The Nordic Liver Transplant Registry (NLTR)

Annual report 2016

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1. Source of data

The numbers and graphs included in the present report are based on data extracted from the Nordic Liver Transplant Registry (NLTR) in June 2017. Prior to the export, data were subjected to extensive integrity and quality control. Entry of missing data and correction of all identified errors were performed by transplant coordinators at all centers prior to the final data extraction.

2. Data content NLTR 2016

The registry comprises complete data from the liver transplantation activity at all transplantation centers in Denmark, Sweden, Norway and Finland since 1982. Before 1990, only patients that were transplanted were 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 securely at Scandiatransplant in Århus (www.scandiatransplant.org).

Up to December 31st 2016, data from a total of 7227 patients had been entered into NLTR. Of these, 6280 patients had received a first liver graft, 635 (10.1%) had been transplanted more than once, and 94 (1.5%) had been transplanted more than twice. A total of 168 living donor transplantations had been performed. Children below 16 years constituted 642 (10.2%) of the transplanted patients in the registry.

3. Transplantation activity 2016

The total number of patients who received a first liver graft in 2016 was 367 (Figure 1). Of these, 10 were combined liver-kidney transplantations. Of the first liver transplantations in 2016 2 were living donor transplantations and none were domino transplantations.

One of the living donor transplantation was performed in Stockholm and one in Gothenburg. In addition, 52 re-transplantations were performed (Table 2). The total number of 419 liver transplantations represents a new record in the Nordic countries. The relative number of re-transplantations has remained stable in the recent years (Figure 1).

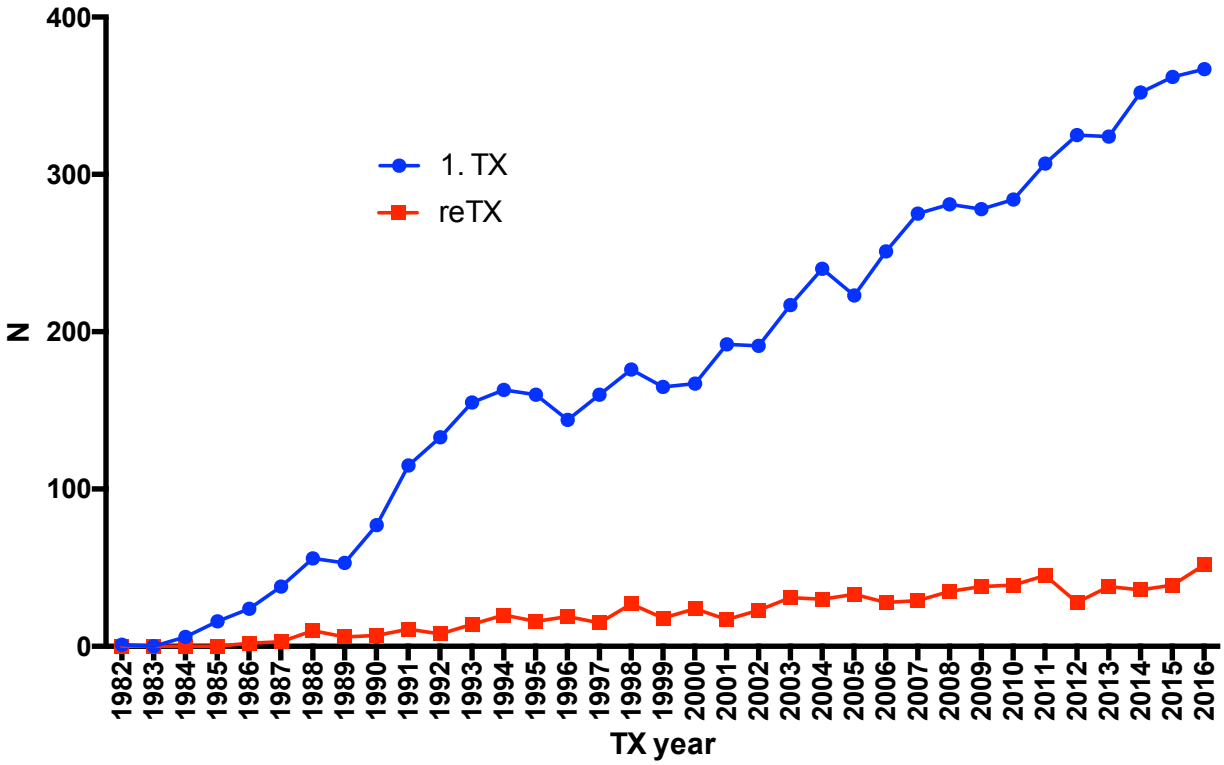

Figure 1. Number of patients receiving a liver allograft 1982-2016. The blue line represents the number of patients receiving a first liver graft while the red line represents the total number of re-transplantations.

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Copenhagen	37	43	37	43	42	44	39	41	55	51
Gothenburg	64	66	78	61	67	75	72	89	86	88
Helsinki	50	42	42	47	52	48	44	56	70	54
Oslo	64	69	69	77	81	89	96	89	72	88
Stockholm	50	52	43	53	65	69	73	77	79	86
Uppsala	8	11	10	3	0	0	0	0	0	0

Table 1. Number of first liver transplantations performed at the individual centers during the last 10 years.

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Copenhagen	5	1	3	4	9	4	3	6	3	9*
Gothenburg	11	10	11	19	16	4	9	8	7	12
Helsinki	3	5	6	3	4	4	5	3	7	6
Oslo	8	10	13	12	8	11	14	11	12	11
Stockholm	2	6	3	1	8	5	7	8	6*	7
Uppsala	1	2	1	0	0	0	0	0	0	0

Table 2. Total number of re-transplantations performed at the individual centers during the last 10 years. * = 1 pts in 2015 and one in 2016 received their first graft outside SCTP

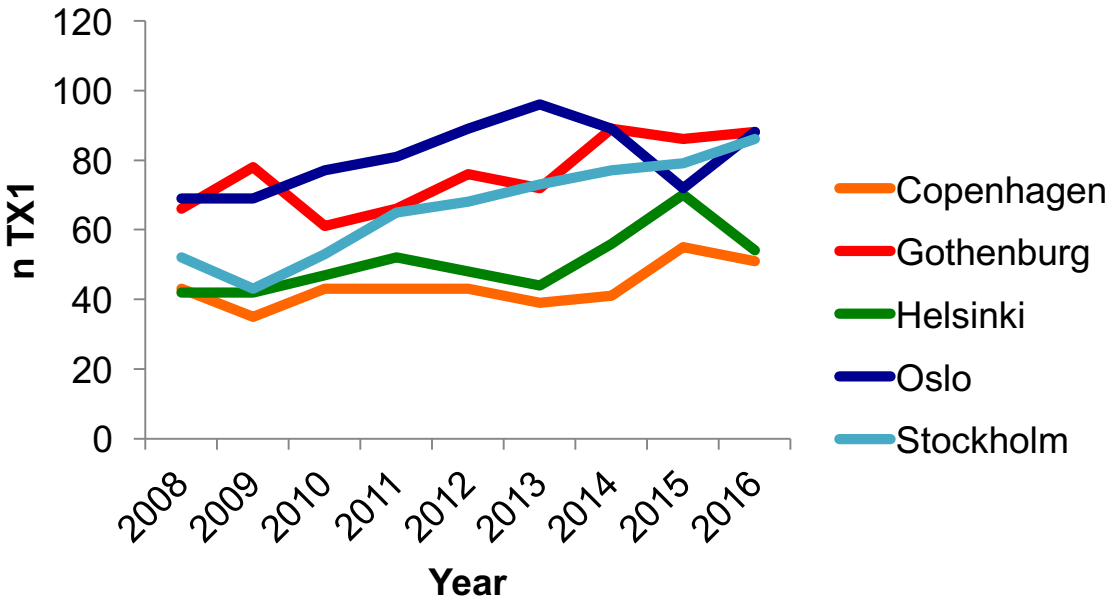

Figure 2. Number of first liver transplantations performed at Nordic centers that are currently performing liver transplantations.

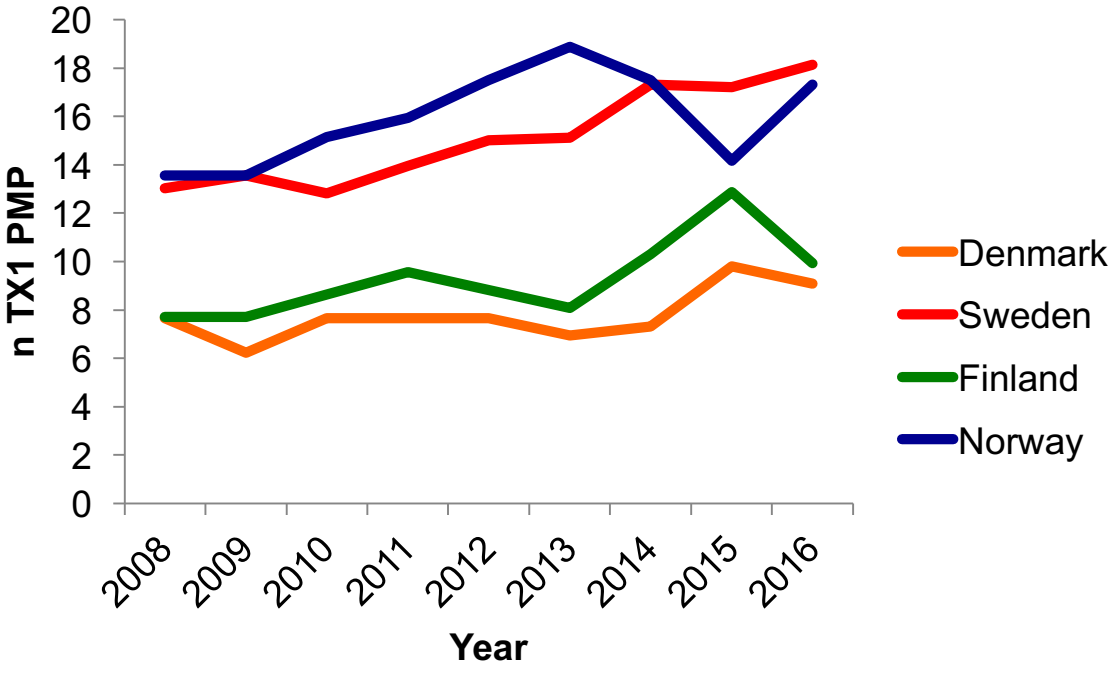

Figure 3. Number of first liver transplantations performed in the Nordic countries according to the country's population. PMP, per million population.

4. The waiting list 2016

In 2016, a total of 407 patients were entered on the waiting list for a first liver transplant (Table 3), this is an increase from the 381 entered in 2015 (Figure 4). Twenty-nine of the patients entered in 2016 were listed as highly urgent.

Active on waiting list	Deceased donor	Living donor	Dead	Permanent withdrawal
79	291	2	12	23

Table 3. *Patients entering the waiting list in 2016 classified by outcome as of December 31st 2016.*

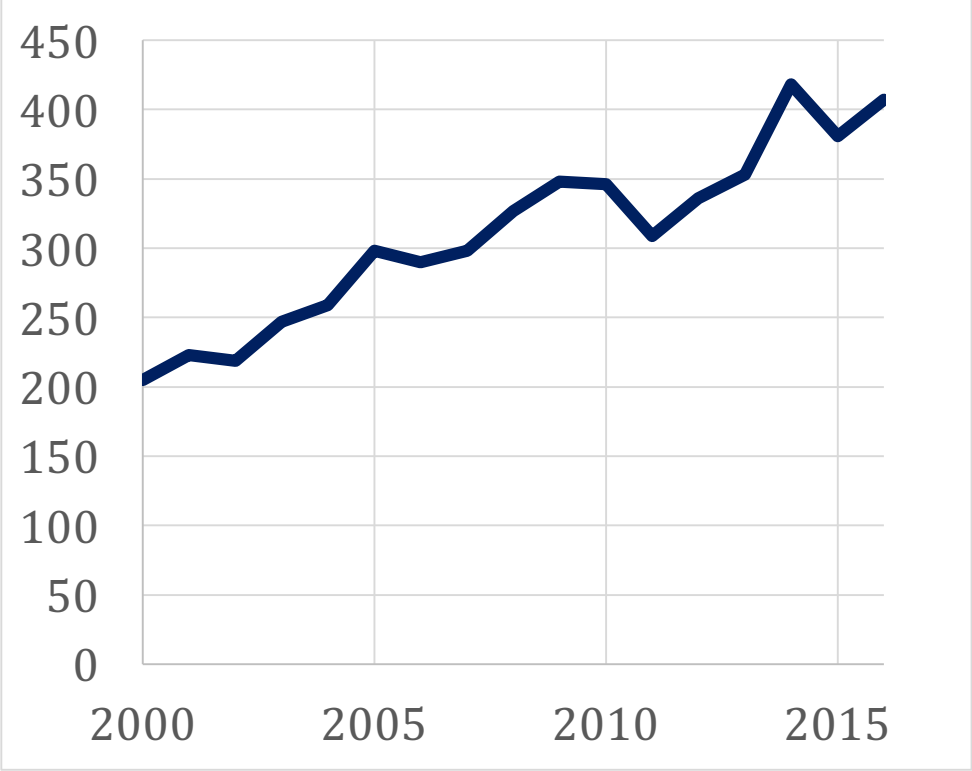

Figure 4. *Number of patients entering the waiting list from 2000-2016.*

The number of deaths among patients waiting for a first liver transplant in 2016 was 12 (Denmark 0, Sweden 3, Finland 2, Norway 7). The absolute number of deaths registered on the waiting list has remained stable since 1990 (Figure 5). When the deaths on the waiting list are evaluated in relation to the total liver transplantation activity it has remained stably low the last years (Figure 6).

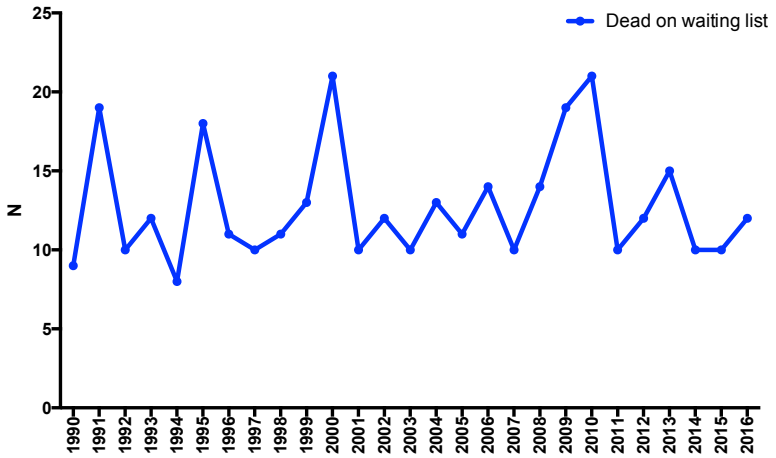

Figure 5. Number of patients registered as dead on the waiting list in the period 1990-2016.

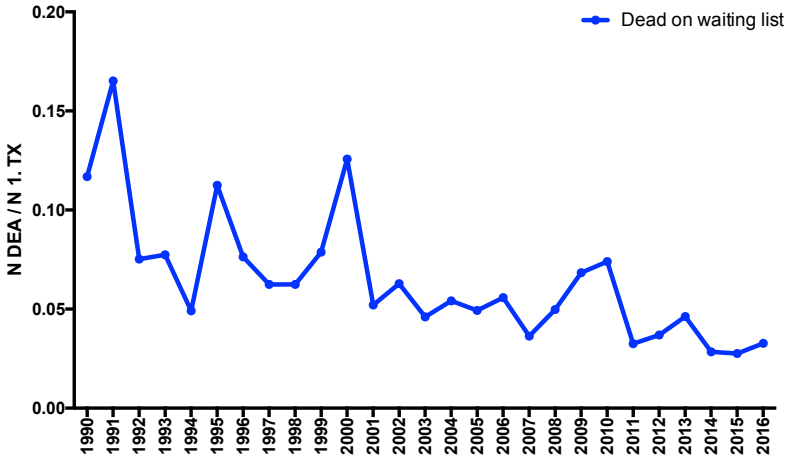

Figure 6. Number of patients registered as dead on the waiting list relative to the total transplantation activity in the period 1990-2016.

The median waiting time in 2016 was 39 days when excluding patients listed for a highly urgent liver transplantation. The differences according to different ABO blood types were as expected (Table 4) with largely similar numbers since 2000 (Figure 7).

0	A	AB	B
101 (1028)	26 (749)	14 (141)	63 (421)

Table 4. Median time on waiting list (days) for patients receiving a first liver allograft in 2016 according to ABO blood type. The number in parenthesis represents the maximum waiting time for the indicated blood type in 2016. (Patients listed as highly urgent are excluded from the calculations.)

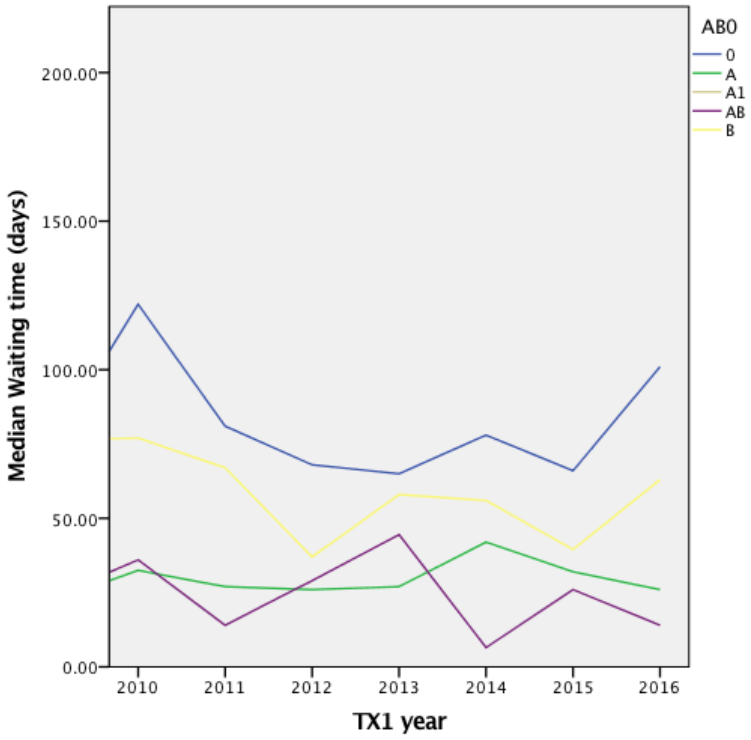

Figure 7. Median waiting time for first liver transplantation according to ABO blood type for 2010-2016. (Patients listed as highly urgent are excluded from the calculations.)

Finland had the lowest waiting time in 2016 while there were only slight differences between the other centers (Table 5). These figures are on the same level as the previous three years (Figure 8).

Copenhagen	Gothenburg	Helsinki	Oslo	Stockholm
43 (1028)	51 (607)	16.5 (287)	41 (612)	44 (482)

Table 5. Median time on waiting list (days) for patients receiving a first liver allograft in 2016 according to transplantation center. The number in parenthesis represents the maximum waiting time for the indicated center in 2016. (Patients listed as highly urgent are excluded from the calculations.)

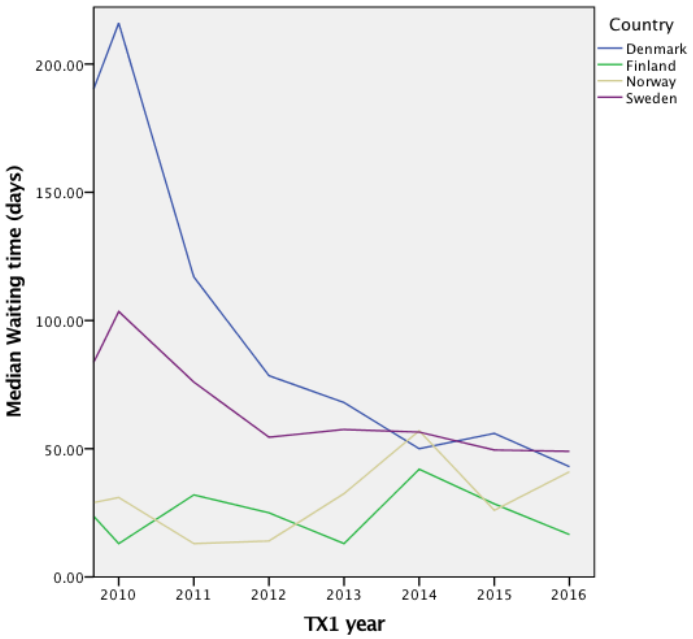

Figure 8. Median waiting time for first liver transplantation according to country for 2000-2016. (Patients listed as highly urgent are excluded from the calculations.)

5. Age of recipients and donors

The mean age of adult liver recipients (≥16 years, first liver transplantation) in 2016 was 52.5 years. Mean age of children (<16 years, first liver transplantation) in 2016 was 5.2 years. Since 1990 the proportion of recipients >60 years of age at the first transplantation has gradually increased (Figure 9). The mean age of the donors has increased since 1990 with a similar trend in all the Nordic countries (Figure 10).

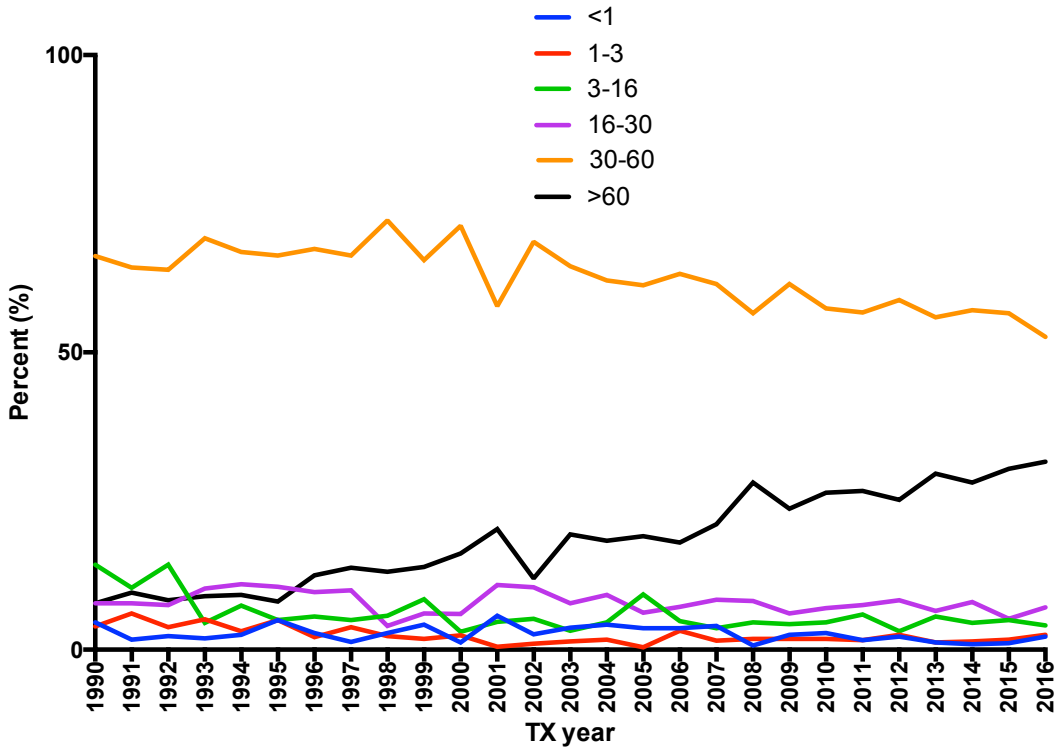

Figure 9. Proportion of liver transplants in the indicated age groups.

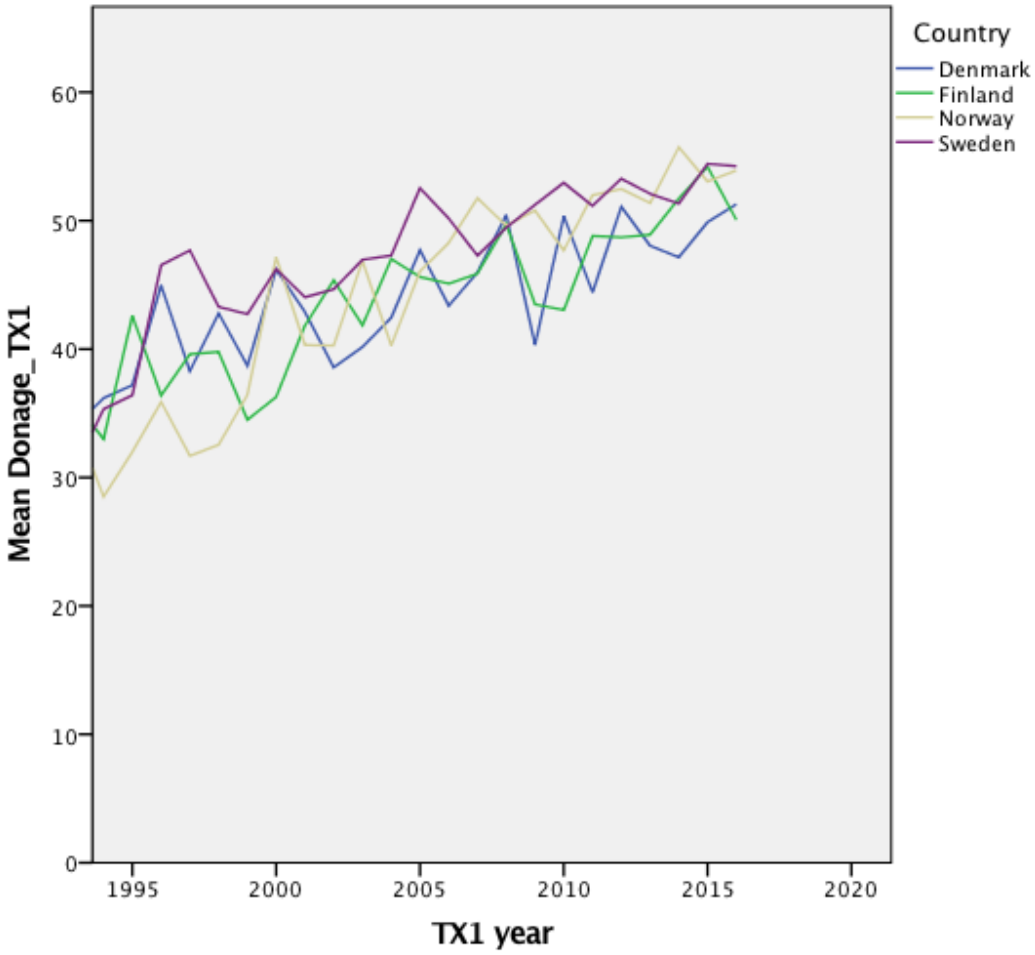

Figure 10. Mean age of donors utilized in the indicated years stratified for the different Nordic countries.

6. Diagnoses

In 2016, primary sclerosing cholangitis and hepatocellular carcinoma were the leading indications for liver transplantation in the Nordic countries (Table 6). Of the patients listed for transplantation with a primary diagnosis of hepatocellular carcinoma (HCC) in 2016 43% were also anti-HCV positive.

	1982-90	1991-96	1997-01	2002-06	2007-11	2012-16	2016
Primary sclerosing cholangitis	10.9%	12.9%	15.5%	14.9%	17.1%	16.3%	17.9%
Hepatocellular carcinoma and cirrhosis	10.9%	4.4%	6.4%	7.4%	11.4%	16.7%	13.5%
Alcoholic cirrhosis	1.9%	8.5%	12.1%	12.6%	11.4%	11.5%	11.3%
Metabolic disease	9.7%	7.4%	6.0%	5.2%	6.9%	7.8%	9.8%
Acute liver failure – other	8.4%	10.1%	8.0%	6.5%	5.5%	5.4%	6.9%
Cirrhosis – unknown	0.6%	3.1%	2.8%	2.4%	5.5%	6.9%	6.6%
Autoimmune cirrhosis	2.8%	4.0%	2.8%	4.3%	4.4%	4.9%	5.2%
Primary biliary cirrhosis	22.5%	13.6%	8.0%	7.4%	6.1%	5.2%	5.2%
Post hepatitis C cirrhosis		3.7%	8.2%	10.7%	9.6%	6.6%	3.4%
Acute liver failure – toxic	0.6%	2.8%	4.4%	4.0%	3.3%	2.9%	3.2%
Extrahepatic biliary atresia	6.9%	5.4%	4.5%	4.5%	2.2%	2.3%	2.7%
Polycystic disease	0.3%	1.2%	0.9%	1.4%	1.4%	2.0%	2.2%
Secondary liver tumors	0.9%	0.5%	0.7%	0.8%	2.3%	1.8%	1.7%
Acute liver failure – viral	1.3%	2.5%	2.2%	0.5%	1.8%	1.1%	1.0%
Cholangiocarcinoma	1.6%	0.9%	0.8%	0.7%	0.7%	0.3%	1.0%
Other liver malignancies	2.5%	2.3%	1.8%	1.4%	1.1%	1.4%	1.0%
Biliary tract carcinoma				0.2%	0.9%	0.5%	0.7%
Congenital disease	1.3%	1.1%	1.1%	0.7%	1.0%	0.8%	0.7%
Post hepatitis D cirrhosis					0.4%	0.6%	0.7%
Post hepatitis B cirrhosis	0.9%	2.6%	3.4%	2.9%	1.4%	1.1%	0.5%
Secondary biliary cirrhosis	0.9%	0.5%	0.2%	0.2%	0.3%	0.4%	0.5%
Others	15.2%	12.7%	10.4%	11.5%	5.4%	3.7%	4.0%

Table 6. *Diagnoses of patients listed for a first liver transplantation in 2016 compared with previous years. In 2016 43% of HCC patients listed for a first liver transplantation were anti-HCV positive.*

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 10 and 11). It is now evident that there is a further increase in the observed survival also in the most recent 5-year period. There are notable differences in the long-term patient and graft survival for different indications for transplantation (Figures 12, 13 and Table 7).

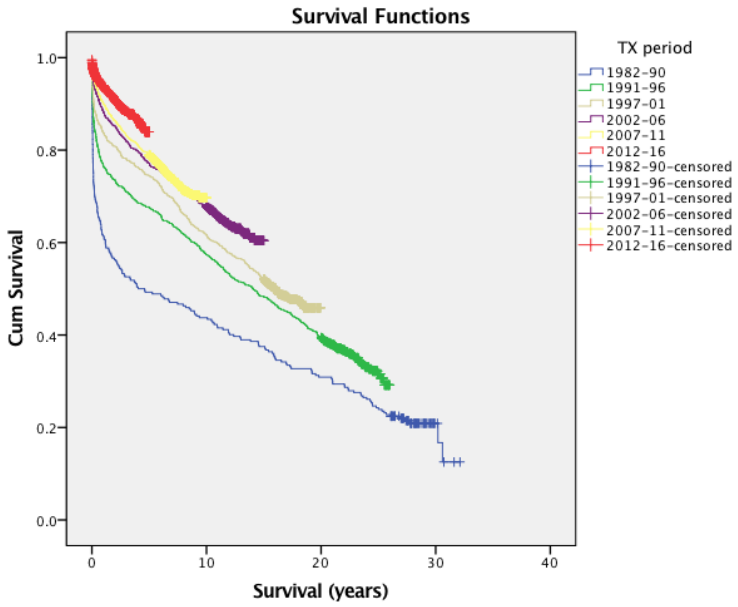

Figure 10. Kaplan-Meier patient survival curve for patients receiving a first liver allograft in the indicated time periods.

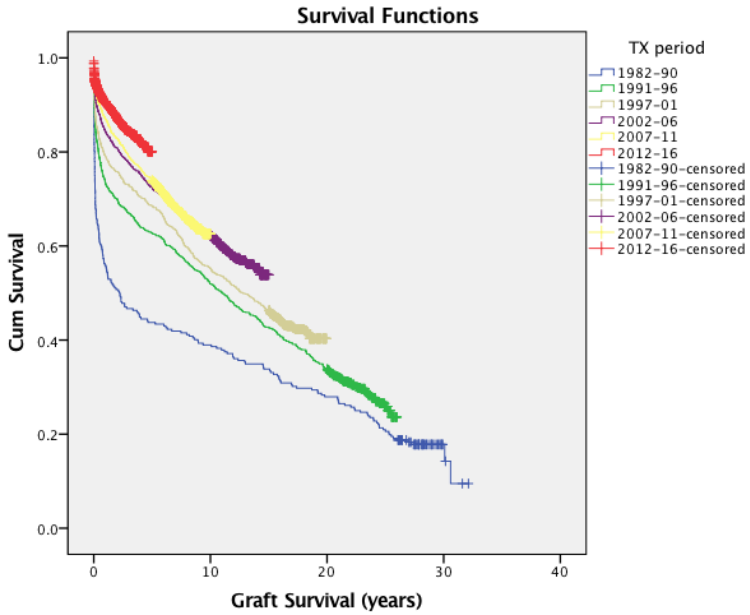

Figure 11. Kaplan-Meier graft survival curve for patients receiving a first liver allograft in the indicated time periods.

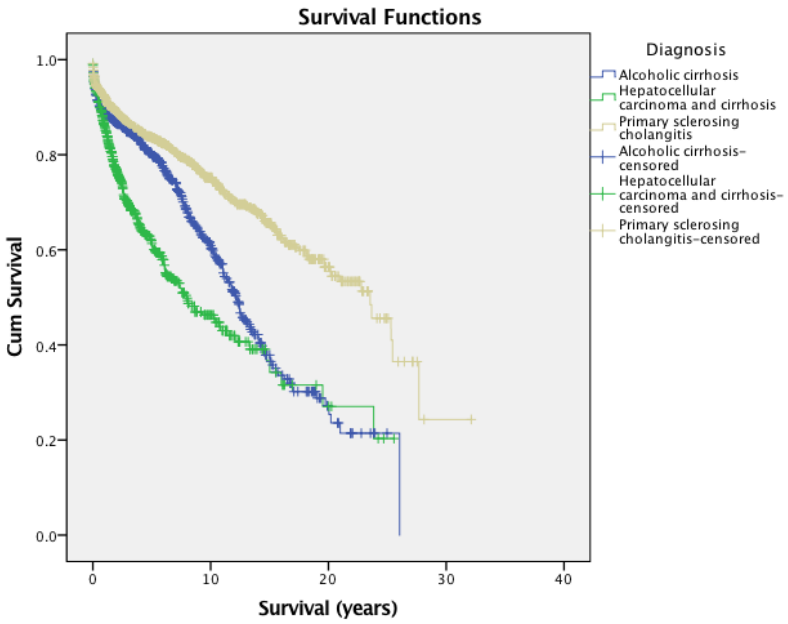

Figure 12. Kaplan-Meier patient survival curve for patients receiving a first liver allograft stratified for the three most common primary diagnoses.

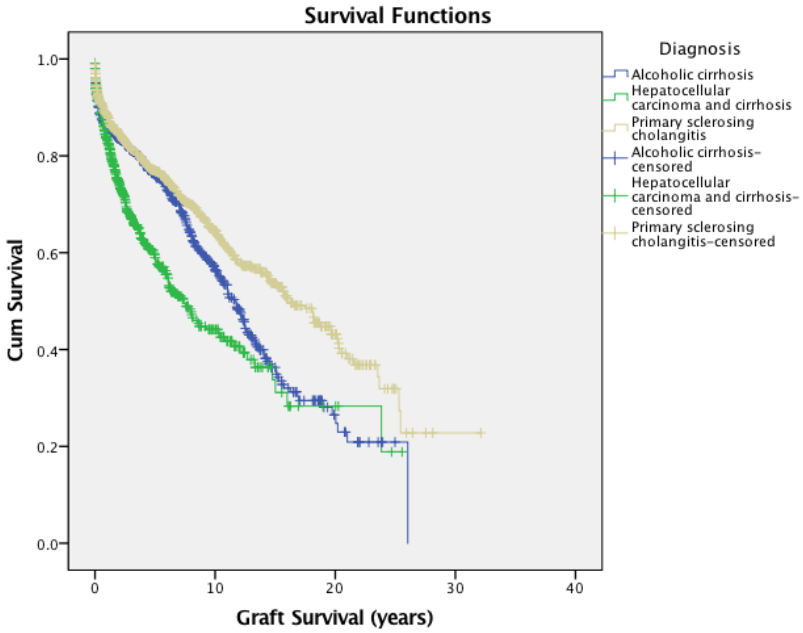

Figure 13. Kaplan-Meier graft survival curve for patients receiving a first liver allograft stratified for the three most common primary diagnoses.

	1990-2004			2005->		
	Median age	**1-year survival (%)**	**5-year survival (%)**	**Median age**	**1-year survival (%)**	**5-year survival (%)**
Primary sclerosing cholangitis	45.4	86 %	78 %	43.3	97 %	89 %
Hepatocellular carcinoma	54.9	72 %	45 %	59.4	93 %	70 %
Alcoholic cirrhosis	52.1	82 %	74 %	57.4	93 %	85 %
Listed as highly urgent	41.7	79 %	69 %	43.0	83 %	78 %

Table 7. *Survival for the patients listed for the three most common diagnoses and those listed as highly urgent divided in two age periods.*

8. Maintenance of the registry

There are differences between each center in terms of how extensively data are entered into the NLTR. Diagnosis information, waiting list/transplantation status and survival data for all patients are now complete for 2016. I am extremely grateful for the meticulous follow-up provided by the transplant coordinators upon my requests during quality control. In Oslo, I particularly want to thank Stein Foss, in Gothenburg Christina Wibeck and Ulla Nyström, in Stockholm Marie Tranäng, in Copenhagen Mette Gottlieb and in Helsinki, Helena Isoniemi is overseeing the maintance of the registry. 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.

9. Acknowledgements - financial support

The NLTR received no financial support in 2016. The maintenance of the Oracle system has been performed by Scandiatransplant. We are extremely grateful for the help and support from Frank Pedersen 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.

10. Organization 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. Utilization 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.

11. Publications based on the NLTR

Full length articles 1990-2016:

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

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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.

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