The Nordic Liver Transplant Registry

Annual report 2007

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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) June 2007. Prior to this export, data were subjected to quality control in terms of presentation of complete data as well as key numbers for 2007 to all transplantation centres with subsequent correction of errors noted by responsible contact persons.

2. Data content NLTR 2007

Up to the 31st of December 2007, data from a total of 4001 patients had been entered to the NLTR. The registry comprises data from all transplantation centres in Denmark, Sweden, Norway and Finland from 1982-2007. For the 219 patients receiving a liver allograft prior to 1990, no waiting list data are available. Among the patients receiving a liver allograft from 1994-2007, a total of 7.6% were listed as "highly urgent" (median waiting list time 2.3 days). A total of 92 living donor transplantations were registered (including 45 domino).

3. Transplantation activity 2007

The total number of patients who underwent first liver transplantation in 2007 was 273 (Figure 1). In addition, 30 re-transplantations were performed. The total number of 303 liver transplantations is the highest ever (Table 1). The number of re-transplantations is not increasing, and constitutes now approximately 10% of the overall activity (Figure 2).

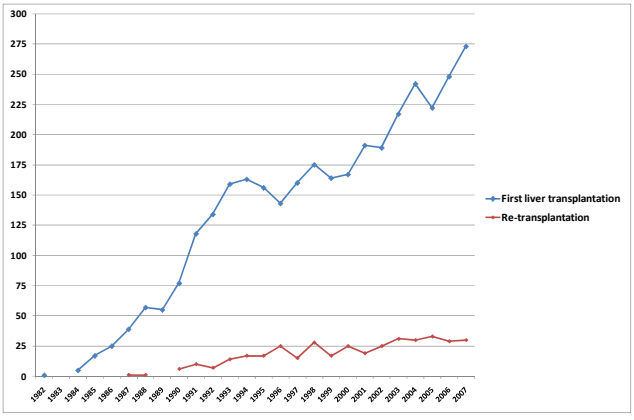

Figure 1. *Number of patients receiving a liver allograft 1982-2007.*

Table 1. *Annual numbers of liver transplantations (TX) 2000-2007.*

	2000	2001	2002	2003	2004	2005	2006	**2007**
First TX	166	194	190	217	241	224	249	**273**
Second TX	22	15	22	25	23	29	23	**22**
Third TX	4	2	1	5	7	2	6	**7**
Fourth TX	0	0	1	1	2	0	0	**1**
Fifth TX	0	0	1	0	0	0	0	**0**
Total TX	192	211	215	248	273	255	278	**303**

Table 2. *Liver transplantations performed per centre 2000-2007.*

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

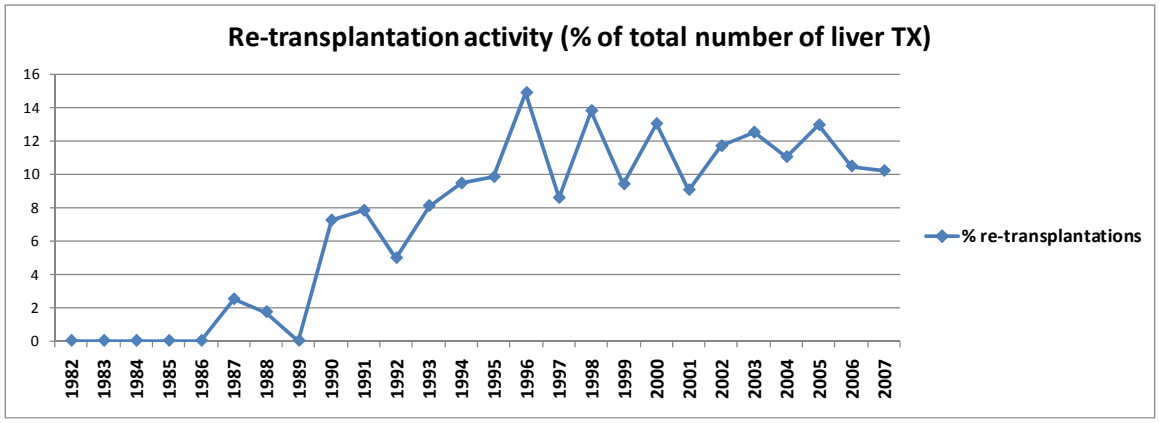

Figure 2. *Fraction of re-transplantations.*

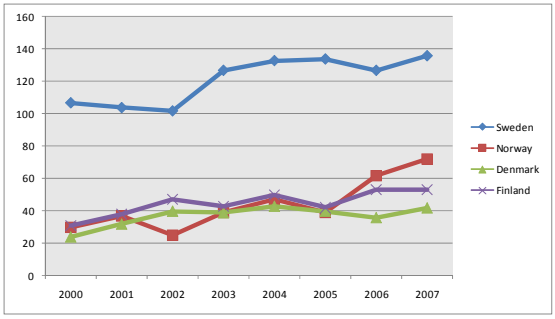

Figure 3. *Total number of liver transplantations per country 2000-2007. Adjusted for population size, the transplantation rates in 2007 were ~15 per million (Norway), ~14 per million (Sweden), ~10 per million (Finland) and ~8 per million (Denmark).*

4. The waiting list 2007

In 2007, a total of 298 patients were entered to the liver transplantation waiting list (31 listed as highly urgent). In addition 8 patients were entered to the waiting list for combined liver+kidney transplantation. A total of 342 patients were withdrawn from the waiting list (Table 3). The number of deaths on the waiting list was only 10 (as compared with 17 in 2006 and 16 in 2005).

Table 3. *Patients withdrawn from the waiting list in 2007 classified by outcome.*

Deceased donor	Living donor	Domino	Dead	Permanent withdrawal
294	4	5	10	28

Patients who received their first liver allograft in 2007 had waited a median of 50 days (excluding patients listed as "highly urgent"). Although this is a slight increase from previous years, there is no trend in the waiting times for the years 2000-2007 (Table 4).

Table 4. *Median time on waiting list (days) for patients receiving first liver allograft (patients listed as highly urgent are excluded in the calculations).*

	2000	2001	2002	2003	2004	2005	2006	2007
All blood types	43	39	52	36	39	41	41	50
Blood type A	43	28	25	27	29	37	26	32
Blood type 0	71	62	104	72	69	60	105	59

There are, however, marked differences in waiting times between the different centres in 2007 (Table 5), with several clear trends for each country notable when 5-year periods are considered (Figure 4).

Table 5. *Median time on waiting list (days) for patients receiving first liver allograft in 2007 (patients listed as highly urgent are excluded in the calculations).*

	Copenhagen	Gothenburg	Helsinki	Oslo	Stockholm	Uppsala
All blood types	173	42	44	20	77	150
Blood type A	68	12	31	12	86	160
Blood type 0	344	57	58	19	72	69

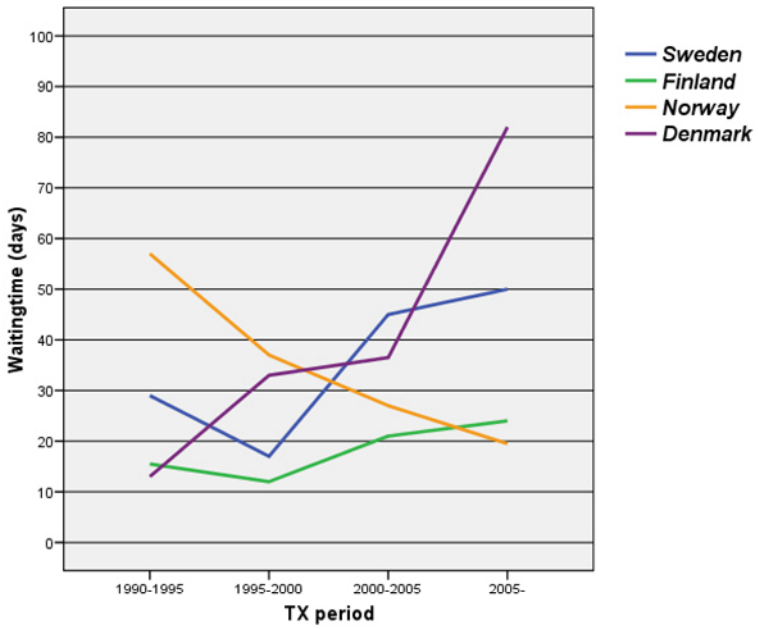

Figure 4. *Median waiting time for first liver transplantation per 5-year period for each country (including all patients, also patients listed as highly urgent).*

5. Age of recipient and donor

The median age at first liver transplantation in 2007 was 51 years as compared with 50 years in 2006 and 51 years in 2005. The median donor age was 53 in 2007 as compared with 51 in 2006 and 50 in 2005. Looking at 5 years intervals, both recipient and donor age have increased throughout the period 1982-2007 (Figure 5).

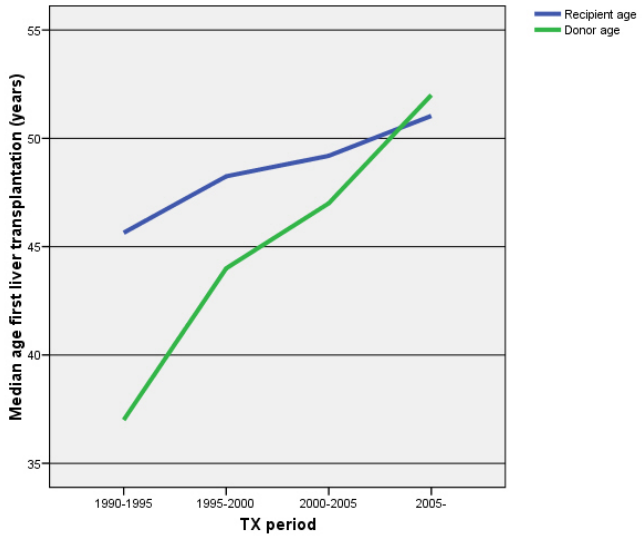

Figure 5. *Recipient and donor age per 5-year period.*

The fraction of first allograft recipients above 60 years of age has steadily increased throughout the entire period 1982-2007 (Figure 6) and was 21.7% in 2007. Probably as a consequence of this, the fraction of children <5 years of age at first liver transplantation has decreased slightly and was in 2007 5.9%.

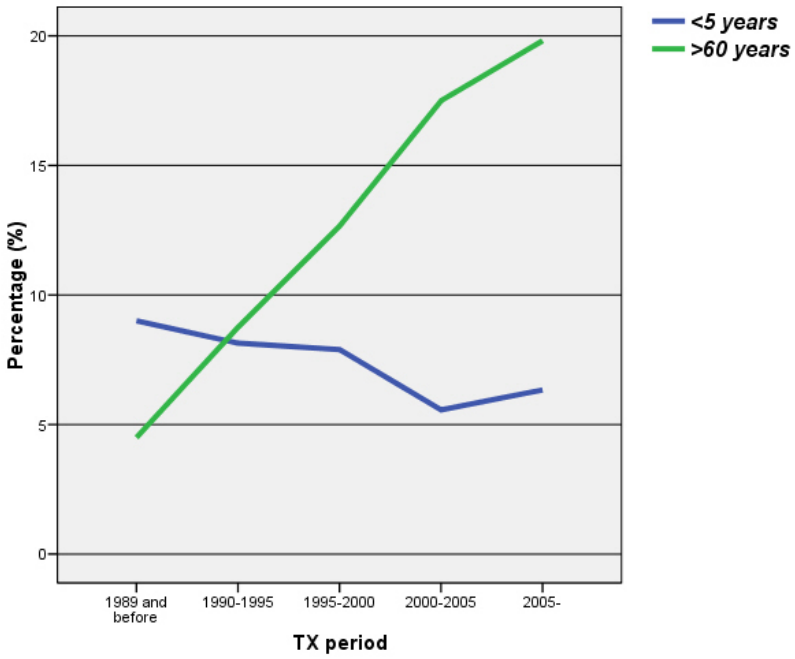

Figure 6. *Fraction of patients <5 and >60 years at first liver transplantation.*

There are some differences in donor and recipient age, and the fraction of old (>60 years) or very young (<5 years) recipients between the centres in 2006 (Table 6).

Table 6. *Age at first liver transplantation for donor and recipient (years) along with fraction of recipients >60 and <5 years in 2007.*

	Median donor age	*Median recipient age*	*% above 60 years (n)*	*% below 5 years (n)*
Copenhagen	49	46	16.2 (6)	0 (0)
Gothenburg	50	54	23.8 (15)	3.2 (2)
Helsinki	54	50	20.4 (10)	10.2 (5)
Oslo	54	51	16.9 (11)	9.2 (6)
Stockholm	54	55	32.0 (16)	6.0 (3)
Uppsala	61	55	12.5 (1)	0 (0)

6. Diagnoses

Primary sclerosing cholangitis (PSC) is still the leading diagnosis for liver transplantation in the Nordic countries in 2007 (Table 7 and 8), closely followed by post-hepatitis C cirrhosis and hepatocellular carcinoma. Co-morbidity (i.e. HCV, HCC, alcohol) complicates the interpretation of the mere diagnosis counts from the registry presented in Table 7. Regarding the 26 patients listed with hepatocellular carcinoma (HCC), positive HCV status was registered for 12 of 20 patients (60%); data was missing for 6 individuals. Regarding the 20 patients listed with alcoholic liver cirrhosis, only negative HCV findings was registered (missing data for 7 individuals). Regarding the 34 patients with HCV cirrhosis, alcohol as a secondary diagnosis was registered for 4 (12%).

Table 7. *Diagnoses of patients (n) receiving the first liver allograft 1997-2007.*

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
PSC	31	24	21	28	37	32	37	42	36	33	50
Alcoholic liver cirrhosis	21	28	13	21	21	29	24	25	26	30	20
Post-hepatitis C cirrhosis	11	17	18	15	11	22	23	26	23	29	34
Hepatocellular carcinoma	10	14	6	11	11	5	13	19	18	20	26
Other malignancies	2	6	6	6	4	10	7	8	2	9	12
Acute liver failure	23	18	20	16	32	15	26	21	15	28	24
PBC	15	16	16	18	11	8	17	18	15	23	17
Other liver diseases (grouped)	13	14	13	11	21	17	20	20	18	22	23
Biliary atresia	5	8	8	6	12	6	9	10	11	12	9
Cryptogenic cirrhosis	9	4	5	9	7	7	10	8	9	11	20
Autoimmune cirrhosis	5	1	10	6	4	10	7	12	12	8	15
Metabolic liver disease	6	15	15	11	9	10	9	14	20	8	15
Budd-Chiari	1	5	3	0	5	4	1	2	2	5	1
Post-hepatitis B cirrhosis	5	5	8	6	4	8	5	11	5	5	3
Diagnosis missing	0	0	1	0	1	7	8	4	11	5	3

Table 8. *Diagnoses of patients (%) receiving first liver allograft in 2006 and 2007.*

Diagnosis	2007 (%)	2006 (%)
PSC	18.4	13.3
Alcoholic liver cirrhosis	7.4	11.7
Post-hepatitis C cirrhosis	12.5	12.1
Hepatocellular carcinoma	9.6	8.1
Other Malignancies	4.4	3.6
Acute liver failure	8.8	11.3
PBC	6.3	9.3
Other liver diseases (grouped)	8.5	8.1
Biliary atresia	3.3	4.8
Cryptogenic cirrhosis	7.4	4.8
Autoimmune cirrhosis	5.5	3.2
Metabolic liver disease	5.5	3.6
Budd-Chiari	0.4	2.0
Post-hepatitis B cirrhosis	1.1	1.6
Diagnosis missing	1.1	2.4

There are marked differences between the Nordic countries in the fraction of patients transplanted for HCV cirrhosis, HCC and acute liver failure (Table 9).

Table 9. *Diagnoses of patients (%) receiving the first liver allograft 2007 (each center).*

Diagnosis	Copenhagen (%)	Gothenburg (%)	Helsinki (%)	Oslo (%)	Stockholm (%)	Uppsala (%)
PSC	18.9	19.0	14.3	24.6	12.0	25.0
Alcoholic liver cirrhosis	16.2	11.1	6.1	4.6	2.0	0.0
Post-hepatitis C cirrhosis	***2.7***	***19.0***	***4.1***	***7.7***	***20.0***	***50.0***
Hepatocellular carcinoma	***2.7***	***6.3***	***10.2***	***7.7***	***22.0***	***0.0***
Other Malignancies	0.0	3.2	0.0	13.8	2.0	0.0
Acute liver failure	***8.1***	***3.2***	***20.4***	***12.3***	***2.0***	***0.0***
PBC	10.8	6.3	12.2	3.1	0.0	12.5
Other liver disease (grouped)	16.2	7.9	6.1	4.6	12.0	0.0
Biliary atresia	0.0	1.6	4.1	9.2	0.0	0.0
Cryptogenic cirrhosis	8.1	9.5	10.2	4.6	6.0	0.0
Autoimmune cirrhosis	5.4	6.3	6.1	6.2	4.0	0.0
Metabolic liver disease	8.1	1.6	2.0	1.5	18.0	0.0
Budd-Chiari	2.7	0.0	0.0	0.0	0.0	0.0
Diagnosis missing	0.0	1.6	4.1	0.0	0.0	0.0

The high fractions of HCV and HCC transplantations in Sweden and liver transplantation for acute liver failure in Finland (as compared with the other countries), are also evident when adjusting numbers for population size (Table 10).

Table 10. *Number of first liver transplantations per million inhabitants performed in the years 2000-2007 (sum of numbers 2000-2007).*

	HCV cirrhosis	HCC	Acute liver failure
Sweden	***15.4***	***9.3***	4.6
Denmark	1.8	1.3	7.1
Finland	1.7	3.8	***11.7***
Norway	5.1	2.3	7.2

7. Patient 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) has constantly improved and is still improving (Figure 6). The 1-year survival rate for patients receiving the first liver allograft in 2006 was 91%.

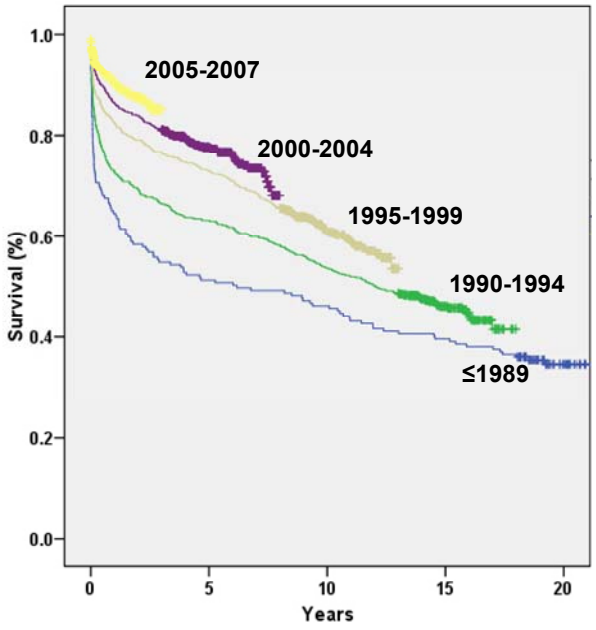

Figure 6.
Kaplan-Meier patient survival curves per 5-years period.

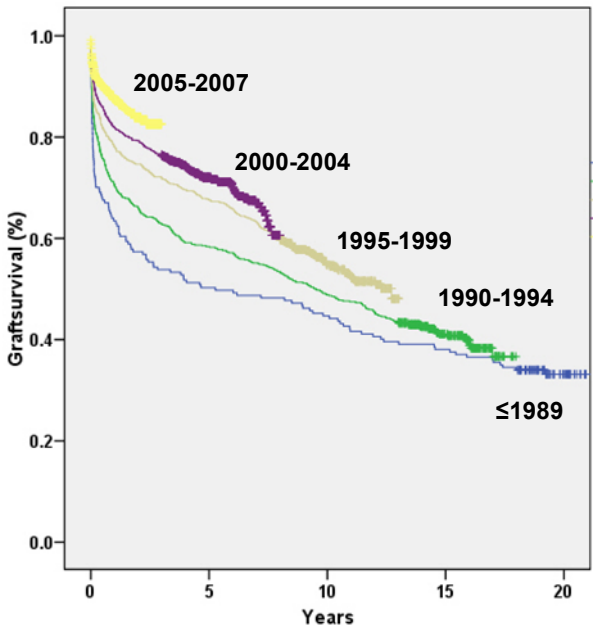

Figure 7.
Kaplan-Meier graftsurvival curves per 5-years period.

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 malignant disease, HVC cirrhosis and acute liver failure (Table 8).

Table 11. *Patient survival rates (1 year and 5 years) according to diagnosis for the entire period 2000-2007. Age at first liver transplantation as well as re-transplantation rate for the same period is given for each diagnosis.*

	2000-2007		2000-2007	2000-2007
	% (1 year survival)	% (5 years survival)	Median age (years)	Re-TX rate
PSC	92%	86%	45	8.1%
Alcoholic liver cirrhosis	91%	79%	55	5.6%
Post-hepatitis C cirrhosis	81%	64%	53	8.7%
Hepatocellular carcinoma	81%	57%	56	4.9%
Acute liver failure	81%	75%	43	11.6%
PBC	92%	86%	57	5.5%
Biliary atresia	85%	79%	1	10.7%
Cryptogenic cirrhosis	87%	81%	55	3.7%
Metabolic liver disease	94%	92%	46	3.1%
Autoimmune cirrhosis	89%	87%	40	5.4%
Budd-Chiari	90%	90%	40	5.0%
Post-hepatitis B cirrhosis	98%	90%	51	6.5%

For domino transplantations (1992-2007), a slightly worse outcome could be observed as compared with all other liver transplantations performed in the same period (i.e. no matching of the groups was performed) (Figure 8). For living donor transplantations (1993-2007), a slightly better outcome could be observed in children <16 years of age (Figure 9), whereas survival in adult patients transplanted so far (n=14) was relatively poor (Figure 10).

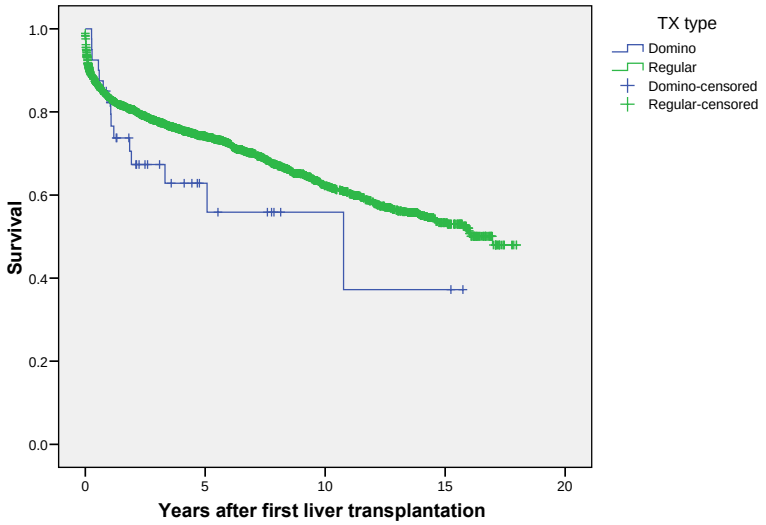

Figure 8. *Kaplan-Meier patient survival curves for domino versus regular liver transplantation 1990-2007.*

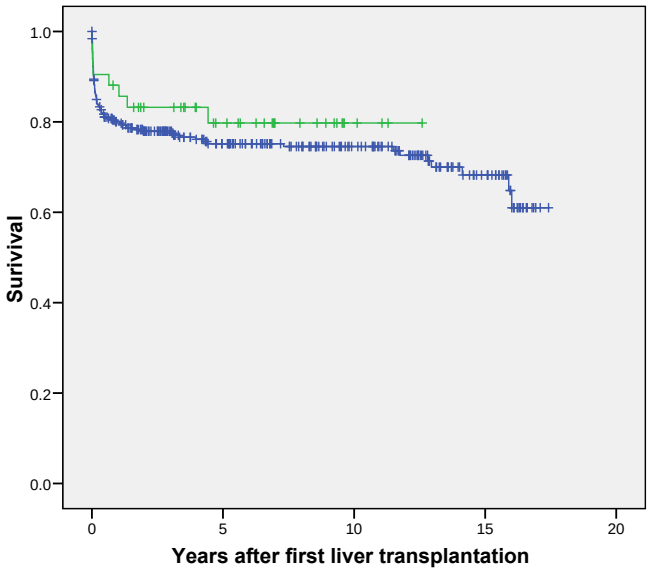

Figure 9. *Kaplan-Meier patient survival curves for children (<16 years); living donor (LDT) versus cadaveric (CDT) liver transplantation.*

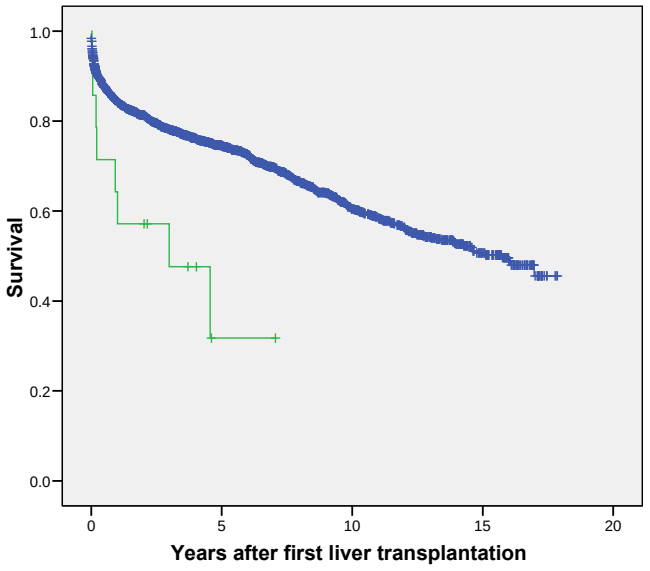

Figure 10. *Kaplan-Meier patient survival curves for adults (>16 years); living donor (LDT) versus cadaveric (CDT) liver transplantation.*

8. Maintenance of the registry

Most centres are relatively up to date with data entry, and waiting list/transplantation status and survival data for all patients are now complete for 2007 (except for one patient). Quality control of existing data and ensuring completeness of remaining parameters is a continuous priority, and in the preparation of this report, a particular emphasis was put into ensuring integrity of the survival data, including cause of death.

Throughout 2007, Christian Mondrup and Frank Pedersen at Scandiatransplant implemented the revised data entry forms (which can be downloaded from http://www.scandiatransplant.org/FINAL_REVISED_NLTR_FORMS_181207.pdf) into a test system. Following several rounds of quality control by Tom Hemming Karlsen and Stein Foss in Oslo, the "new" NLTR was released December 18th. The main changes as compared with the previous system are:

a) *Reduced number of parameters.* The NLTR should only keep an updated record of parameters critical to finding patients of particular characteristics for a study ("identifiers"). This means that for a scientific study to be conducted, usually patient records will have to be consulted. Rationale for choosing not to implement more parameters was to reduce work-load for transplant co-ordinators entering data into the system, as well as the fact that for most specific scientific contexts, data would
b) *Thoroughly revised Form C.* A major weakness of the present system is the lack of follow-up data. Systematic use of Form C at 1, 3, 5, 10, 15, 20, 25 and 30 years follow-up consultations, will over time generate a valuable source for studying long-term complications of liver transplantation (e.g. biliary and vascular complications, disease recurrence, malignancy etc.). Critical to the actual use of Form C is the implementation of the form into the follow-up logistics at each individual liver transplant center.
c) *ELTR/HUSLTR compatibility.* The old diagnosis and death codes used in NLTR were incompatible with current ELTR standards as well as the Helsinki-based HUSLTR system. For data transfer between these systems to become possible, a minimum requirement is compatibility at this level.

The experience after a few months with the new system points to two critical issues that need to be resolved: 1) While NLTR diagnosis and death codes are now ELTR compatible, the main Scandiatransplant system still uses the old codes. Due to the ongoing update project of the main Scandiatransplant system, revision of these obsolete codes has not yet been possible. As soon as formalities allow for the revision of the

Scandiatransplant system as to this regard, the update will be performed. 2) Some of the new points at Form C (PSC/PBC/AIH recurrence, HCV recurrence and new onset renal failure) are ambiguous in the absence of a consensus definition. At the NLTG meeting in Oslo 13. April 2008, it was agreed that definitions for PSC/PBC/AIH recurrence would be drafted by Erik Schrumpf/Kirsten Muri Boberg, definitions for HCV recurrence by Styrbjørn Friman and new onset renal failure by Gustav Herlenius, for discussion and implementation at the next NLTG meeting.

The principal maintenance effort to be performed in 2008 is to ensure automated and reliable data transfer from HUSLTR to NLTR, to ensure completeness of Finnish data in the system. Another important activity scheduled for 2008 is the user meeting in Århus in September, where Tom Hemming Karlsen, Frank Pedersen and Christian Mondrup will work through content-related and technical issues of the system with transplant coordinators from all centers.

10. Acknowledgements - financial support

The maintenance of the software has been performed by Scandiatransplant. We are extremely grateful for the help and support from Frank Pedersen and Christian Mondrup in Aarhus. Without their assistance it would not have been possible to maintain the registry. Transplant nurses and transplant coordinators at the individual centres have also made an enormous effort in updating and maintaining the registry. The existence of the registry depends completely on their work and dedication.

11. Organisation and data ownership

It should be emphasised that the registry (software) is the property of Scandiatransplant, while the data in the registry are the property of the Nordic Liver Transplantation Group. Utilisation of data should be censored by the latter. The data presented here should not be used without permission from the Nordic Liver Transplantation Group.

12. Publications based on the NLTR

Full length articles 1990-2007:

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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9. Olausson M, Mjornstedt L, Backman L, Lindner P, Olsson R, Krantz M, Karlsen KL, Stenqvist O, Henriksson BA, Friman S. Liver transplantation--from experiment to routine care. Experiences from the first 500 liver transplantations in Gothenburg. Lakartidningen 2001;98:4556-62
10. Brandsæter B , K Höckerstedt, BG Ericzon, S Friman, P Kirkegaard, H Isoniemi, 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.
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.
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