The Nordic Liver Transplant Registry

(NLTR)

Annual report 2012

Report prepared by Tom H. Karlsen April 2013

Responsible contact persons:

Scandiatransplant Denmark - Århus; Frank Pedersen
TX Denmark - Copenhagen; Allan Rasmussen
TX Sweden - Gothenburg; Michael Olausson
TX Sweden - Stockholm; Bo-Göran Ericzon
TX Finland - Helsinki; Helena Isoniemi
TX Norway - Oslo; Aksel Foss
NLTR; Tom Hemming Karlsen, t.h.karlsen@klinmed.uio.no, Oslo, Norway

1. Source of data

Numbers and graphs in the present report are based on data extracted from the Nordic Liver Transplant Registry (NLTR) March 2012. 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 2012

The registry comprises complete data from the liver transplanpation 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 Scandiatransplant in Århus (www.scandiatransplant.org).

Up to the 31st of December 2012, data from a total of 5750 patients had been entered to the NLTR. Of these, 4868 patients had been transplanted. Of these, 569 (11.7%) had been transplanted more than once, and 86 (1.8%) had been transplanted more than twice. A total of 82 living donor transplantations (7 in 2012) and 75 domino transplantations (4 in 2012) had been performed up to 31st of December 2012. Children below 16 years constituted 509 (10.9%) of the transplanted patients in the registry.

3. Transplantation activity 2012

The total number of patients who underwent first liver transplantation in 2012 was 325 (Figure 1). Of these, 4 were combined liver-kidney transplantations. In addition, 27 re-transplantations were performed. The total number of 353 liver transplantations represents a substantial increase from the 323 liver transplantations performed in 2010 (Table 1, Figure 2), but is comparable to the overall number as in 2011 (352).

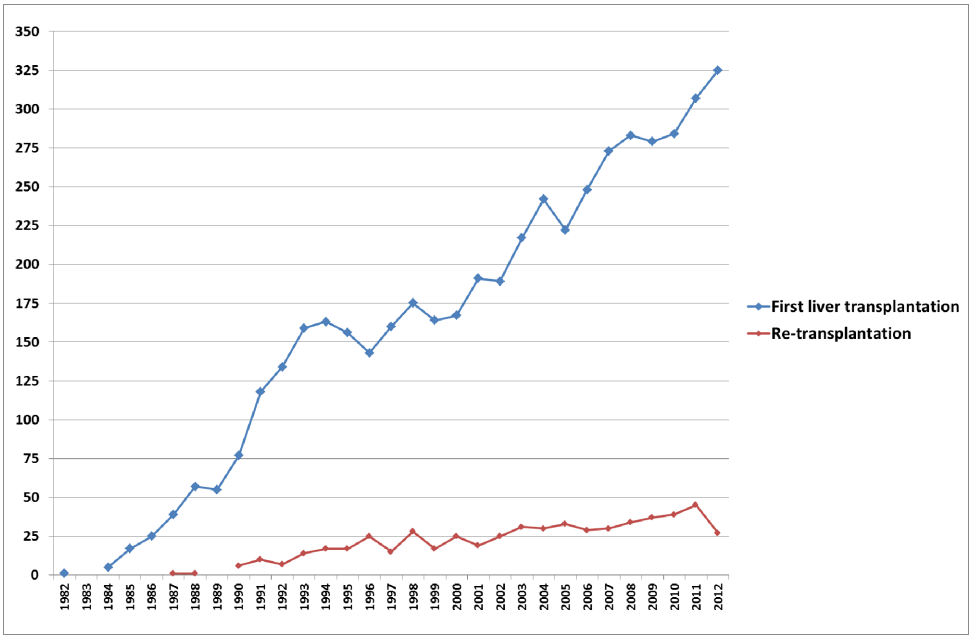

Figure 1. *Number of patients receiving a liver allograft 1982-2012.*

Table 1. *Liver transplantations performed per center the last 10 years.*

	Number of first liver transplantations										*Number of re-transplantations*									
	2003	2004	2005	2006	2007	2008	2009	2010	2011	**2012**	2003	2004	2005	2006	2007	2008	2009	2010	2011	**2012**
Copenhagen	36	37	36	32	37	43	37	43	42	**44**	3	6	4	4	5	1	3	4	9	**4**
Gothenburg	62	59	53	52	64	66	78	61	67	**75**	7	11	14	8	11	10	11	19	16	**4**
Helsinki	40	46	39	49	50	42	42	47	52	**48**	3	4	3	4	3	5	6	3	4	**4**
Oslo	31	43	32	52	64	69	69	77	81	**89**	8	4	7	10	8	10	13	12	8	**11**
Stockholm	41	45	56	56	50	52	43	53	65	**69**	9	7	4	3	2	6	3	1	8	**5**
Uppsala	7	11	7	8	8	11	10	3	0	**0**	1	0	0	0	1	2	1	0	0	**0**
Total number	217	241	223	249	273	283	279	284	307	**325**	31	32	32	29	30	34	37	39	45	**28**

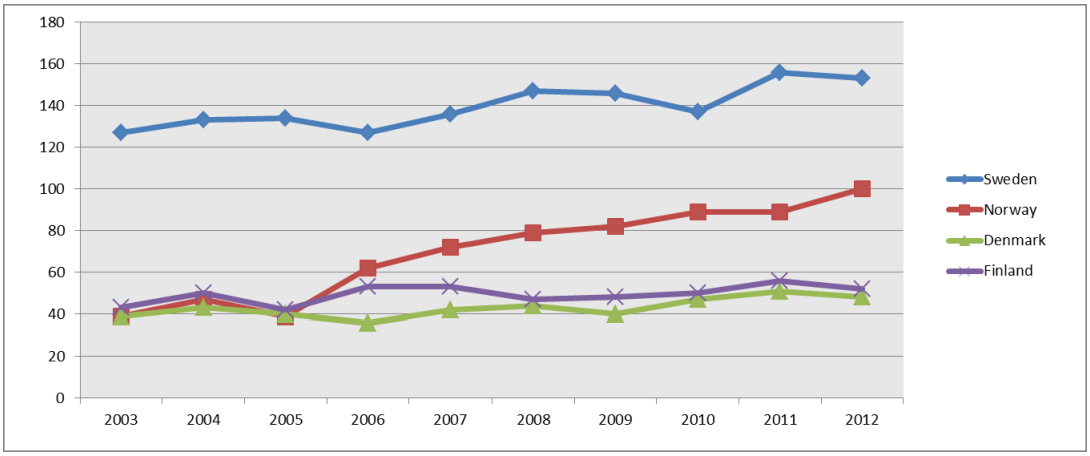

Figure 2. *Total number of liver transplantations per country 2000-2012. Adjusted for population size, annual transplantation rates in 2012 were 16.9 per million for Sweden, 19.8 per million Norway, 9.6 per million for Finland and 8.7 per million for Denmark.*

4. The waiting list 2012

A total of 391 withdrawals were made from the waiting list (Table 2). The number of deaths on the waiting list in 2012 was 15 (Denmark 3, Sweden 9, Finland 0, Norway 3).

Table 2. *Patients withdrawn from the waiting list in 2012 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.*

Deceased donor	Living donor	Domino	Dead	Permanent withdrawal
342	7	4	15	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).*

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
All blood types	**38**	**40**	**41**	**41**	**51**	**58**	**44**	**64**	**46**	**39**
Blood type A	27	29	38	26	33	56	24	33	27	26
Blood type 0	74	71	60	105	62	76	80	119	98	81
Blood type AB	43	10	23	42	52	44	24	36	14	29
Blood type B	33	44	44	28	63	84	83	90	67	38

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 2012 (patients listed as highly urgent are excluded from the calculations, numbers in brackets are 2011 numbers for comparison).*

	Copenhagen	Gothenburg	Helsinki	Oslo	Stockholm
Blood type A	65 (55)	40 (33)	21 (30)	9 (7)	30 (66)
Blood type 0	187 (272)	257 (174)	79 (30)	26 (23)	99 (171)
Blood type AB	16 (84)	NA (17)	29 (31)	6 (1)	18 (29)
Blood type B	27 (265)	69 (49)	4 (107)	33 (17)	118 (257)

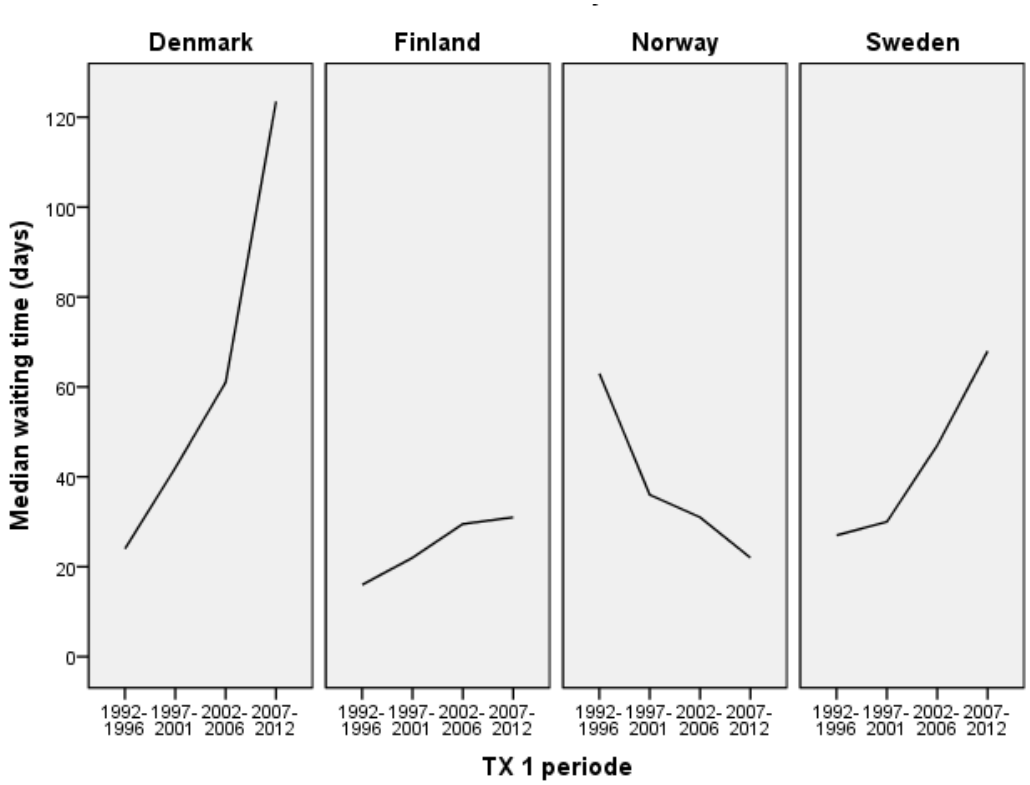

Figure 4. *Median waiting time for first liver transplantation per 5-year period for each country (patients listed as highly urgent are excluded from the analysis).*

5. Age of recipients and donors

Both recipient and donor age have increased throughout the period 1982-2012 (Figure 5), but are now reasonably stable over the recent years. Median age of adult liver recipients (≥16 years, first liver transplantation) in 2012 was 53.2 years. Median age of children (<16 years, first liver transplantation) in 2012 was 2.0 years.

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

6. Diagnoses

In 2012, primary sclerosing cholangitis (PSC) and hepatocellular carcinoma were the leading indications for liver transplantation in the Nordic countries (Table 5). Of the 47 patients transplanted with a primary diagnosis of hepatocellular carcinoma (HCC) in 2012, slightly less than half of the patients (n=20) were registered with a positive history of hepatitis C infection (missing data on HCV serology for 1 patient). Hepatitis C related disease accounted for a total of 16.9% (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 2012 compared with 2010, 2011 and the remainder of the last decade and previous years.Top indications were PSC, HCC, HCV and alcoholic cirrhosis. * HCC: 20 pos. HCV, 1 ND (26 neg. HCV), Alcohol: 2 pos. HCV, 2 ND (35 neg. HCV); i.e. 55 (16.9%) HCV related*

Diagnosis	*1982-1999 (n)*	*1982-1999 (%)*	*2000-2009 (n)*	*2000-2009 (%)*	*2010 (n)*	*2010 (%)*	*2011 (n)*	*2011 (%)*	*2012 (n)*	*2012 (%)*
Acute liver failure	210	12,7	234	10,1	36	12,6	19	6,2	30	9,2
Alcoholic liver cirrhosis	144	8,7	257	11,1	33	11,6	39	12.7*	42	12,9
Autoimmune cirrhosis	60	3,6	100	4,3	11	3,9	11	3,6	9	2,8
Biliary atresia	84	5,1	87	3,8	7	2,5	5	1,6	11	3,4
Budd-Chiari	35	2,1	27	1,2	1	0,4	3	1,0	6	1,8
Hepatocellular carcinoma	92	5,6	172	7,4	47	16,5	49	16.0*	47	14,5
Metabolic liver disease	141	8,6	146	6,3	24	8,4	18	5,9	17	5,2
Other liver diseases (grouped)	175	10,6	276	12	25	8,8	41	11,8	42	12,9
Other malignancies	54	3,2	78	3,4	17	6,0	14	4,6	12	3,7
PBC	253	15,4	170	7,4	12	4,2	13	4,2	21	6,5
Polycystic liver disease	19	1,2	33	1,4	2	0,7	5	1,6	6	1,8
Post-hepatitis B cirrhosis	43	2,6	56	2,4	1	0,4	6	2,0	1	0,3
Post-hepatitis C cirrhosis	72	4,4	247	7,4	19	6,7	24	7,8	33	10,2
PSC	219	13,3	389	16,8	45	15,8	64	20,9	47	14,5

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.

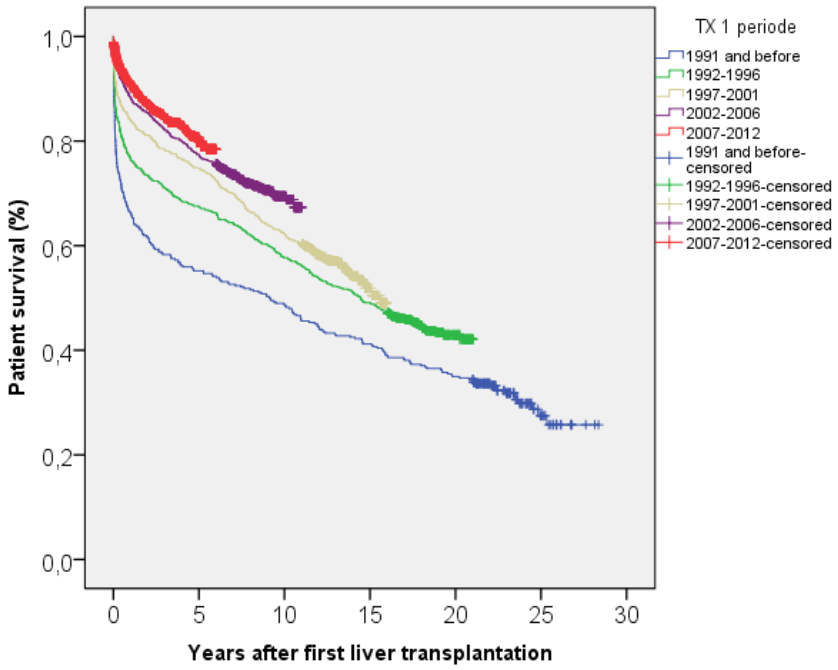

Figure 6. *Kaplan-Meier patient survival curves per 5-years period (first liver transplantation).*

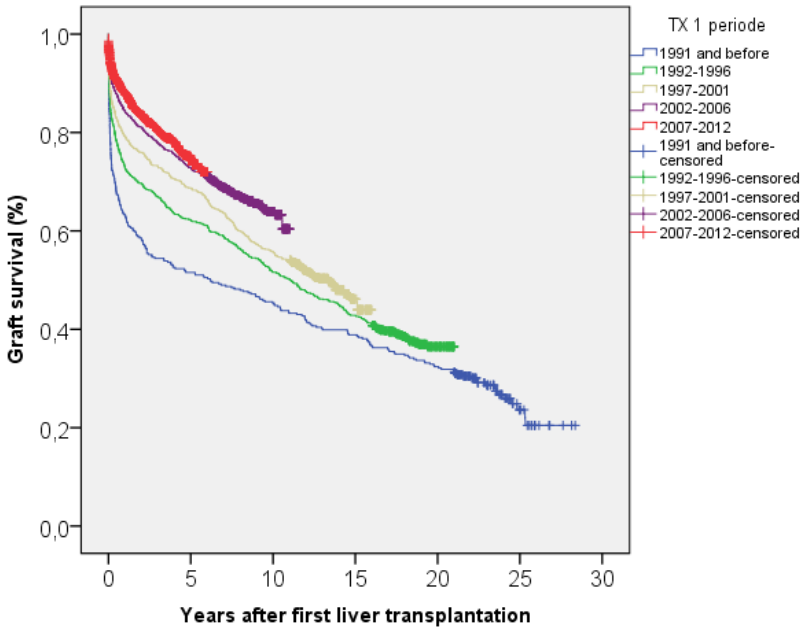

Figure 7. *Kaplan-Meier graftsurvival curves per 5-years period (first liver transplantation).*

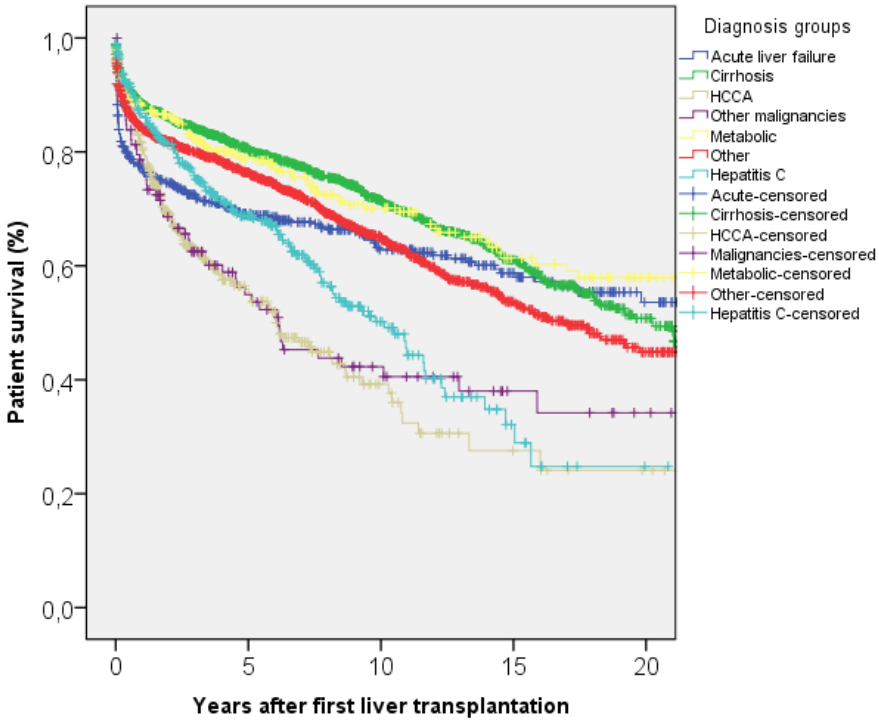

Figure 8. *Kaplan-Meier patient survival curves per diagnosis category (first liver TX during 2003 to 2012).*

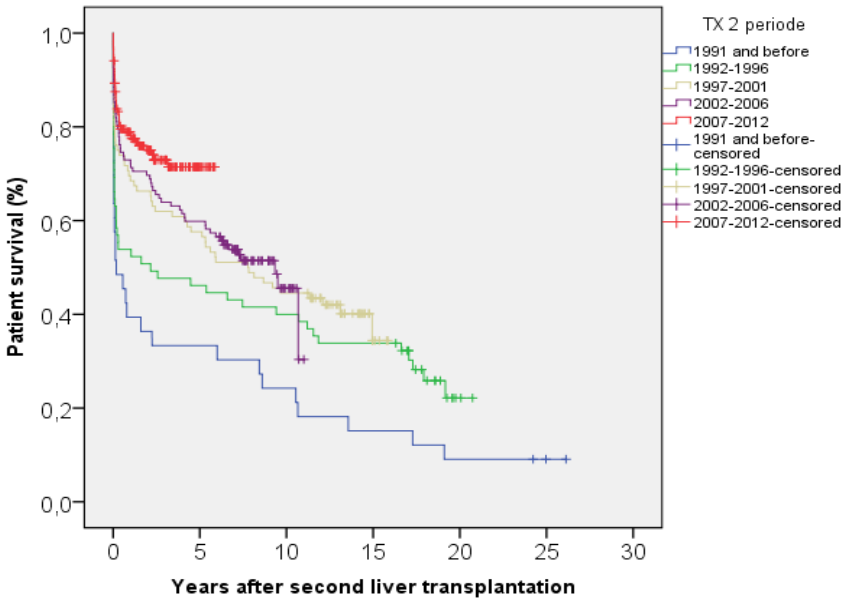

Figure 9. *Kaplan-Meier graft survival curves per diagnosis category (second liver TX), legend categories as in Figure 8.*

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 2003-2012 (the piggy-back technique was standard after 2002). Age at first liver transplantation as well as re-transplantation rates for the same period are given for each diagnosis.*

	2003-2012		2003-2012	2003-2012	1982-2002	1982-2012
	% (1 year survival)	% (5 years survival)	Median age (years)	Re-TX	Re-TX	% alive
Acute liver failure	83,0%	77,9%	44	10,5 %	19,9 %	59,6 %
Alcoholic liver cirrhosis	93,1%	83,2%	57	3,7 %	7,4 %	60,2 %
Autoimmune cirrhosis	87,4%	83,5%	40	7,0 %	11,3 %	66,4 %
Biliary atresia	83,6%	77,8%	0.9	5,7 %	19,4 %	63,2 %
Budd-Chiari	92.4%	77.0%	34	20,7 %	15,9 %	63,6 %
Hepatocellular carcinoma	86,9%	66,1%	58	4,5 %	8,4 %	56,5 %
Metabolic liver disease	93,6%	86,1%	50	2,8 %	14,8 %	70,7 %
PBC	93,7%	86,6%	57	6,6 %	10,0 %	61,5 %
Post-hepatitis B cirrhosis	91,7%	84,2%	51	6,3 %	14,8 %	62,8 %
Post-hepatitis C cirrhosis	89,2%	71,4%	54	7,6 %	16,0 %	57,1 %
PSC	95,8%	85,5%	43	7,8 %	18,8 %	72,3 %

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 2012. 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 Mette Gottlieb 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 remainder of the registry must be maintained at a level set at the discretion of each individual center and contact person. Data transfer between NLTR and local registries and the ELTR needs to be established.

10. Acknowledgements - financial support

The NLTR received no financial support in 2012. 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 Ilse Duus Weinreich and the rest of the Scandiatransplant team 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 Scandiatransplant.

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, 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 1990-2012:

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
2. Hockerstedt K, Ericzon BG, Eriksson LS, Flatmark A, Isoniemi H, Karlberg I, Keiding N, Keiding S, Olsson R, Samela K. Survival after liver transplantation for primary biliary cirrhosis: use of prognostic indices for comparison with medical treatment. Transpl Proc 1990; 22:1499-500
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
4. Bjøro K, Friman S, Höckerstedt K, Kirkegaard P, Keiding S, Schrumpf E, Olausson M, Oksanen A, Isoniemi H, Hjortrup A, Bergan A, Ericzon BG. Liver transplantation in the Nordic countries, 1982-1998: Changes of indications and improving results. Scand J Gastroenterol 1999;34:714-722
5. Bjøro K, Höckerstedt K, Ericzon BG, Friman S, Hjortrup A, Keiding S, Schrumpf E, Duraj F, Olausson M, Mäkisalo H, Bergan A, Kirkegard P. Liver transplantation in patients over 60 years of age. Transpl Int 2000; 13, 165-170
6. Bjøro K, Kirkegaard P, Ericzon BG, Friman S, Schrumpf E, Isoniemi H, Herlenius G, Olausson M, Rasmussen A, Foss A, Höckerstedt K. Is a 3-day limit for highly urgent liver transplantation for fulminant hepatic failure appropriate – or is the diagnosis in some cases incorrect? Transpl Proceed 2001;33:2511-3
7. Ericzon BG, Bjøro K, Höckerstedt K, Hansen B, Olausson M, Isoniemi H, Kirkegaard P, Broome U, Foss A, Friman S. Time to request AB0-identity when transplanting for fulminant hepatic failure? Transpl Proc 2001;33:3466-7
8. Leidenius M, Broome U, Ericzon B-E, Friman S, Olausson M, Schrumpf E, Höckerstedt K. Hepatobiliary carcinoma in primary sclerosing cholangitis: a case control study. J Hepatol 2001; 34: 792-8.
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.
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.
15. Bjøro K, Schrumpf E. Liver transplantation for primary sclerosing cholangitis. J Hepatol. 2004;40:570-7.
16. Brandsaeter B, Isoniemi H, Broomé U, Olauson M, Bäckmann L, Hansen B, Oksanen A, Ericzon BG, Höckerstedt K, Mäkisalo H, Kirkegaard P, Friman S, Bjøro K, Schrumpf E (Nordic Liver Transplantation Group). Chemopreventive effect of ursodeoxycholicacid in primary sclerosing cholangitis? Falk Symposium 141. Bile Acid Biology and its Therapeutic Implications. XVIII International Bile Acid Meeting (2005; page 242-249).
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.
18. Bjøro K, Brandsaeter B, Foss A, Schrumpf E. Liver transplantation in primary sclerosing cholangitis. Semin Liver Dis. 2006;26:69-79.
19. Melum E, Friman S, Bjøro K, Rasmussen A, Isoniemi H, Gjertsen H, Bäckman L, Oksanen A, Olausson M, Duraj FF, Ericzon BG. Hepatitis C impairs survival following liver transplantation irrespective of concomitant hepatocellular carcinoma. J Hepatol. 2007 Dec;47(6):777-83.
20. Friman S, Foss A, Isoniemi H, Olausson M, Höckerstedt K, Yamamoto S, Karlsen TH, Rizell M, Ericzon BG. Liver transplantation for cholangiocarcinoma: selection is essential for acceptable results. Scand J Gastroenterol. 2011 Mar;46(3):370-5.
21. Jørgensen KK, Lindström L, Cvancarova M, Castedal M, Friman S, Schrumpf E, Foss A, Isoniemi H, Nordin A, Holte K, Rasmussen A, Bergquist A, Vatn MH, Boberg KM. Colorectal neoplasia in patients with primary sclerosing cholangitis undergoing liver transplantation: a Nordic multicenter study. Scand J Gastroenterol. 2012 Sep;47(8-9):1021-9.