

The Nordic Liver Transplant Registry (NLTR)

Annual report 2021

Report prepared by Espen Melum May 2022

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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 March 2022. 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 at all centers prior to the final data extraction.

2. Data content NLTR 2021

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. From October 1st 2017 data on patients transplanted in Estonia are prospectively included, patients transplanted in Estonia prior to this date have been retrospectively included. All data are stored securely at Scandiatransplant in Århus (www.scandiatransplant.org).

Up to December 31st 2021, data from a total of 9293 patients had been entered into NLTR. Of these, 8144 patients had received a first liver graft, 843 (10.4%) had been transplanted more than once, and 122 (1.5%) had been transplanted more than twice. Of the 843 patients receiving a second liver graft, 8 had received their first graft outside of the Scandiatransplant area. A total of 210 living donor transplantations had been performed. Children below 18 years constituted 867 (10.6%) of the transplanted patients in the registry.

3. Transplantation activity 2021

The total number of patients who received a first liver graft in 2021 was 347 (Figure 1). Of these, 17 were combined liver-kidney transplantations. Of the first liver transplantations performed in 2021 three were living donor transplantations and none was a domino transplantation. The three living donor transplantations were performed in Copenhagen, Oslo and Gothenburg. Seven patients received a DCD graft. In addition, 49 re-transplantations were performed (Table 2). The total number of liver transplantations was 396, which is a slight decrease compared to the 413 transplants performed in 2020 and it can be speculated that this might be due to the pandemic.

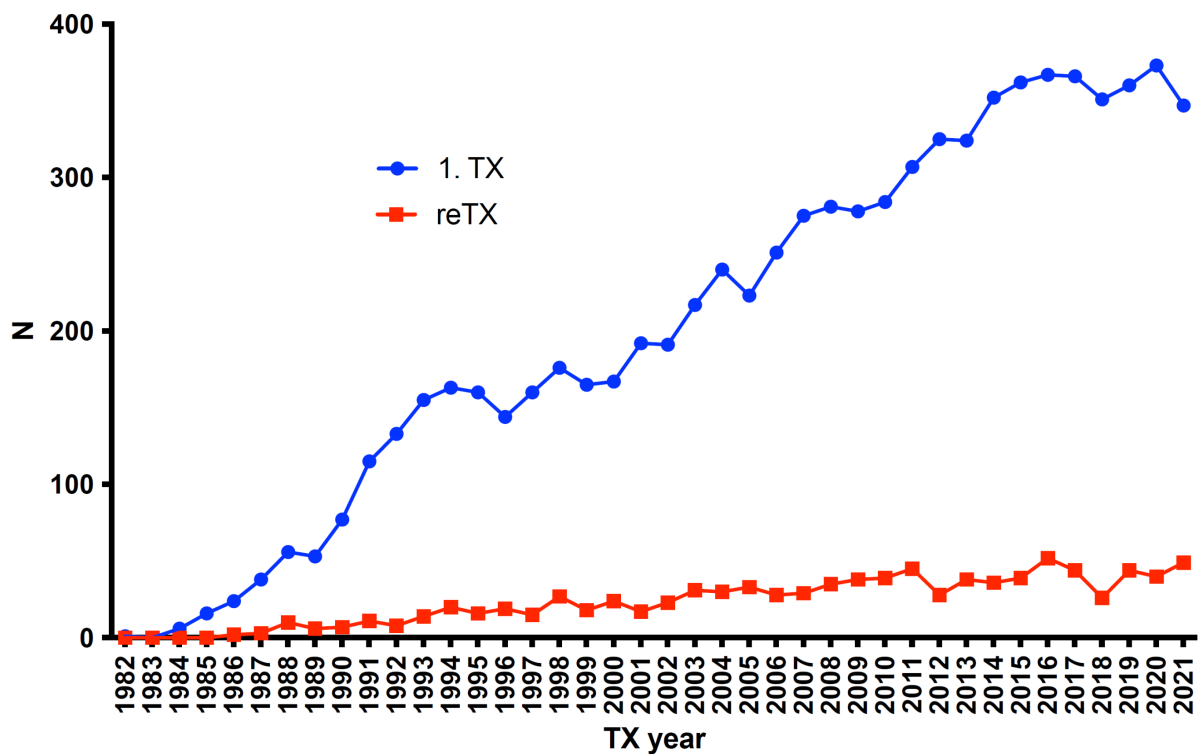


Figure 1. Number of patients receiving a liver allograft 1982-2021. The blue line represents the number of patients receiving a first liver graft while the red line represents the total number of re-transplantations.

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Copenhagen	43	39	41	55	51	52	39	61	59	45
Gothenburg	76	72	89	86	88	84	83	80	72	87
Helsinki	48	44	56	70	54	57	60	56	71	65
Oslo	89	96	89	72	88	85	87	75	76	83
Stockholm	68	73	77	79	86	82	73	78	84	63
Tartu					0	6	9	10	11	4

Table 1. Number of first liver transplantations performed at the individual centers during the last 10 years. *Data from Tartu are only included from the time Estonia joined Scandiatransplant

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Copenhagen	4	3	6	3	9*	5	4	3	7	5
Gothenburg	4	9	8	8	17	10	3	15	8	11*
Helsinki	4	5	3	7	7	6	6	9	4	10
Oslo	11	14	11	14	12	17	8	19	12***	15
Stockholm	5	7	8	8*	7	5	4	9	8	8
Tartu**						0	1	0	1	0

Table 2. Total number of re-transplantations performed at the individual centers during the last 10 years. * = 1 pts in 2015, 2016 and 2021 received their first graft outside SCTP **Data from Tartu are only included from the time Estonia joined Scandiatransplant. ***One patient retransplanted in Oslo received his first graft in Stockholm

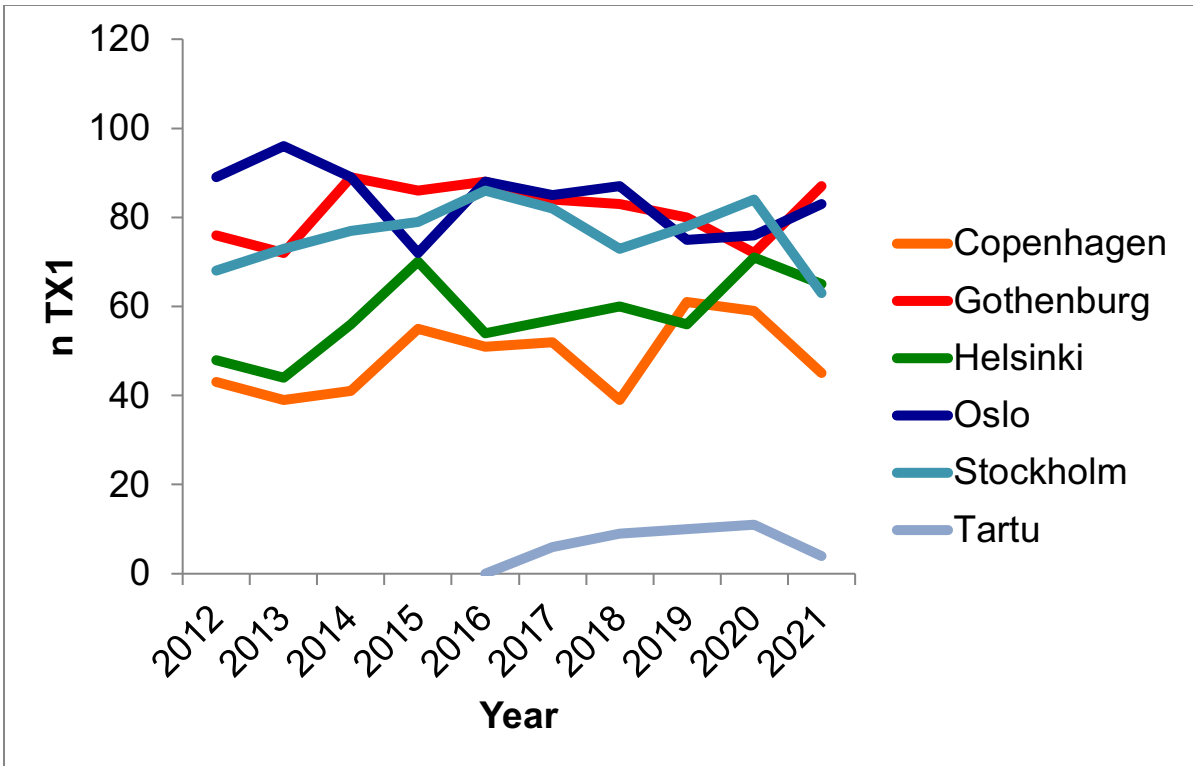


Figure 2. Number of first liver transplantations performed at the Nordic and Estonian centers that are currently performing liver transplantations.

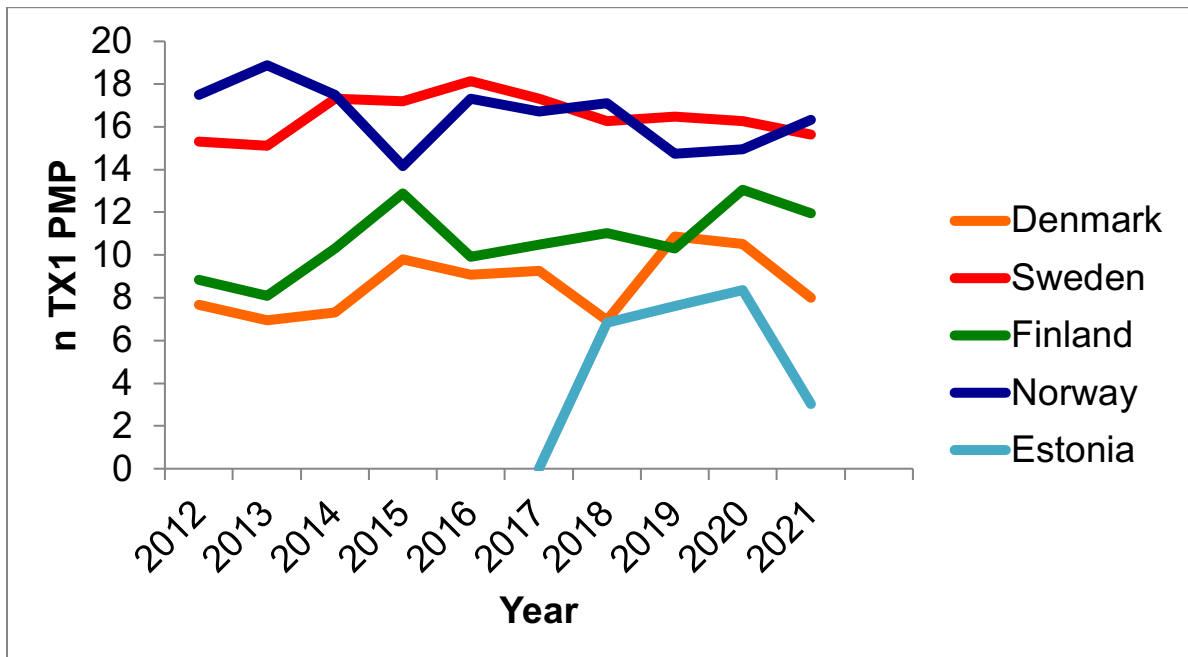


Figure 3. Number of first liver transplantations performed in the ScandiTransplant countries according to the country's population. PMP, per million population.

4. The waiting list 2021

In 2021, a total of 395 patients were entered on the waiting list for a first liver transplant (Table 3), this is a decrease from the 422 entered in 2020 (Figure 4). Sixteen of the patients listed for a first liver transplant in 2021 were listed as highly urgent. This is in line with 2020, but a marked decrease compared to previous years.

Active on waiting list	Deceased donor	Living donor	Dead	Permanent withdrawal
107	254	3	11	20

Table 3. Patients entering the waiting list in 2021 classified by outcome as of December 31st 2021.

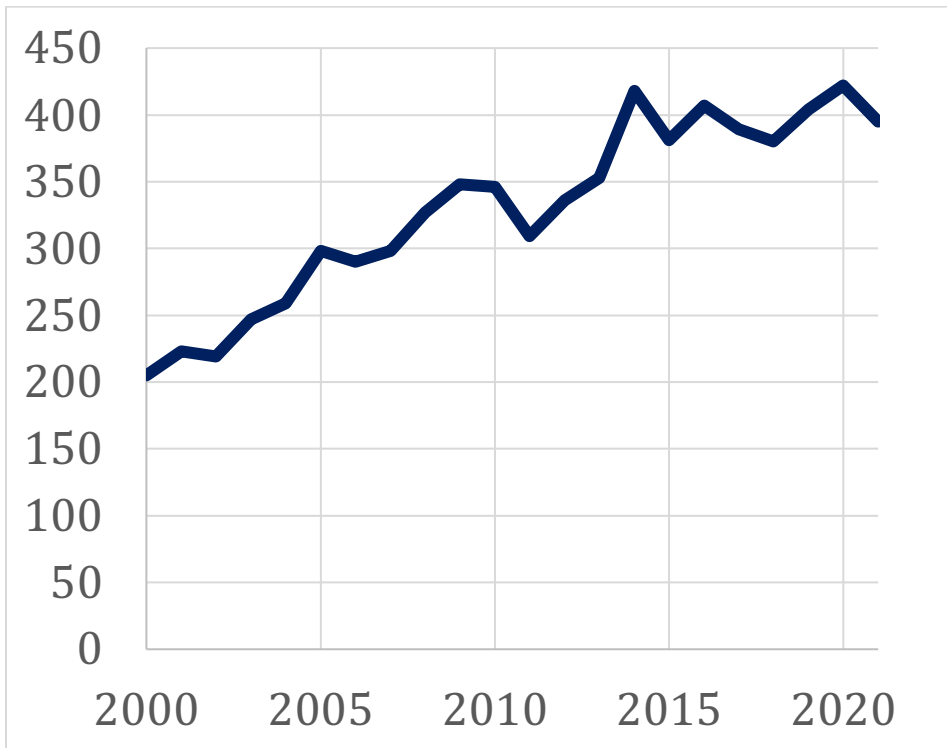


Figure 4. Number of patients entering the waiting list from 2000-2021.

The number of deaths among patients listed in 2021 for a first liver transplant was 9 (Denmark 1, Sweden 1, Finland 2, Norway 6 and Estonia 1). 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 the relative number of deaths on the waiting list remains low (Figure 6).

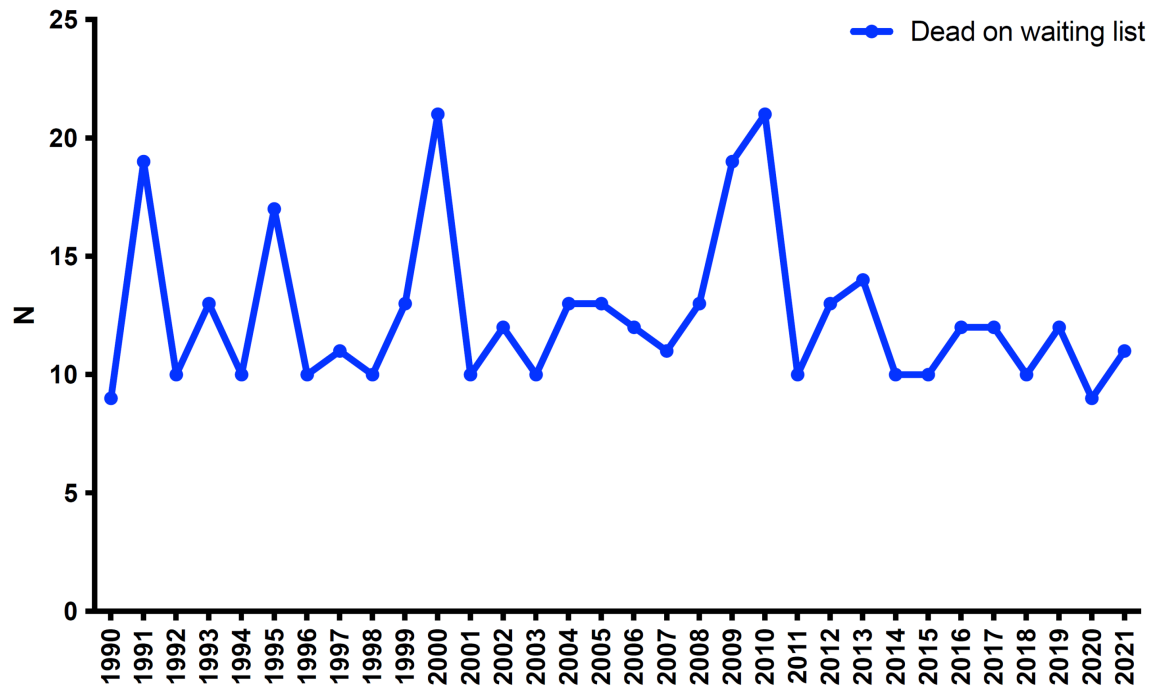


Figure 5. Number of patients registered as dead on the waiting list in the period 1990-2021.

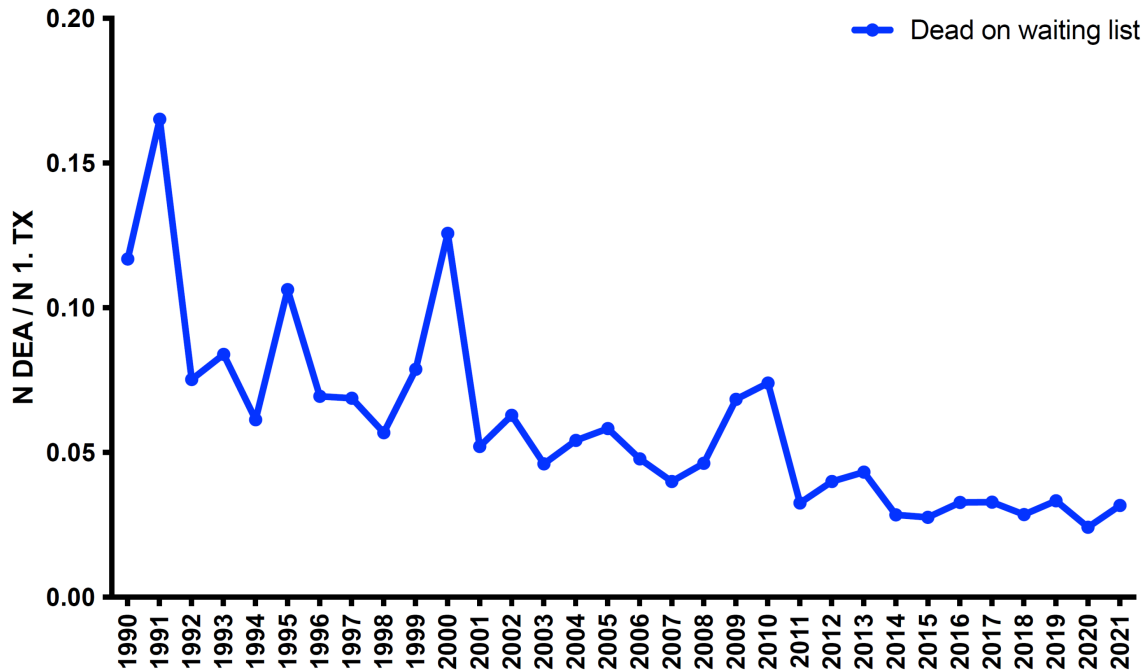


Figure 6. Number of patients registered as dead on the waiting list relative to the total transplantation activity in the period 1990-2021.

The median waiting time in 2021 was 49 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 2012 (Figure 7).

O	A	AB	B
77 (808)	39 (457)	23 (302)	36 (450)

Table 4. Median time on waiting list (days) for patients receiving a first liver allograft in 2021 according to ABO blood type. The number in parenthesis represents the maximum waiting time for the indicated blood type in 2021. (Patients listed as highly urgent are excluded from the calculations).

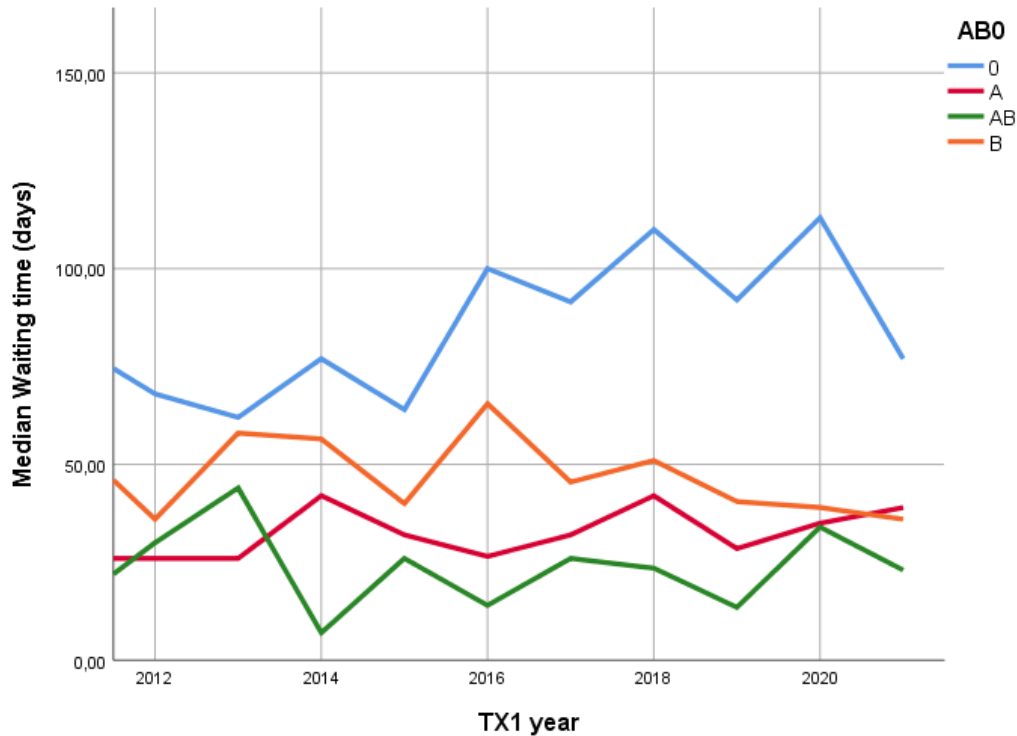


Figure 7. Median waiting time for first liver transplantation according to ABO blood type for 2010-2021. (Patients listed as highly urgent are excluded from the calculations.)

Helsinki had the lowest and Tartu the longest waiting time in 2021 (Table 5). The waiting times in 2021 saw a clear decline in Finland and a clear increase in Estonia while Norway, Sweden and Denmark were large unchanged compared to 2020 (Figure 8). Nevertheless, the waiting times remain remarkably low compared to other programs.

Copenhagen	Gothenburg	Helsinki	Oslo	Stockholm	Tartu
55 (640)	56 (808)	24 (164)	52 (729)	66 (494)	133.5 (450)

Table 5. Median time on waiting list (days) for patients receiving a first liver allograft in 2021 according to transplantation center. The number in parenthesis represents the maximum waiting time for the indicated center in 2021. (Patients listed as highly urgent are excluded from the calculations.)

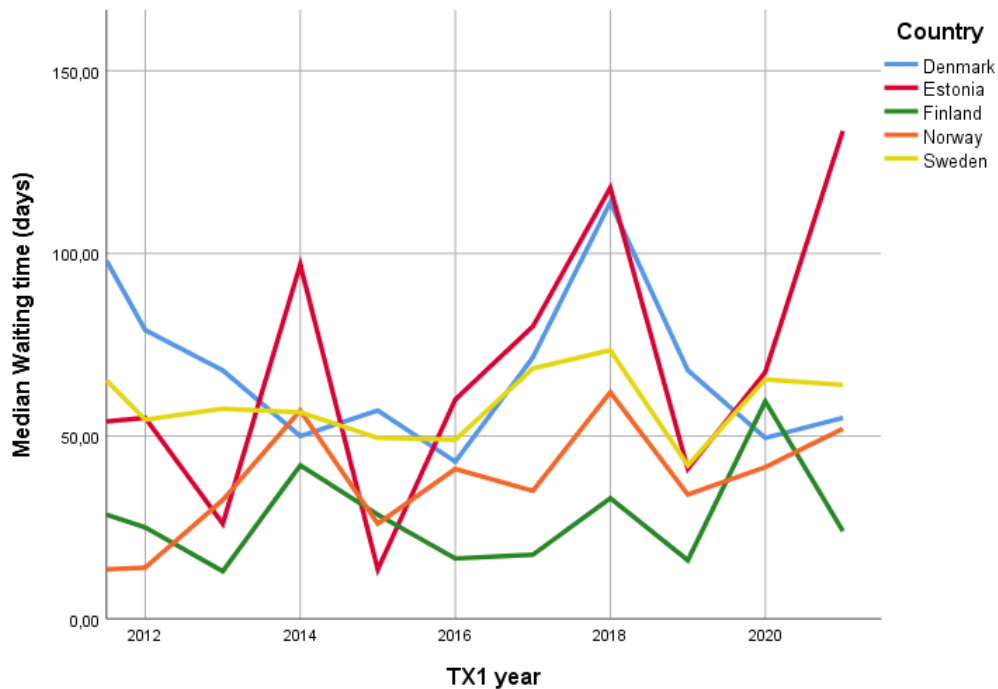


Figure 8. Median waiting time for first liver transplantation according to country for 2010-2021. (Patients listed as highly urgent are excluded from the calculations.)

5. Age of recipients and donors

The mean age of adult liver recipients (>18 years, first liver transplantation) in 2021 was 54.6 years. Mean age of children (<18 years, first liver transplantation) in 2021 was 6.4 years. Since 1990 the proportion of recipients >60 years of age at the first transplantation has gradually increased with a further increase to 35.7% of the patients in 2021 being above 60 years of age (Figure 9). The mean age of the donors has remained stable since 2010 with a median age of 59.0 years in 2021 (Figure 10).

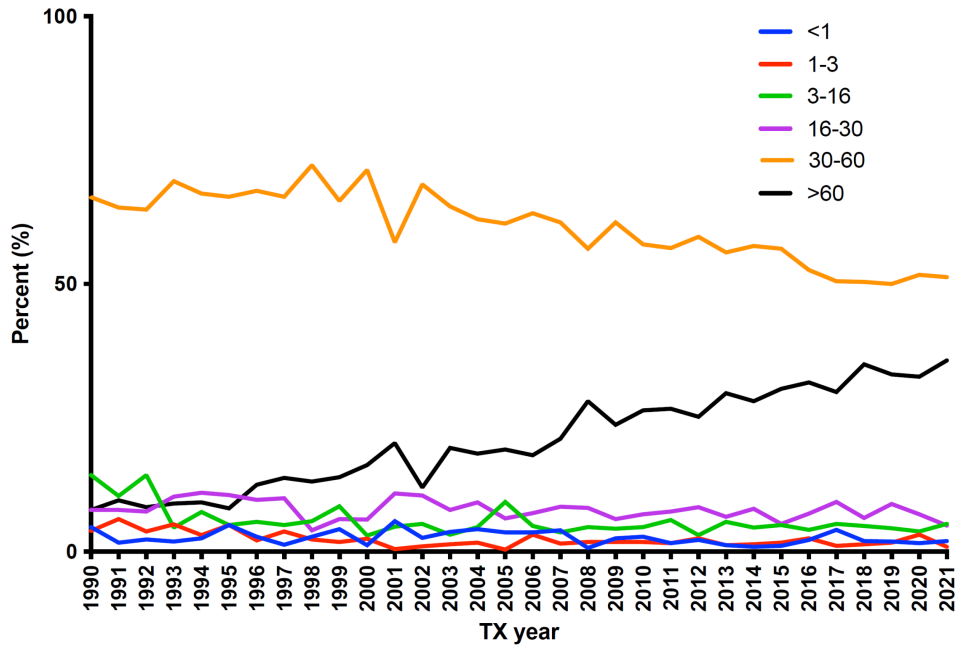


Figure 9. Proportion of liver transplants in the indicated age groups.

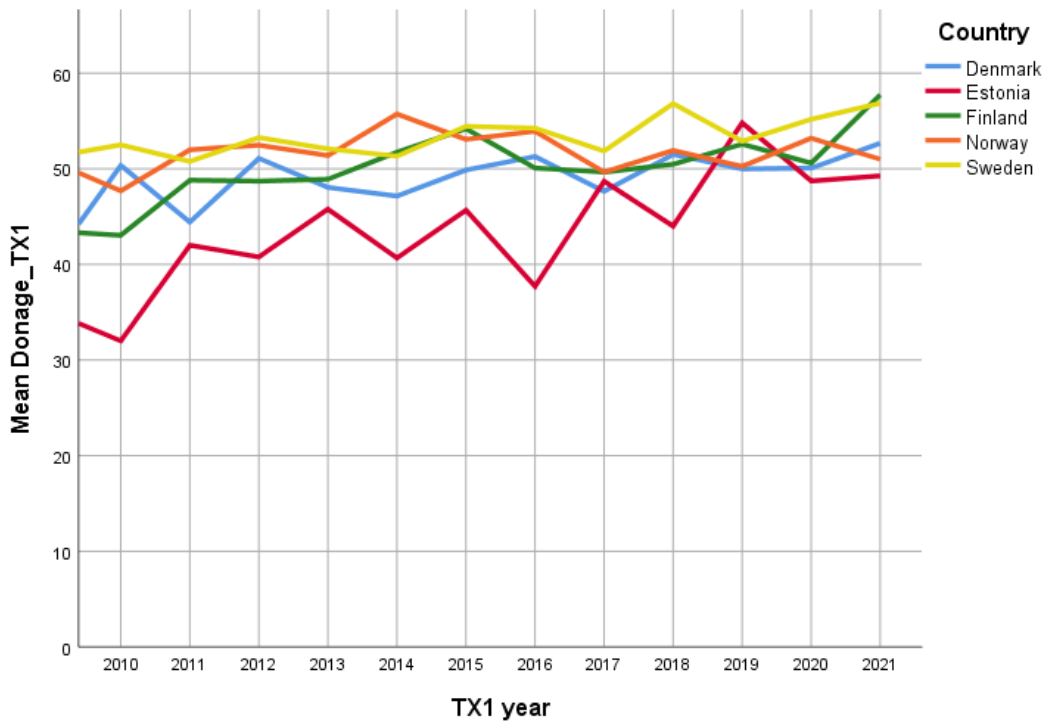


Figure 10. Mean age of donors utilized in the indicated years stratified for the different countries.

6. Diagnoses

In 2021, alcoholic cirrhosis was the leading indication for liver transplantation in Nordic countries (Table 6). Of the patients listed for transplantation with a primary diagnosis of hepatocellular carcinoma in 2021, 22 % were also anti-HCV positive. During the last 7 years the percentage of patients listed for transplantation with a diagnosis of HCV cirrhosis has dramatically declined (Figure 11). This decline coincides with the introduction of direct acting antiviral treatment and HCV cirrhosis has moved from being a major indication in our program to a rather rare indication.

	1982-90	1991-96	1997-01	2002-06	2007-11	2012-16	2017-21	2021
Alcoholic cirrhosis	1.9 %	8.4 %	12.2 %	12.6 %	11.3 %	11.4 %	15.0 %	16.2 %
Primary sclerosing cholangitis	11.1 %	12.9 %	15.6 %	14.6 %	17.3 %	16.1 %	16.4 %	15.2 %
Hepatocellular carcinoma and cirrhosis	10.8 %	4.4 %	6.4 %	7.8 %	11.3 %	16.8 %	15.2 %	12.9 %
Metabolic disease	9.3 %	7.5 %	5.9 %	5.7 %	7.0 %	7.8 %	9.5 %	9.6 %
Cirrhosis - unknown	0.6 %	3.1 %	3.0 %	3.4 %	5.5 %	6.6 %	6.0 %	8.4 %
Acute liver failure - other	8.7 %	10.0 %	7.7 %	6.3 %	5.4 %	5.2 %	6.5 %	6.3 %
Polycystic disease	0.3 %	1.2 %	0.9 %	1.7 %	1.4 %	2.1 %	3.0 %	5.1 %
Autoimmune cirrhosis	2.8 %	4.1 %	2.8 %	4.4 %	4.4 %	4.7 %	4.4 %	3.8 %
Secondary liver tumors	0.9 %	0.5 %	0.8 %	0.8 %	2.2 %	1.8 %	2.2 %	3.5 %
Primary biliary cirrhosis	22.6 %	13.6 %	7.9 %	7.4 %	6.0 %	5.3 %	4.2 %	2.5 %
Post hepatitis C cirrhosis	0.0%	3.7 %	8.2 %	10.6 %	9.7 %	7.4 %	2.4 %	2.5 %
Acute liver failure - toxic	0.6 %	2.8 %	4.4 %	4.1 %	3.3 %	2.9 %	2.6 %	2.3 %
Extrahepatic biliary atresia	6.8 %	5.4 %	4.5 %	4.5 %	2.4 %	2.4 %	2.6 %	1.3 %
Other liver malignancies	2.5 %	2.3 %	1.8 %	1.5 %	1.2 %	1.3 %	1.0 %	1.3 %
Cholangiocarcinoma	1.5 %	0.9 %	0.8 %	0.7 %	0.6 %	0.2 %	0.7 %	1.0 %
Other	18.9 %	19.1 %	17.0 %	13.9 %	10.8 %	8.0 %	8.0 %	6.3 %

Table 6. Diagnoses of patients listed for a first liver transplantation in 2021 compared with previous years. In 2021 22% of HCC patients listed for a first liver transplantation were anti-HCV positive.

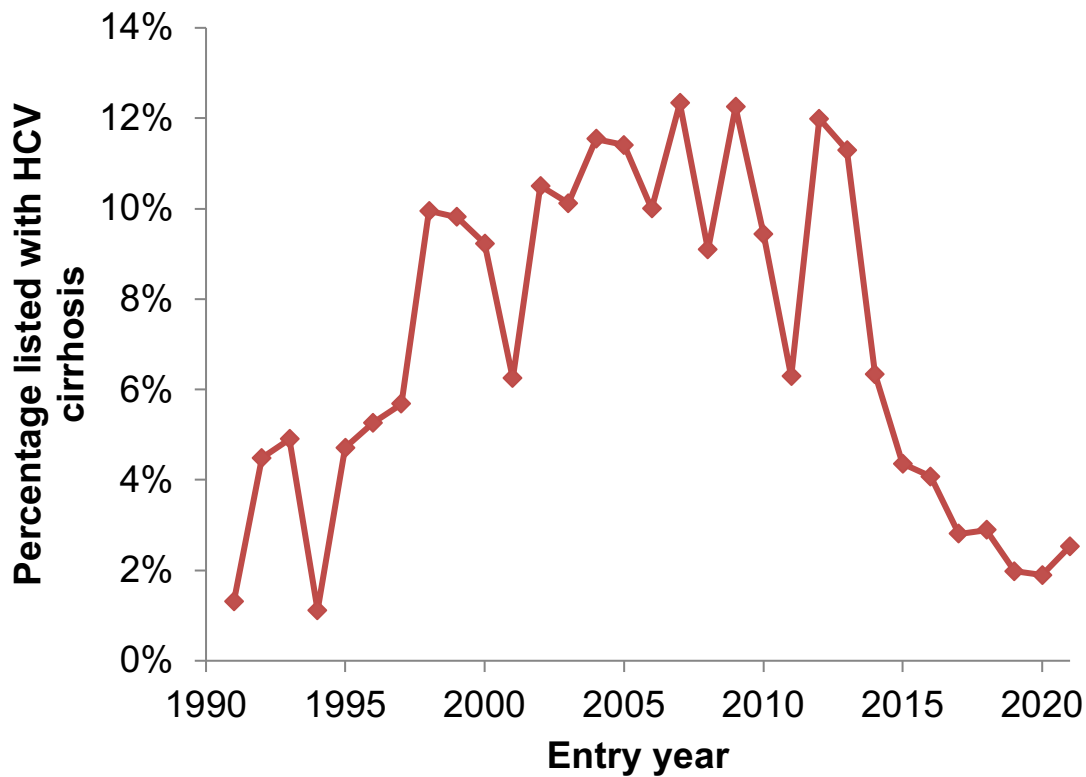


Figure 11. Percentage of patients listed with HCV cirrhosis from 1990-2021.

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 12 and 13). For the two last 5-year periods the survival is quite similar. There are notable differences in the long-term patient and graft survival for different indications for transplantation (Figures 14, 15 and Table 7). The survival following retransplantation is reduced compared to the primary transplantation, this is particularly evident during the first months after the transplantation (Figure 16). Similar to the survival

following the primary transplantation, the survival following retransplantation is markedly better in the recent time-periods compared to the start of the program. In an intention-to-treat analysis analysing survival from the listing for transplantation, the survival is lower but encompasses all events following listing and gives an indication of the performance of the program (Figure 17).

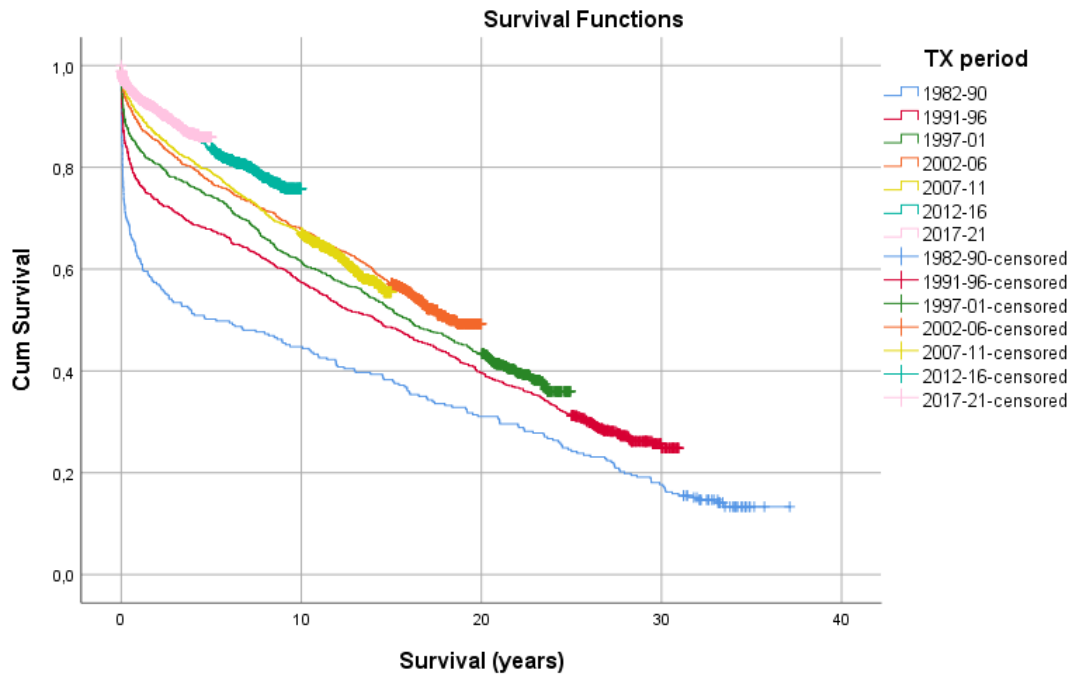


Figure 12. Kaplan-Meier patient survival curve for patients receiving a first liver allograft in the indicated time periods.

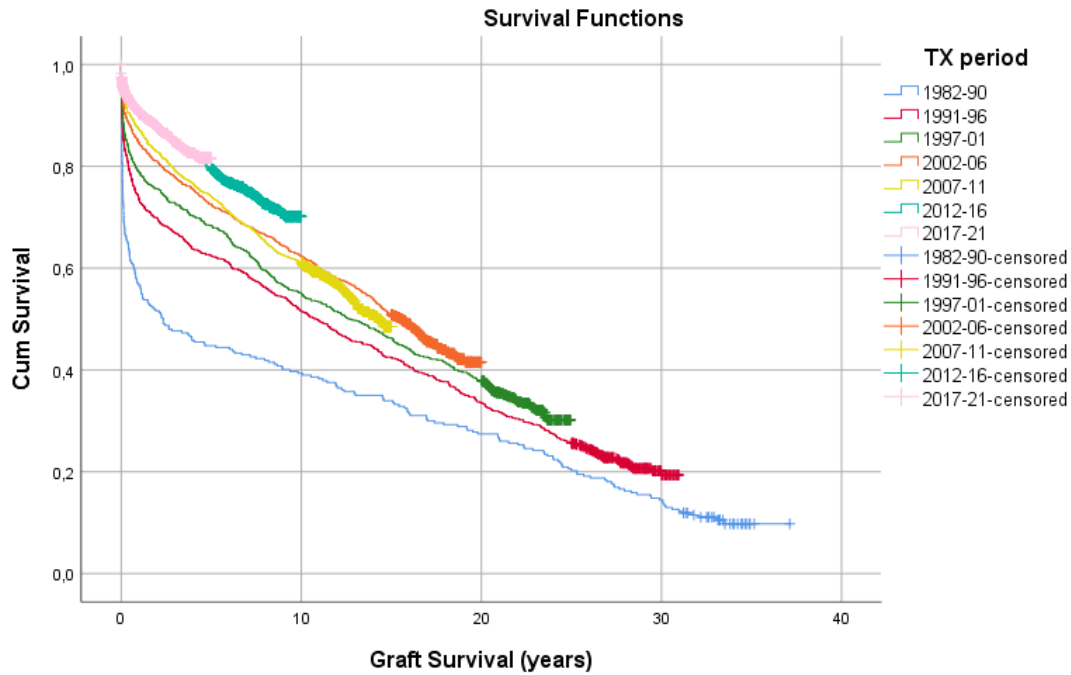


Figure 13. Kaplan-Meier graft survival curve for patients receiving a first liver allograft in the indicated time periods.

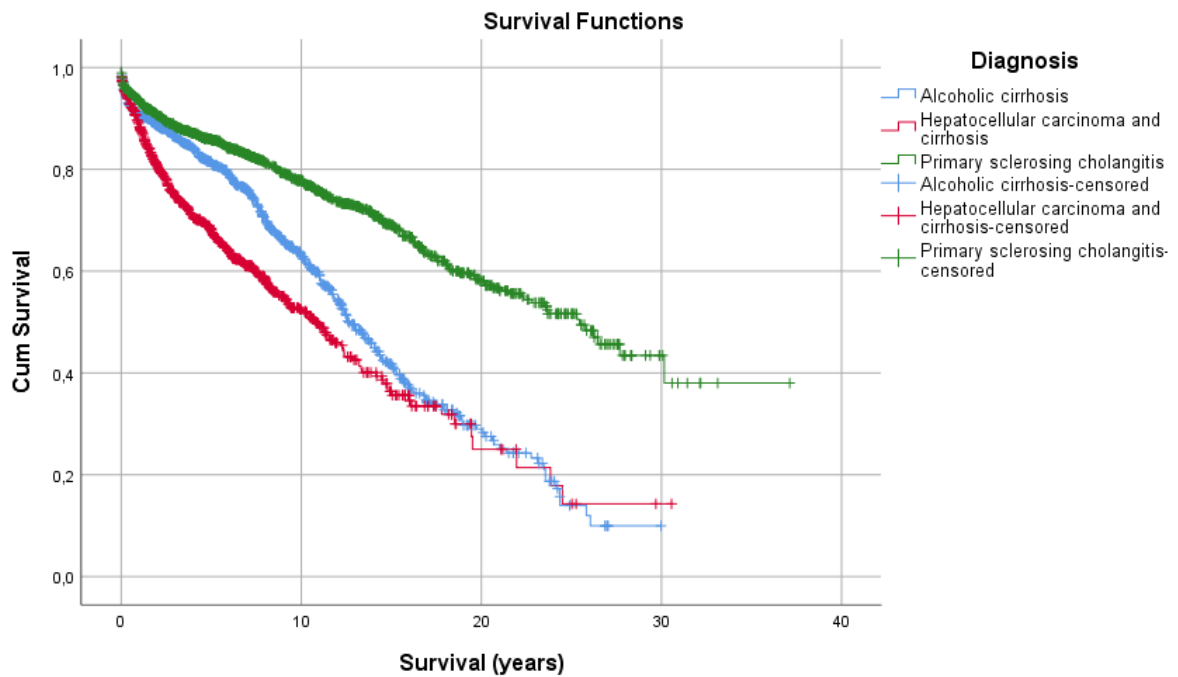


Figure 14. Kaplan-Meier patient survival curve for patients receiving a first liver allograft stratified for the three most common primary diagnoses.

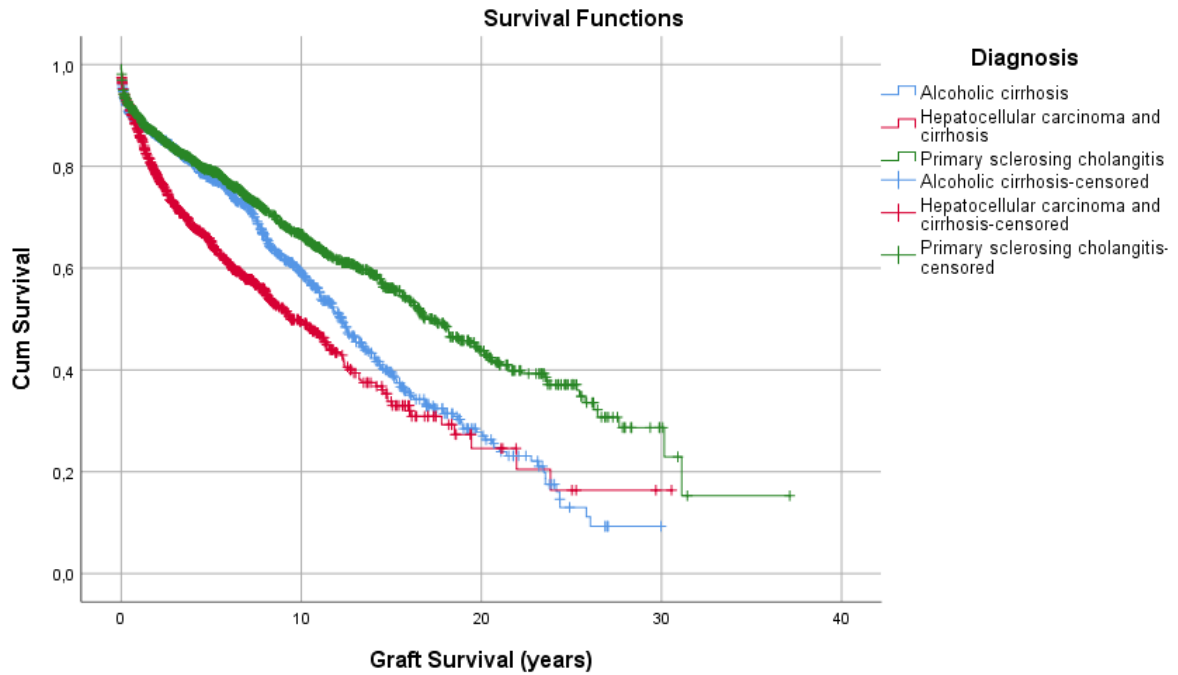


Figure 15. Kaplan-Meier graft survival curve for patients receiving a first liver allograft stratified for the three most common primary diagnoses.

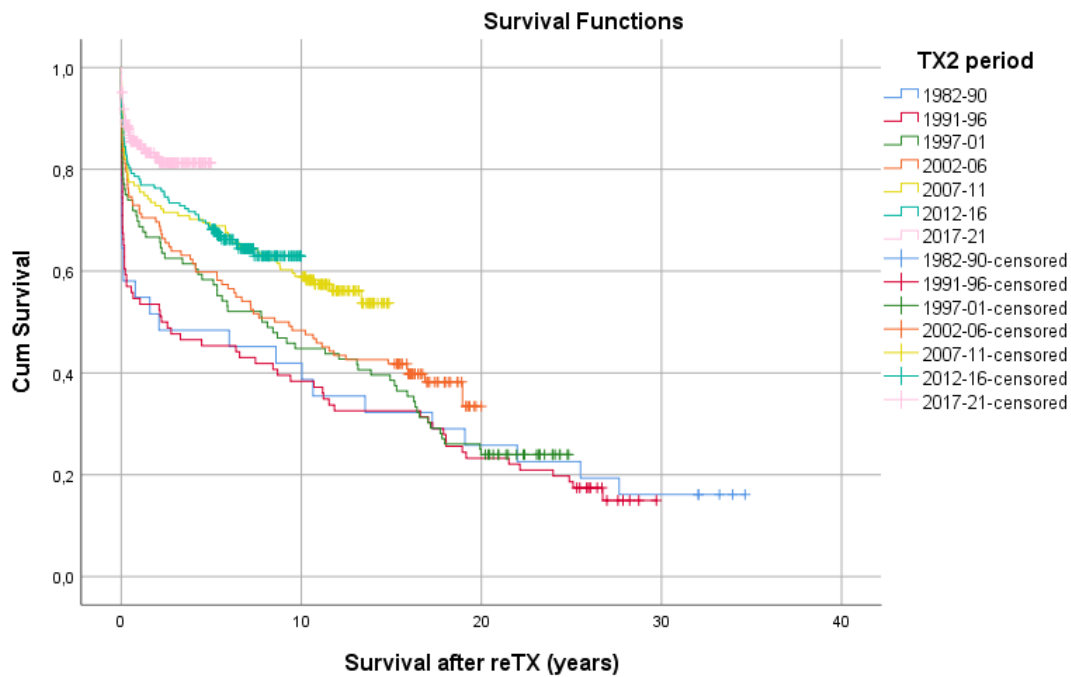


Figure 16. Kaplan-Meier patient survival curve for patients following retransplantation in the indicated time periods.

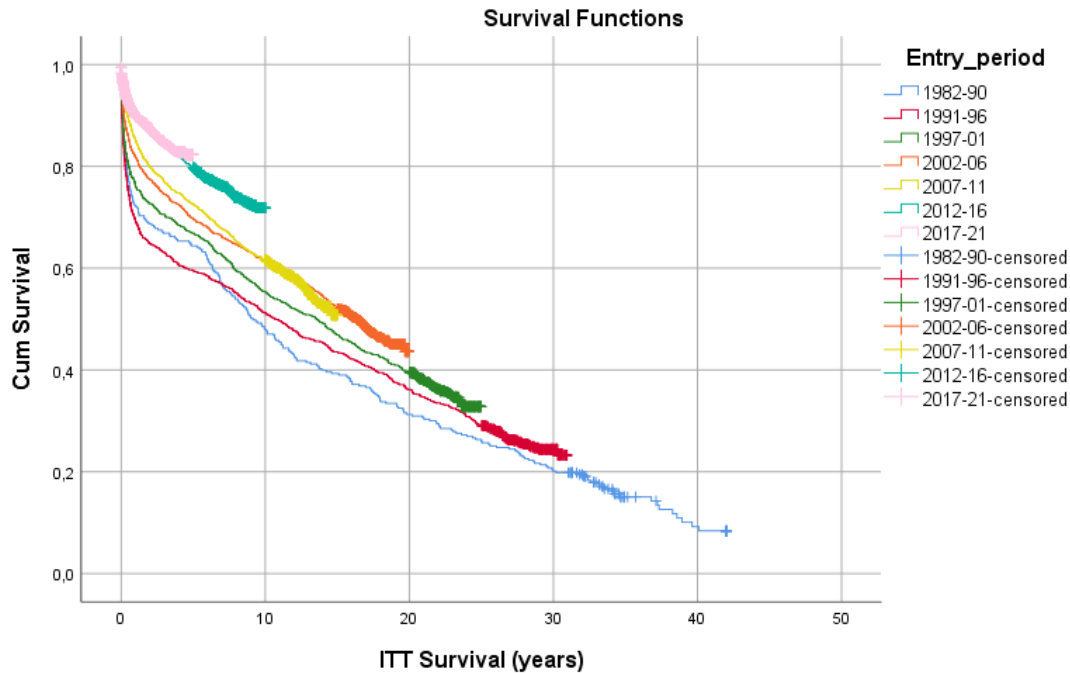


Figure 17. Kaplan-Meier patient intention-to-treat survival curve following listing for transplantation.

	Median age	1-year survival (%)	5-year survival (%)
Primary sclerosing cholangitis	45.3	98 %	90 %
Hepatocellular carcinoma and cirrhosis	61.5	94 %	78 %
Alcoholic cirrhosis	57.8	95 %	85 %
Metabolic disease	52.1	96 %	91 %
Cirrhosis - unknown	56.9	93 %	85 %
Autoimmune cirrhosis	51.5	95 %	86 %
Primary biliary cholangitis	56.4	93 %	89 %
Extrahepatic biliary atresia	1.2	91 %	91 %
Polycystic disease	54.1	96 %	95 %
Post hepatitis C cirrhosis	54.6	89 %	75 %
Listed as highly urgent	41.0	83 %	79 %

Table 7. Age at transplant and survival for the patients listed 2012-2021 for ten selected diagnoses and those listed as highly urgent

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 2021. I am extremely grateful for dedicated follow-up provided by the transplant coordinators upon my requests during quality control. In Oslo, I particularly want to thank Monika Olofsson, in Gothenburg Ulla Nyström, in Stockholm Marie Tranäng, in Copenhagen Mette Gottlieb, in Helsinki Leena Toivonen and in Tartu Virge Pall takes care of the registry. The work with the registry has not been impacted by the ongoing COVID-19 pandemic in 2020 and 2021. 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. The export of data from NLTR to ELTR is now fully functional and has reduced the burden with dual data collection at all the centers.

9. Acknowledgements - financial support

The NLTR received no financial support in 2021. The maintenance of the Oracle system has been performed by Scandiatransplant. We are extremely grateful for the help and support from 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 1990-2021:

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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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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