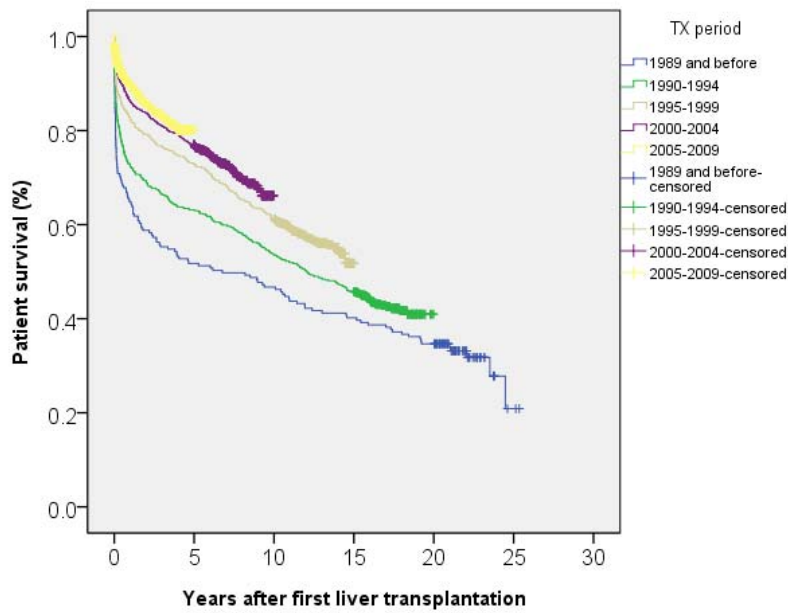


Figure 6. Kaplan-Meier patient survival curves per 5-years period (first liver transplantation).

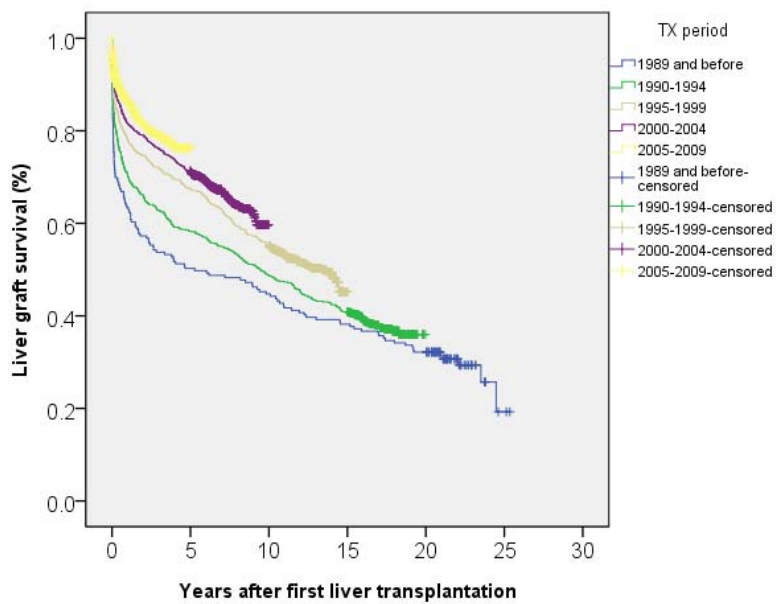


Figure 7. Kaplan-Meier graft survival curves per 5-years period (first liver transplantation).

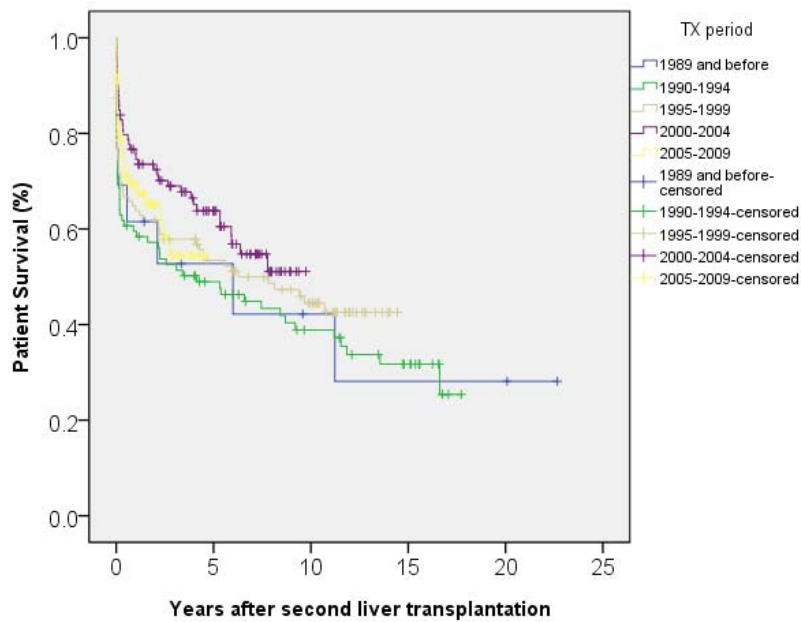


Figure 8. Kaplan-Meier patient survival curves per 5-years period (second liver transplantation).

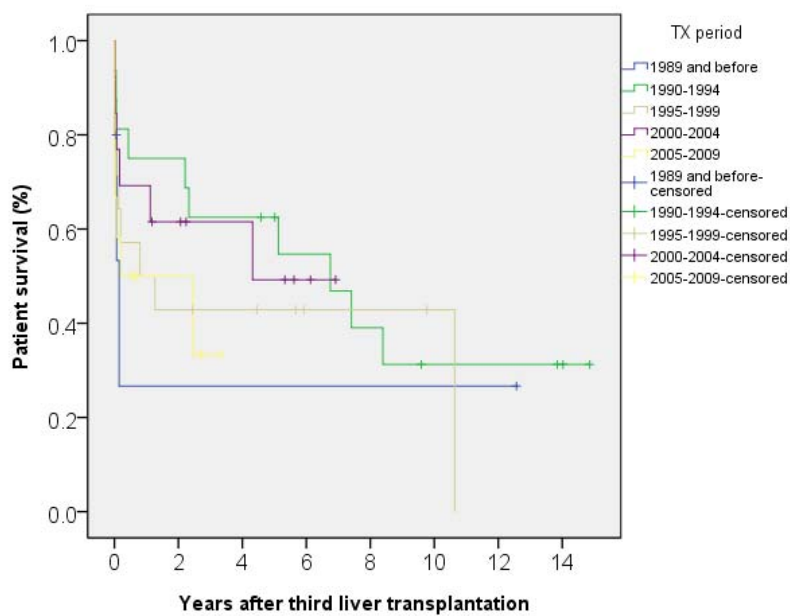


Figure 9. Kaplan-Meier patient survival curves per 5-years period (third liver transplantation).

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 and malignant disease (Table 8). Median patient survival in the overall population of transplant recipients in the Nordic countries (1982-2009) was 17 years.

Table 8. Patient survival rates (1 year and 5 years) according to diagnosis for patients transplanted during the six years period 2003-2009. Age at first liver transplantation as well as re-transplantation rates for the same period is given for each diagnosis.

	2003-2009		2003-2009	2003-2009	2003-2009
	% (1 year survival)	% (5 years survival)	Median age (years)	Re-TX	Re-TX >1x
Acute liver failure	83.8%	80.7%	44	11.7%	2.3%
Alcoholic liver cirrhosis	91.9%	81.7%	57	4.8%	0
Autoimmune cirrhosis	89.6%	89.6%	42	6.3%	0
Biliary atresia	80.3%	73.9%	1	6.3%	3.2%
Budd-Chiari	94.4%	77.3%	34	16.3%	0
Hepatocellular carcinoma	81.3%	57.4%	57	5.6%	0.7%
Metabolic liver disease	92.9%	86.2%	51	2.6%	1.7%
PBC	93.7%	88.7%	57	5.3%	0
Post-hepatitis B cirrhosis	89.0%	82.6%	53	5.3%	0
Post-hepatitis C cirrhosis	88.2%	66.0%	54	6.0%	1.5%
PSC	94.0%	83.5%	43	6.5%	1.4%

8. Maintenance of the registry

There are notable differences between each center 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 2009. 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.

The initiative regarding data transfer from the Helsinki Liver Transplant registry system (HUSLTR) to the NLTR is slowly progressing. Helena Isoniemi and Jouni Lang are

responsible for this effort from the side of HUSLTR, Frank Pedersen and Christian Mondrup are responsible from the side of NLTR. At present, the technical problems from the side of Scandiatransplant has been resolved, and the implementation of the export facility in the HUSLTR is pending. Once settled, similar systems will be established for data transfer in Stockholm and, at some point, Gothenburg (who is in the process of establishing a local database).

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 centers 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 2009. 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 and Bo Hedemark Pedersen 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 1990-2009:

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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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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