The Nordic Liver Transplant Registry

Annual report 2008

Report prepared by Tom Hemming Karlsen

tom.hemming.karlsen@rikshospitalet.no

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Responsible contact persons:

Denmark - Copenhagen; Preben Kirkegaard
Sweden - Gothenburg; Styrbjörn Friman
Sweden - Stockholm; Bo-Göran Ericzon
Sweden - Uppsala; Frans Duraj
Finland - Helsinki; Krister Höckerstedt
Norway - Oslo; Aksel Foss
Scandiatransplant – Århus; Frank Pedersen

1. Source of data

Numbers and graphs in the present report are based on data extracted from the Nordic Liver Transplant Registry (NLTR) April 2009. Prior to this export, data were subjected to quality control by Tom Hemming Karlsen with subsequent contribution of missing data and correction of obvious errors by transplant coordinators at all centers.

2. Data content NLTR 2008

The registry comprises data from all transplantation centres in Denmark, Sweden, Norway and Finland from 1982-2008. Data are stored at Scandiatransplant in Århus (www.scandiatransplant.org).

Up to the 31st of December 2008, data from a total of 4335 patients had been entered to the NLTR. Of these, 3678 patients had been transplanted. Of these, 351 (9.5%) had been transplanted more than one time, and 50 (1.4%) had been transplanted more than two times. For the 219 patients receiving a liver allograft prior to 1990, no waiting list data are available. Highly urgent calls were performed in 9.0% of first listings (n=330), and 245 of these patients were transplanted with a median waiting list time of 2.0 days. A total of 105 living donor transplantations were registered (including 55 domino). Children below 16 years constituted 11.7% (n=430) of the transplanted patients.

3. Transplantation activity 2008

The total number of patients who underwent first liver transplantation in 2008 was 283 (Figure 1). Of these, 8 were combined liver-kidney transplantations. In addition, 34 re-transplantations were performed. The total number of 317 liver transplantations is the highest ever (Table 1). The number of re-transplantations is relatively stable and constitutes now 10.7% of the overall activity (Figure 2).

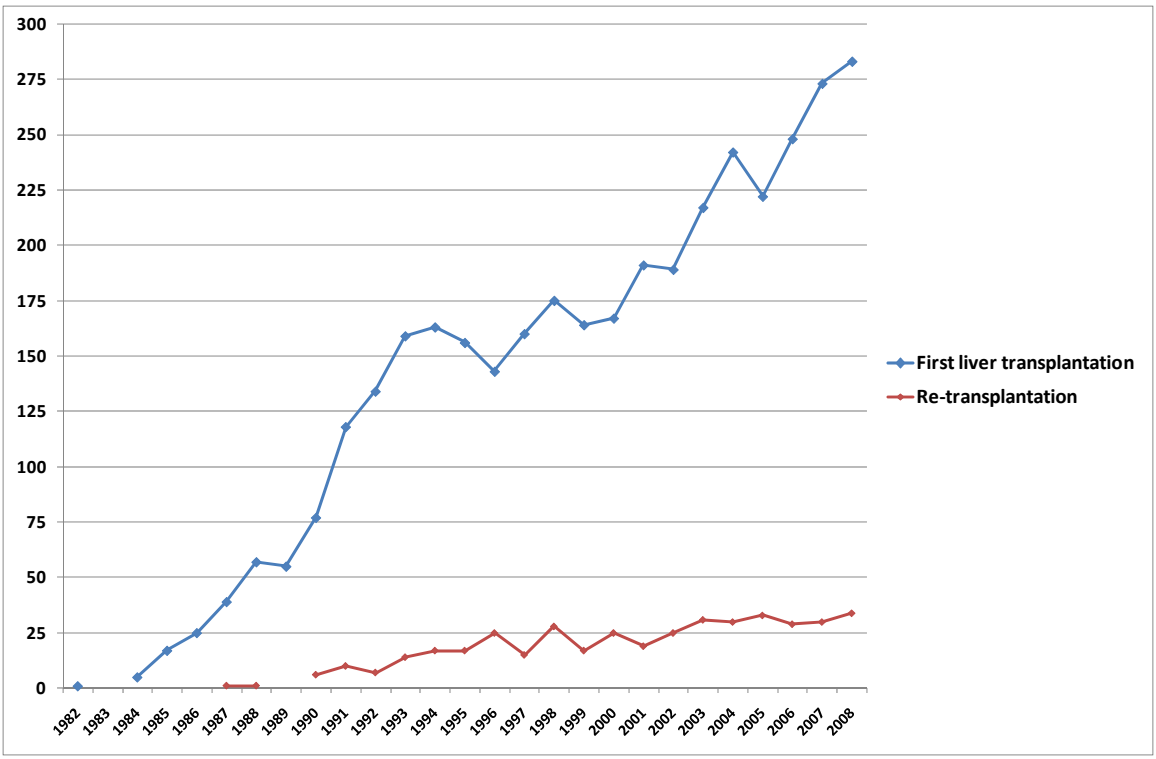

Figure 1. *Number of patients receiving a liver allograft 1982-2008.*

Table 1. *Annual numbers of liver transplantations (TX) 2000-2008.*

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

Table 2. *Liver transplantations performed per centre 2000-2008.*

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

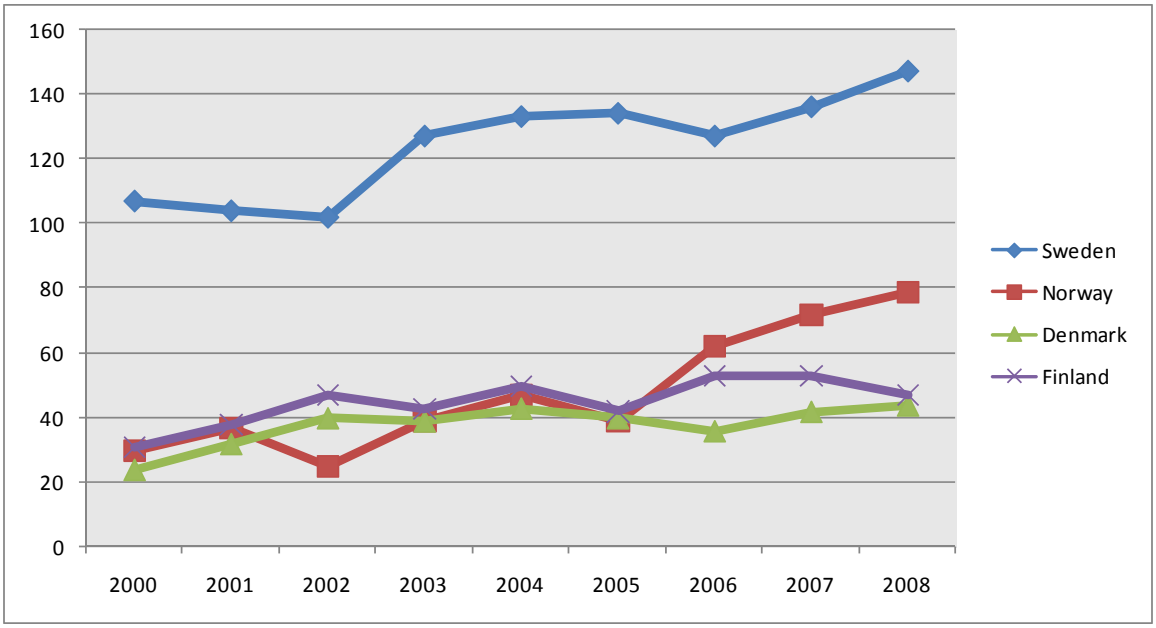

Figure 3. *Total number of liver transplantations per country 2000-2008. Adjusted for population size, annual transplantation rates in 2008 were approximately 16 per million for Norway and Sweden, approximately 9 for Finland and approximately 8 for Denmark.*

4. The waiting list 2008

In 2008, a total of 323 patients were entered to the liver transplantation waiting list (25 listed as highly urgent). A total of 351 patients were withdrawn from the waiting list (Table 3). The number of deaths on the waiting list was 14 (Denmark 4 [1 child], Sweden 9 [1 child], Finland 1, Norway 0).

Deceased donor	*Living donor*	*Domino*	*Dead*	*Permanent withdrawal*
303	6	7	14*	21

Table 3. *Patients withdrawn from the waiting list in 2008 classified by outcome. *Number of deaths on the waiting list is relatively stable; 10 in 2007, 17 in 2006 and 16 in 2005.*

Patients who received their first liver allograft in 2008 had waited a median of 58 days (excluding patients listed as "highly urgent"). As such, there is now a slight trend towards increasing waiting list times (Table 4).

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

	2000	*2001*	*2002*	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*
All blood types	**43**	**39**	**52**	**38**	**40**	**41**	**41**	**51**	**58**
Blood type A	39	32	26	27	29	38	26	33	56
Blood type 0	76	56	102	74	71	60	105	62	76
Blood type AB	22	61	16	43	10	23	42	52	44
Blood type B	35	49	75	33	44	44	28	63	84

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 2008 (patients listed as highly urgent are excluded from the calculations).*

	Copenhagen	*Gothenburg*	*Helsinki*	*Oslo*	*Stockholm*	*Uppsala*
All blood types	95	55	45	30	116	95
Blood type A	58	58	49	36	94	97
Blood type 0	478	65	12	27	189	110

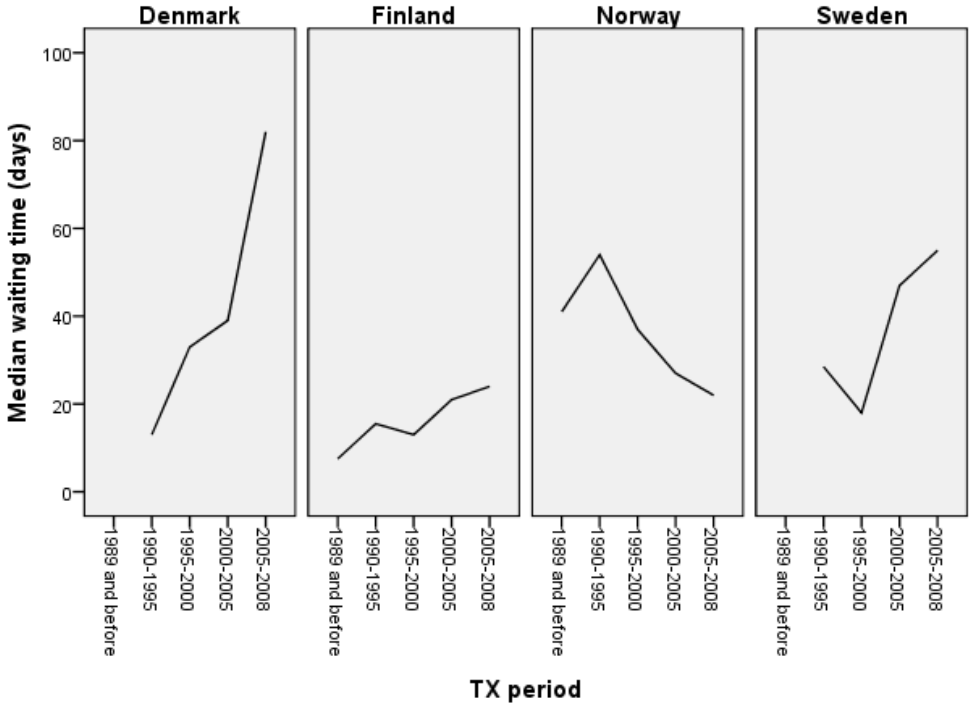

Figure 4. *Median waiting time for first liver transplantation per 5-year period for each country (including all patients, also patients listed as highly urgent).*

5. Age of recipients and donors

Looking at 5 years intervals, both recipient and donor age have increased throughout the period 1982-2008 (Figure 5). Median age of adult liver recipients (≥16 years, first liver transplantation) in 2008 was 54 years (oldest patient 71.8 years). Median age of children (<16 years, first liver transplantaion) in 2008 was 3.9 years (youngest patient 4.5 months).

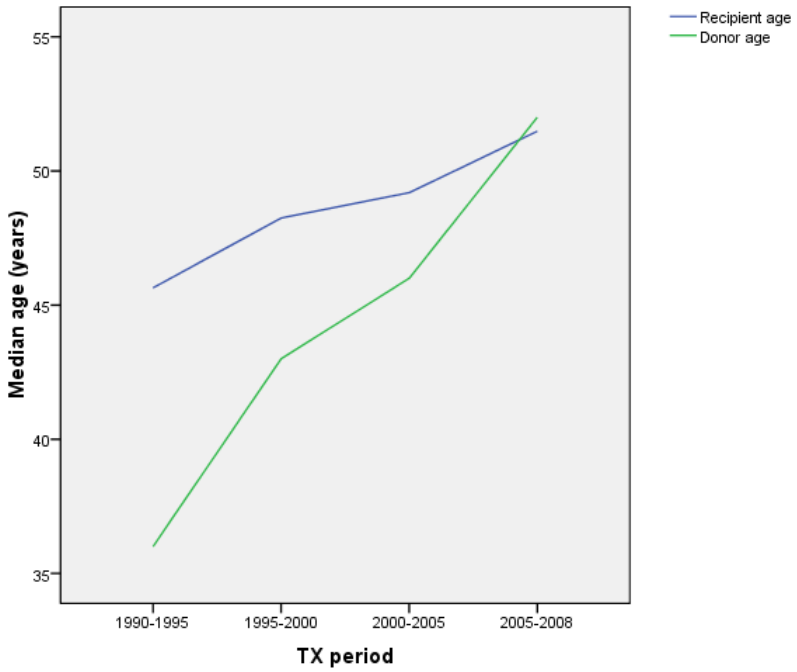

Figure 5. *Recipient and donor age per 5-year period.*

The fraction of first allograft recipients above 60 years is increasing and was 28.7% in 2008. Table 6 summarizes the distribution across other age categories.

Age (years)	*Fraction (%)*
<1	0.7
1-3	1.8
3-15	4.6
16-29	8.2
30-59	56.4
≥60	28.2

Table 6. *First liver transplantation in 2008 according to age.*

6. Diagnoses

Primary sclerosing cholangitis (PSC) was the leading diagnosis for liver transplantation in the Nordic countries in 2008 (Table 7). Other important diagnoses were alcoholic liver cirrhosis, post-hepatatis C cirrhosis and hepatocellular carcinoma. Of the 23 patients transplanted on the basis of hepatocellular carcinoma in 2008, approximately 1/3 (n=7) were registered with a positive history of hepatitis C infection.

Table 7. *Diagnoses of patients receiving the first liver allograft in 2008 compared with the remainder of this decade and previous years.*

Diagnosis	*1982-1999 (n)*	*1982-1999 (%)*	*2000-2007 (n)*	*2000-2007 (%)*	*2008 (n)*	*2008 (%)*
Acute liver failure	210	12.7	178	10.2	31	11.0
Alcoholic liver cirrhosis	144	8.7	196	11.2	30	10.6
Autoimmune cirrhosis	60	3.6	75	4.3	14	4.9
Biliary atresia	84	5.1	75	4.3	4	1.4
Budd-Chiari	35	2.1	20	1.1	3	1.1
Cryptogenic cirrhosis	69	4.2	82	4.7	1	0.4
Hepatocellular carcinoma	92	5.6	126	7.2	23	8.1
Metabolic liver disease	141	8.6	103	5.9	18	6.4
Other liver diseases (grouped)	106	6.4	126	7.2	33	11.7
Other malignancies	54	3.2	58	3.3	6	2.1
PBC	253	15.4	128	7.3	21	7.4
Polycystic liver disease	19	1.2	22	1.3	8	2.8
Post-hepatitis B cirrhosis	43	2.6	46	2.6	5	1.8
Post-hepatitis C cirrhosis	72	4.4	185	10.6	29	10.2
PSC	219	13.3	295	16.9	52	18.4

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) 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).

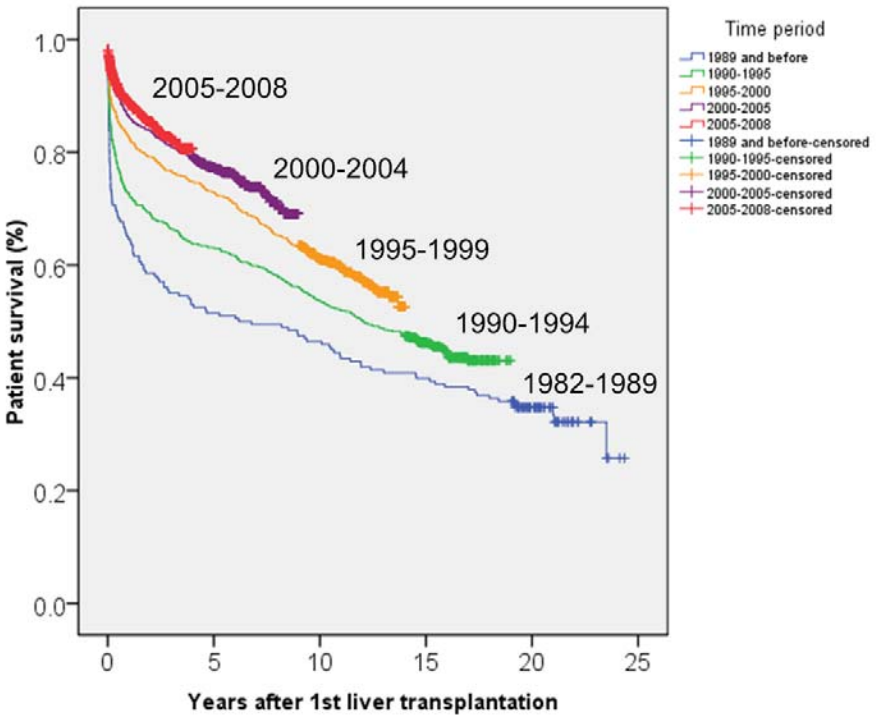

Figure 6. *Kaplan-Meier patient survival curves per 5-years period.*

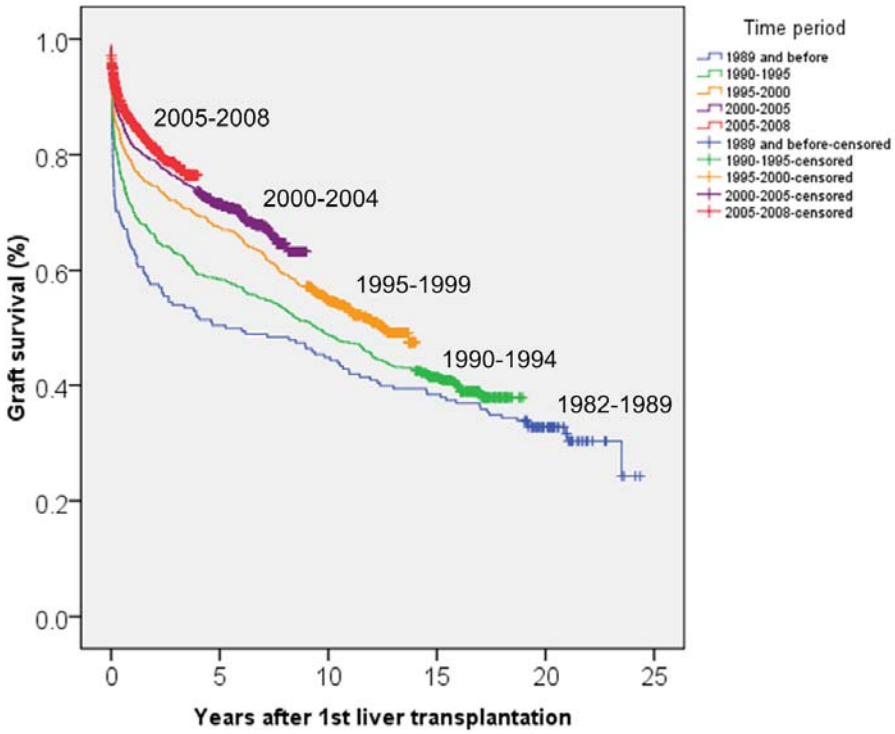

Figure 7. *Kaplan-Meier graft survival curves per 5-years period.*

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 HCV cirrhosis and malignant disease (Table 8).

Table 8. *Patient survival rates (1 year and 5 years) according to diagnosis for patients transplanted during 2001-2008. Age at first liver transplantation as well as re-transplantation rate for the same period is given for each diagnosis.*

	2001-2008		2001-2008	2001-2008
	% (1 year survival)	% (5 years survival)	Median age (years)	Re-TX rate
Acute liver failure	81.4%	74.3%	44	11.9
Alcoholic liver cirrhosis	87.8%	74.8%	56	5.9
Autoimmune cirrhosis	88.9%	87.3%	43	4.8
Biliary atresia	84.7%	77.7%	0.8	9.6
Budd-Chiari	91.3%	83.7%	35	8.7
Cryptogenic cirrhosis	85.1%	77.1%	56	2.7
Hepatocellular carcinoma	80.1%	56.9%	57	6.5
Metabolic liver disease	94.3%	89.0%	47	3.8
PBC	92.7%	89.1%	57	3.1
Post-hepatitis B cirrhosis	90.8%	82.8%	52	4.4
Post-hepatitis C cirrhosis	83.2%	66.5%	54	7.0
PSC	93.1%	87.0%	44	7.8

Patient survival is comparable with data from the remainder of Europe (Table 9).

Table 9. *Survival data for selected patient groups from the European Liver Transplant Registry as compared with data from NLTR. Data from 2001-2007 (data from 2008 not yet available from ELTR). Note that NLTR data are also reported to the ELTR and thus included in the ELTR statistics.*

	Survival (%) ELTR		Survival (%) NLTR	
Diagnosis	1 year	5 years	1 year	5 years
Post-HCV cirrhosis	82	65	83	65
Acute liver failure	76	70	83	75
Alcoholic cirrhosis	87	77	90	77
Non-viral, non-malignant	88	81	92	87
PSC	90	84	93	87

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 2008. 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. 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.

An initiative has finally been set up with regard to data transfer from the Helsinki Liver Transplant registry system (HUSLTR) to the NLTR. 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. In principle, bulk data will be exported from the HUSLTR and subsequently semi-manually (script) imported to the NLTR. When completed, NLTR data for Finland will be annually transferred (at present, only core Scandiatransplant parameters and survival status are systematically entered).

The 15th and 16th of September 2008 Scandiatransplant hosted a NLTR user group meeting at Skejby Hospital in Aarhus. Transplant coordinators from all Nordic centers were present. Day 1 focused on content of the NLTR (Form A-D were discussed in detail as to the interpretation of the parameters). Day 2 focused on technical aspects of the NLTR (challenges related to functionality of the Oracle system).

Definition of "Event" parameters in Form D were discussed at recent NLTG user group meetings in Stockholm (October 6th 2008) and Gothenburg (March 30th 2009). 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": Dialysis or kidney transplantation (add to form: GFR)
- "Recurrent PSC": Histology + cholangiography required
- "Recurrent PBC": Histology required
- "Recurrent AIH": Histology required
- "Recurrent HCV": Infection (HCV RNA) + histologically verified liver injury

Routine cholangiography and histology at 3-5-10 years was proposed, but not concluded mandatory. 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).

10. Acknowledgements - financial support

The NLTR received no financial support in 2008. 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 lately also Bo Hedemark Pedersen in Aarhus. Without their assistance it would not have been possible to maintain the registry. Transplant nurses and transplant coordinators at the individual centres make an enormous effort in updating and maintaining the registry. The existence of the registry depends completely on their work and dedication. I particularly want to thank Inger Palfelt in Copenhagen, Stein Foss in Oslo, Kerstin Larsson and Susanne Klang in Stockholm, Catharina Gehlin in Uppsala, Christina Wibeck in Gotheburg and Helena Isoniemi in Helsinki for fast replies whenever I have questions related to their data.

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 1990-2008:

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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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

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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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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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