ANNUAL REPORT 2016

The
Norwegian Renal Registry

(Norsk Nyreregister)

This report will also be available on:
http://www.nephro.no/registry.html

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Preface

The Norwegian Renal Registry (Norsk Nefrologiregister) was formally constituted in 1994 as a collaboration between The Norwegian Renal Association (Norsk Nyremedisinsk Forening) and Oslo University Hospital-Rikshospitalet, with the latter as the formal owner. National data on renal replacement therapy (RRT) had been collected within The Renal Association since 1980 in a less formalised manner, and the transplant centre had stored data on transplanted patients since the late sixties. Further, Norwegian renal units had reported to the ERA-EDTA-registry since the late sixties.

Since the mid-90ies, a process of transition from a pure epidemiological registry into a quality-oriented registry has progressed. With the present way of collecting and processing quality data, they cannot be collected in time to be included in the annual report, but selected data may be included in the next years report; others will be theme for quality-seminars and special reports.

National organisation and policy

Norway has 5.237 mill. inhabitants (July 2016) and 19 counties with populations ranging from 76.000 to 662.500. Each county, except one, has a central renal unit and some have two, further some have satellite units run in close contact with the central unit. There is only one transplant centre (two during 1963-82). Pre-transplant work-up, as well as post-transplant follow-up beyond 2-3 months, is handled by the county-centres.

The centres, at present 25, are responsible for reporting data from day 1 on all patients receiving renal replacement therapy (RRT) for chronic renal failure within their area. Based on annual cross-checks, reporting is considered to be complete. Treatment of acute renal failure is not reported unless the failure turns out to be irreversible, in which case the whole treatment period is included. Minor changes of treatment modality, e.g. from HD to HDF or between CAPD and APD, are not reported. Similarly, temporary changes to HD for PD-patients are not reported. At intervals, cross-checking for unreported deaths is performed against official census data.

Transplantation has always been considered the treatment of choice, if possible with a living related donor. Since 1984, also unrelated donors have been used. Acceptance criteria for transplantation have been wide, strict age limits have not been applied. Over time, an increasing number of non-transplantable patients have also been offered life-long dialysis.

Incidence and prevalence calculations in this report are based on the national population data from July 2016, although this in some instances may be slightly misleading since population changes have not been uniform in all counties during the period.

Incidence figures for 2016

During 2016 a total of 554 new patients (in 2015: 514) entered renal replacement therapy (RRT), i.e. 105.8 per mill. inhabitants.

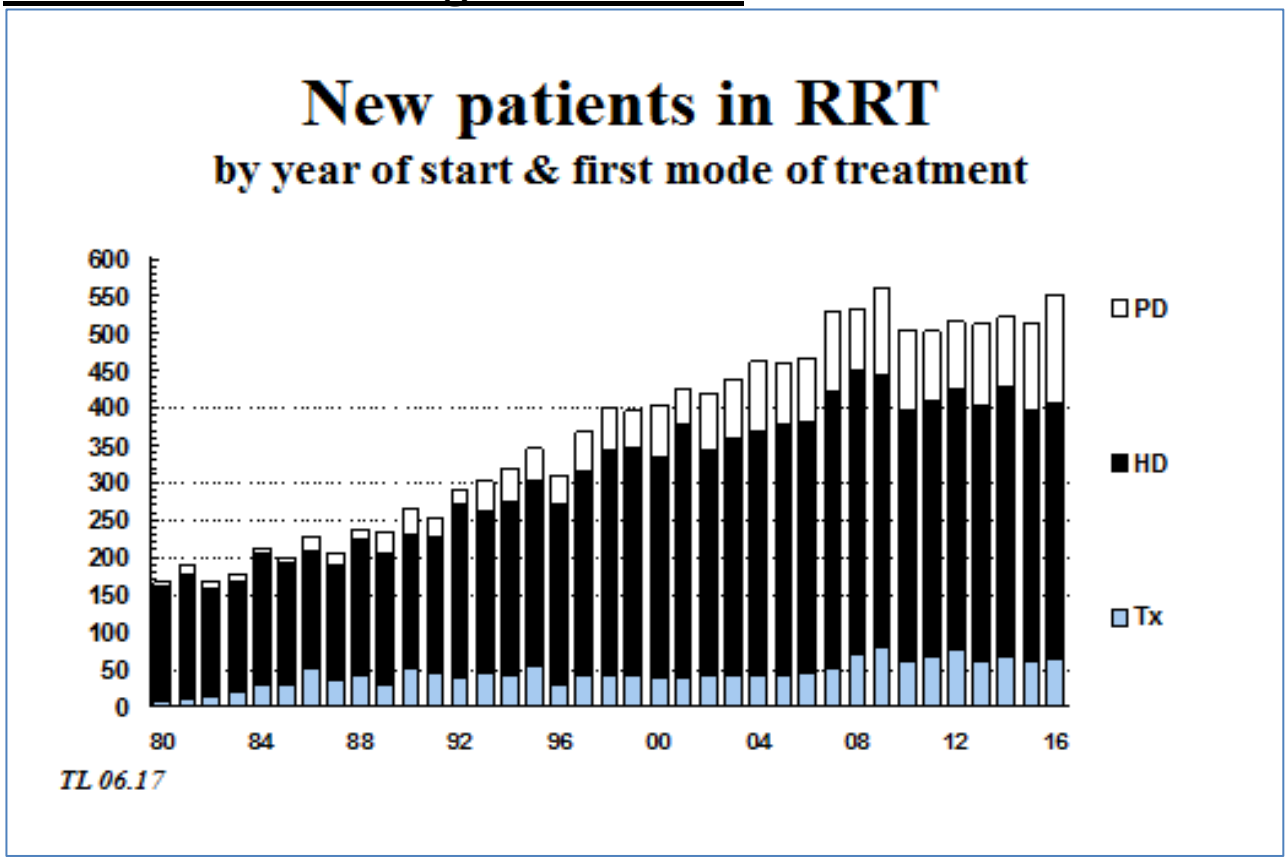
A majority of 362 (65.3 %) were males and 192 (34.7 %) females. Median age at start was 66.6 years, mean 63.2 years, ranging from one to 91.9 years.

Tabulated by first mode of treatment, and age at start of treatment:

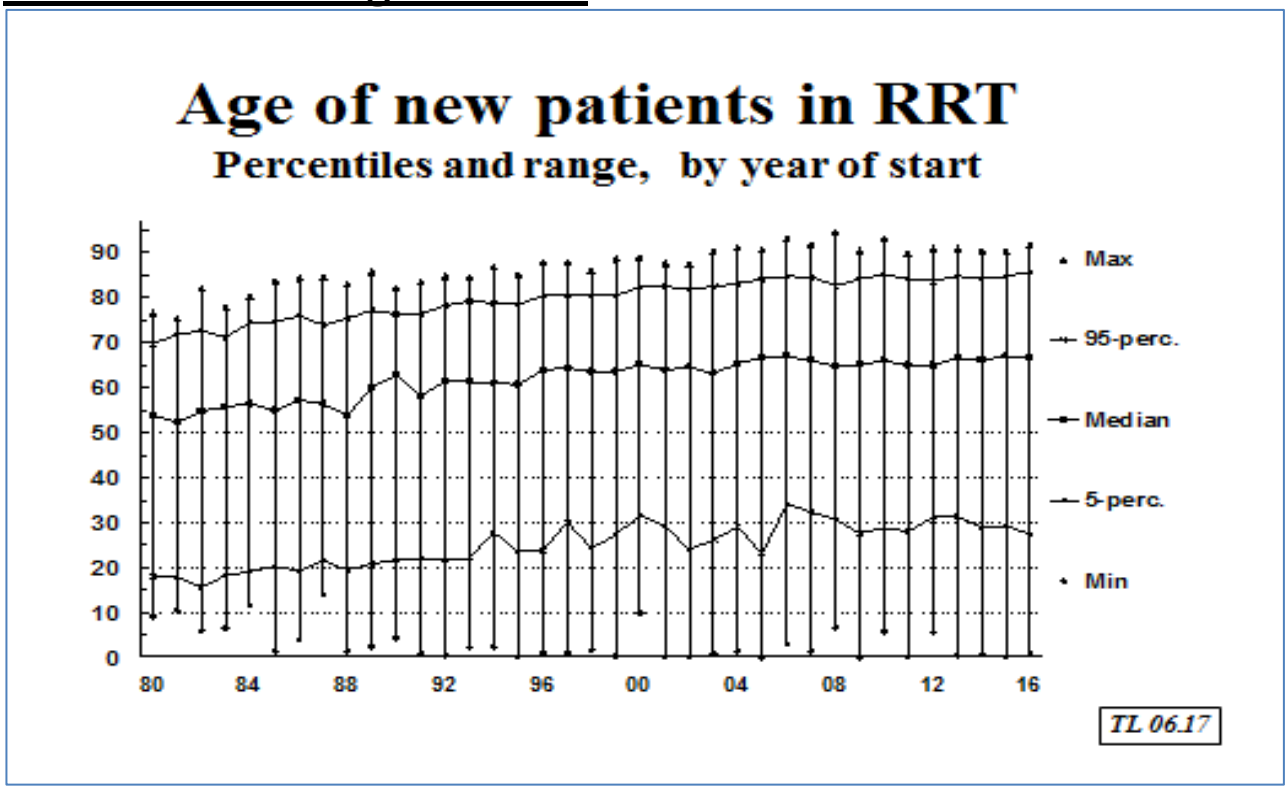
	< 15	15-24	25-34	35-44	45-54	55-64	65-74	75-84	85+	Total	in %
HD	0	9	14	23	30	77	90	74	23	340	61.4
PD	1	2	9	6	18	17	43	41	12	149	26.9
TX	4	4	4	8	11	18	13	3	0	65	11.7
Total	5	15	27	37	59	112	146	118	35	554	100
in %	0.9	2.7	4.9	6.7	10.6	20.2	26.4	21.3	6.3	100	

At start of treatment, 303 (55 %) were considered by their nephrologist to be a potential candidate for transplantation, while 251 (45 %) were accepted for life-long dialysis (the latter constituting 54% of those starting with HD and 46 % of those starting PD).
Among the 489 patients starting dialysis in 2016, 80 % had been under control by the renal unit for at least four months, while 20 % were previously unknown and counted as "late referrals".

Incidence data: Changes 1980-2016:



Incidence data: Age at start:



Since registration started in 1980 there has been a continuous shift in patient age. Both the maximum and the median age at start of RRT have increased. Also the 5-percentile and 95-percentile values (i.e. including the majority of patients) have increased with a similar number of years. But also smaller children have been accepted; the youngest ever started PD in 2011 at age two days. Five children below 15 years started RRT in 2016.

Incidence data: Primary renal disease

	1980-89	1990-99	2000-09	2010-14	2015	2016
Glomerulonephritis	35%	27%	18%	16%	12%	17%
Pyelo/interstitial nephr.	15%	11%	10%	9%	9%	9%
Polycystic diseases	10%	9%	8%	8%	10%	8%
Diabetic nephropathy	13%	11%	15%	17%	18%	16%
Amyloidosis	6%	5%	2%	2%	3%	2%
Vascular/hypertensive	7%	21%	30%	35%	32%	34%
Immune/systemic	5%	5%	4%	4%	6%	3%
Kidney tumour	1%	1%	2%	1%	2%	1%
Myelomatosis	2%	2%	3%	1%	2%	2%
Other defined	4%	4%	4%	4%	5%	5%
Unknown	3%	3%	4%	3%	2%	3%
N:	2018	3234	4705	2570	514	554

The main change over time has been an increase of vascular/hypertensive nephropathy and a relative reduction of glomerulonephritis. Whether this only reflects changed coding practice or a true shift is not known. Amyloidosis seems again to increase, caused by chronic infections in i.v.-drug abusers.

Diabetic nephropathy has contributed 10-18 % per year. In 2016, 17 out of these were registered as having Type I and 70 as Type II diabetes, 83 patients with other types of primary renal disease were recorded as having diabetes as a co-morbid factor (2 Type I and 81 Type II), thus 30.7 % of new patients were diabetics.

The time from onset of diabetes to start of RRT differed considerably. For the 17 with Type I diabetes the mean time was 33 years, for the 70 with Type II diabetic nephropathy the mean time was 19 years. The 81 Type II diabetics judged to have a primary renal disease other than diabetic nephropathy, most often hypertensive, in mean had 13 years of pre-RRT diabetes duration.

Cardiovascular disease is often present at start of RRT. Coronary heart disease was reported in 161 (29%), one had a previous heart-tx. and 100 (18%) had anamnestic heart failure. Echo-verified left ventricular hypertrophy was reported in 138 (25%). Cerebrovascular disease was reported in 66 (12%) and peripheral atherosclerotic disease in 75 patients (14%) while 60 (11%) had chronic obstructive lung disease.

Prevalence data: Status by 31.Dec. 2016.

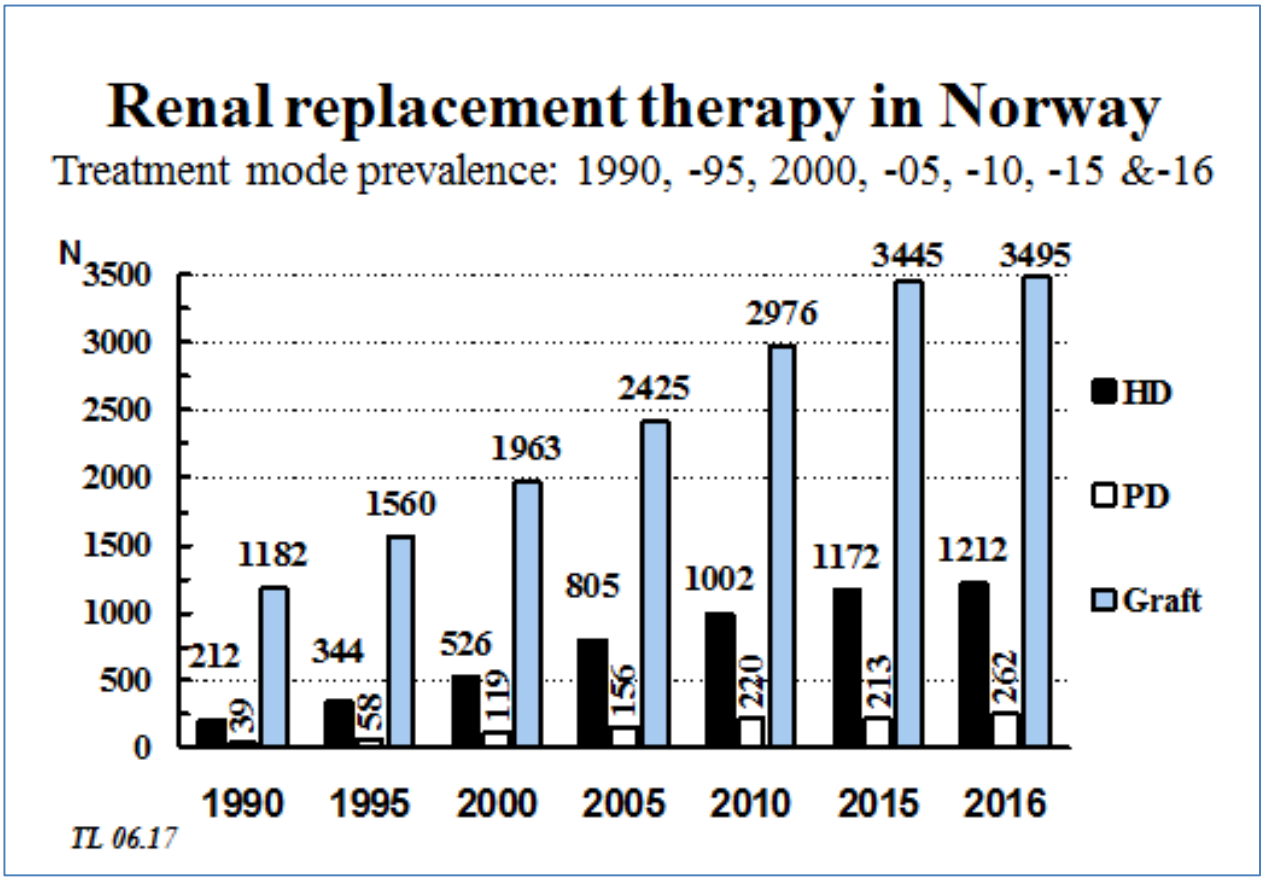
By the end of 2016, 4969 patients in Norway received renal replacement therapy, i.e. 948.9 per million inhabitants. This represents an increase of 140 patients or 2.9 % since 2015.

Tabulated by last mode of treatment and age by end of 2016:

	< 15	15-24	25-34	35-44	45-54	55-64	65-74	75-84	85+	Total	in %
HD	0	19	45	79	142	209	331	280	107	1212	24.4
PD	2	5	13	9	29	37	68	68	31	262	5.3
TX	51	79	202	414	722	846	837	326	18	3495	70.3
Total	53	103	260	502	893	1092	1236	674	156	4969	100
In %	1.1	2.1	5.2	10.1	18.0	22.0	24.9	13.6	3.1	100	

Median age by the end of the year was 61.5 years, mean 59.4 years and range 1.25 to 94.0 years. Gender: 65.0 % males and 35.0 % females.

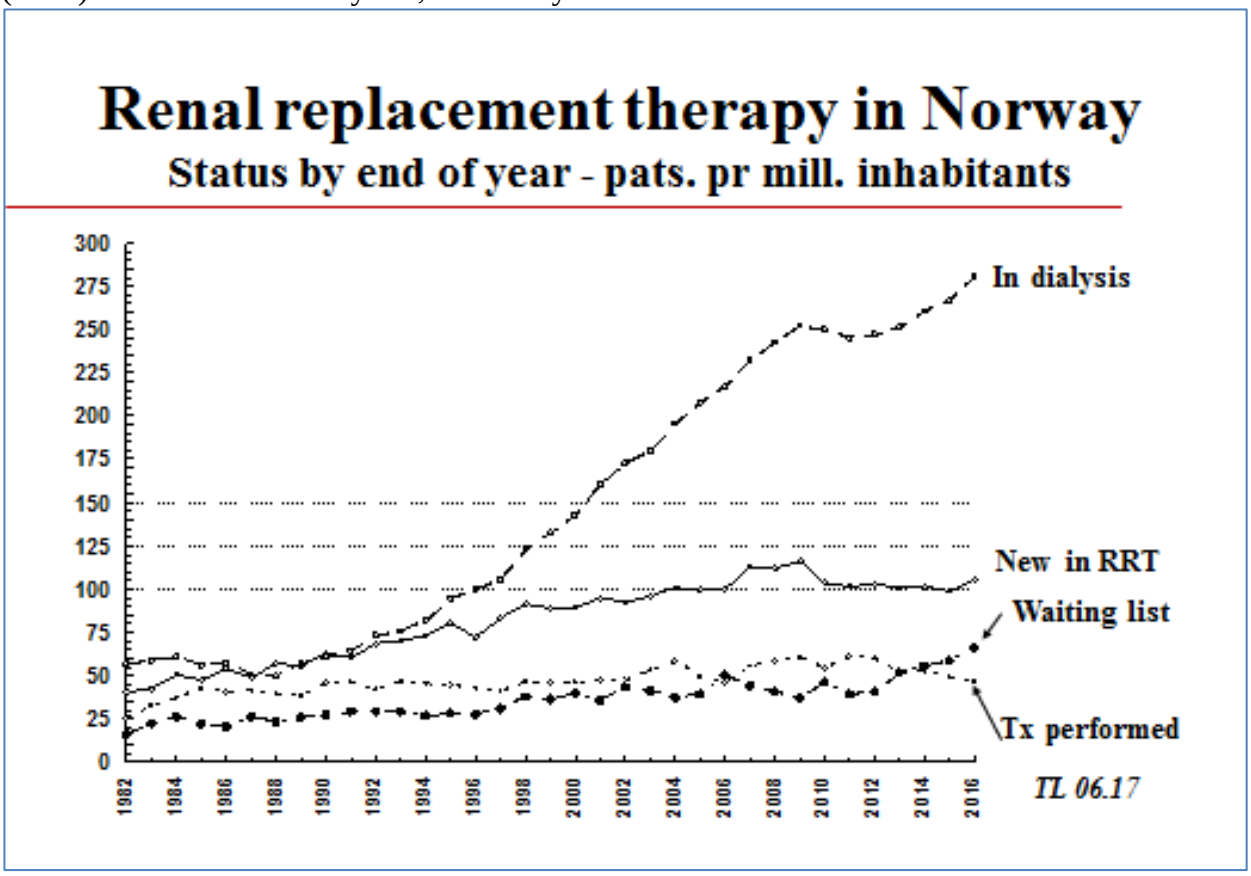
Dialysis modalities: Dialysis-treatment in Norway is part of public speciality-service, there are no private facilities. Due to long travelling distances, some centres have satellite-units (see table in appendix), in total 24% of HD-patients are treated in satellites (up to 75% in one centre). Seventeen patients were in home-HD by end of 2016 (same as in 2015). By end of 2016 39% of HD-patients used haemodiafiltration (HDF).
Not all centres offer PD-treatment, such centres may refer actual patients to neighbouring centres. In total 17.8% of dialysis patients were in PD, constituting 35% in the most active centre. 66% of PD-patients used automated (APD) treatment.
Shifts during 2016: 24 patients went from HD to PD, mostly (22) due to preference. 47 patients went from PD to HD, most often due to or unsatisfactory effect/poor adherence (24), infections (14), access problems (4) or leakage (5).



Transplantation and waiting lists in 2016:

A total of 240 renal transplants were performed at Oslo University Hospital Rikshospitalet in 2016, i.e. 45.8 per million inhabitants. In 47 (19.6%) the graft came from a living donor (LD), 17 of those were biologically unrelated to the recipient (15 were spouses). Among the LD-graft recipients 24 out of 41 first graft recipients were grafted pre-emptively, 2 out of 6 re-graft recipients did not receive dialysis. 193 patients received a deceased donor (DD) graft, 41 out of the 167 first graft recipients were pre-emptively transplanted (25 %), while 1 out of 26 had a re-graft without entering dialysis. There were 208 first grafts (41 LD and 167 DD), 24 were second grafts (6 LD, 18 DD), six third grafts and two fourth grafts (all DD).
Simultaneous kidney + pancreas (SPK) transplantation was performed in 16 patients.

In principle, transplantation is offered to all patients considered to profit from it, with no strict upper or lower age limit. The age of the 167 first-DD-graft recipients in 2016 ranged from 1 to 82 years, with a mean age of 54 y. Out of these, 30 % were above the age of 65 and 5 % were 75 or older. The 41 recipients of a first LD-graft were from 1 to 77 years, mean 45 y. Re-graft recipients (n=32) were from 27 to 73 years, mean 52 y.



By end 2016, 344 patients (65.7 per mill.) were on the active waiting list for a DD renal graft. This represented an increase of 39 patients (13 %) since 2015. Among those waiting by Dec.31, median time on the list was 10.5 months. 32 % had waited less than 6 months, 56 % less than one year and 16 % more than two years. The 193 recipients given a DD-graft in 2016 had a median waiting time of 16 months and a maximum of 107 months at the time of grafting.
Among the 1474 patients in dialysis treatment by Dec.31, 764 (52 %) were for various reasons not considered candidates for a (new) renal graft.

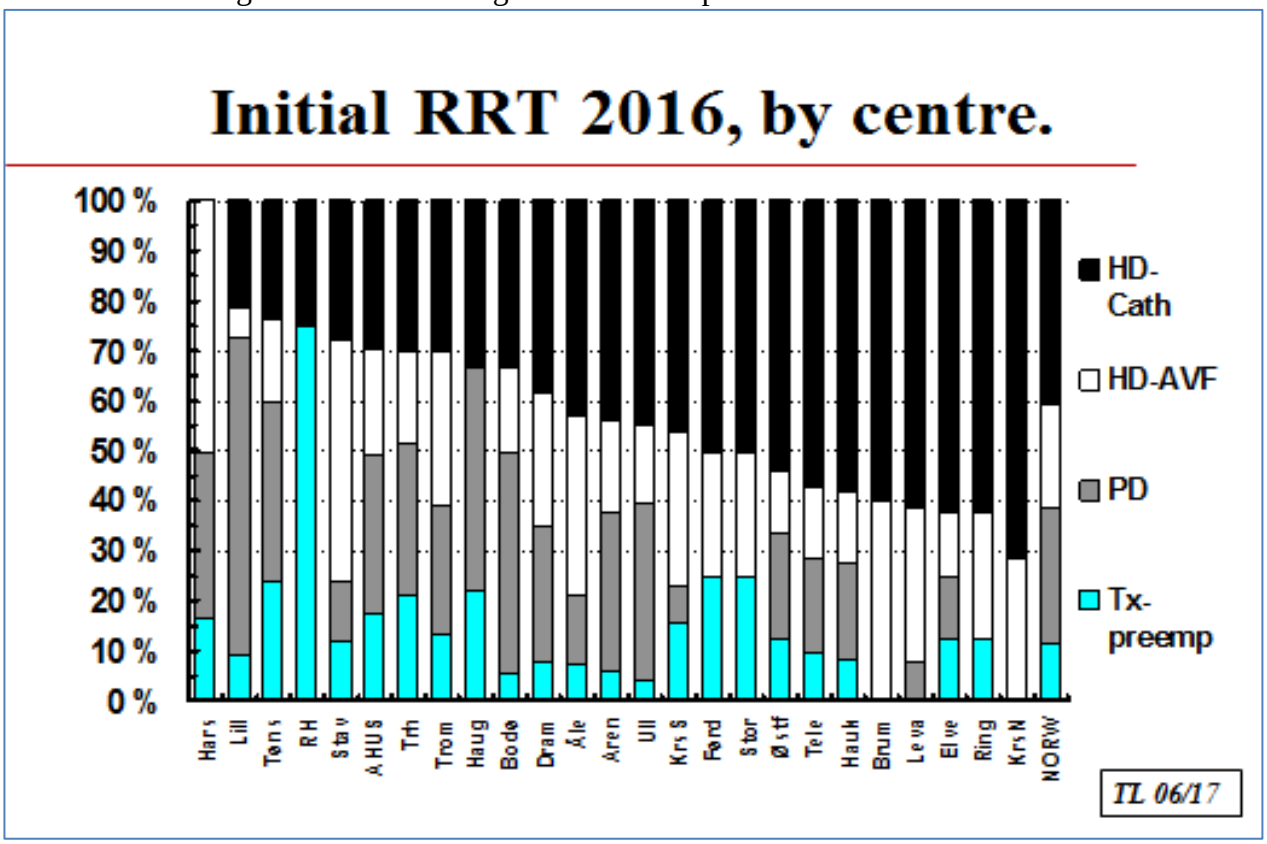
New patients in 2016 – status at start of RRT.

A total of 554 patients started RRT in 2016. Among the 340 starting haemodialysis, the access was via catheter in 227 patients (67 %), while 113 had AV-fistula or graft (33 %) as access.

Status at start of RRT	Total (n:554)	HD (n:340)	PD (n:149)	Tx (n:65)
Creatinine (mean)	636 µmol/l	670	612	516
eGFR (mean), (excl. children)	8.8	8.6	8.7	10.7
Albumin (mean)	36 g/L	34	37	42
Haemoglobin (mean)	10.2 g/dL	9.9	10.4	11.6
Haemoglobin - % <11 g/dL	69 %	76 %	69 %	32 %
ESA use	55 %	54 %	60 %	48 %
Active D vitamin use	67 %	62 %	75 %	79 %
Statin use	58 %	52 %	69 %	60 %
Not on antihypertensive drugs	9 %	12 %	3 %	8 %
Using >2 antihypertensive drugs	51 %	53 %	55 %	31 %

As might be anticipated, pre-emptively transplanted patients had a somewhat lower serum creatinine, thus higher GFR, and a higher haemoglobin and albumin than those starting dialysis. Among patients known less than four months, 85 % had haemoglobin <11 g/dL.

While pre-emptive transplantation is considered the best initial RRT, HD by catheter may be seen as the poorest alternative. In the following figure, individual centres are ranged by the proportion starting with catheter (NORW = country) from "best" to "poorest". Admittedly, small centres and centres not offering PD are disadvantaged in such comparisons.



Transplantation and graft survival:

While the first renal transplantation in Norway was performed as early as in 1956, an organised national transplant programme was first started in 1969. At the same time, the exchange organisation 'Scandiatransplant', having all transplantation centres in Denmark, Finland, Sweden and Norway as members, came in effect.
Until the introduction of cyclosporine in 1983, two centres in Norway performed renal transplants, since then all transplants have been performed in one centre only. Over time immunosuppressive protocols have changed, as have acceptance criteria for recipients and donors. Thus, the Kaplan-Meier survival curves shown in this report will demonstrate the combined effects of several factors. Time of censoring is 01.04.2017; patient death with functioning graft is counted as graft loss in all curves.

"Transplant vintage":

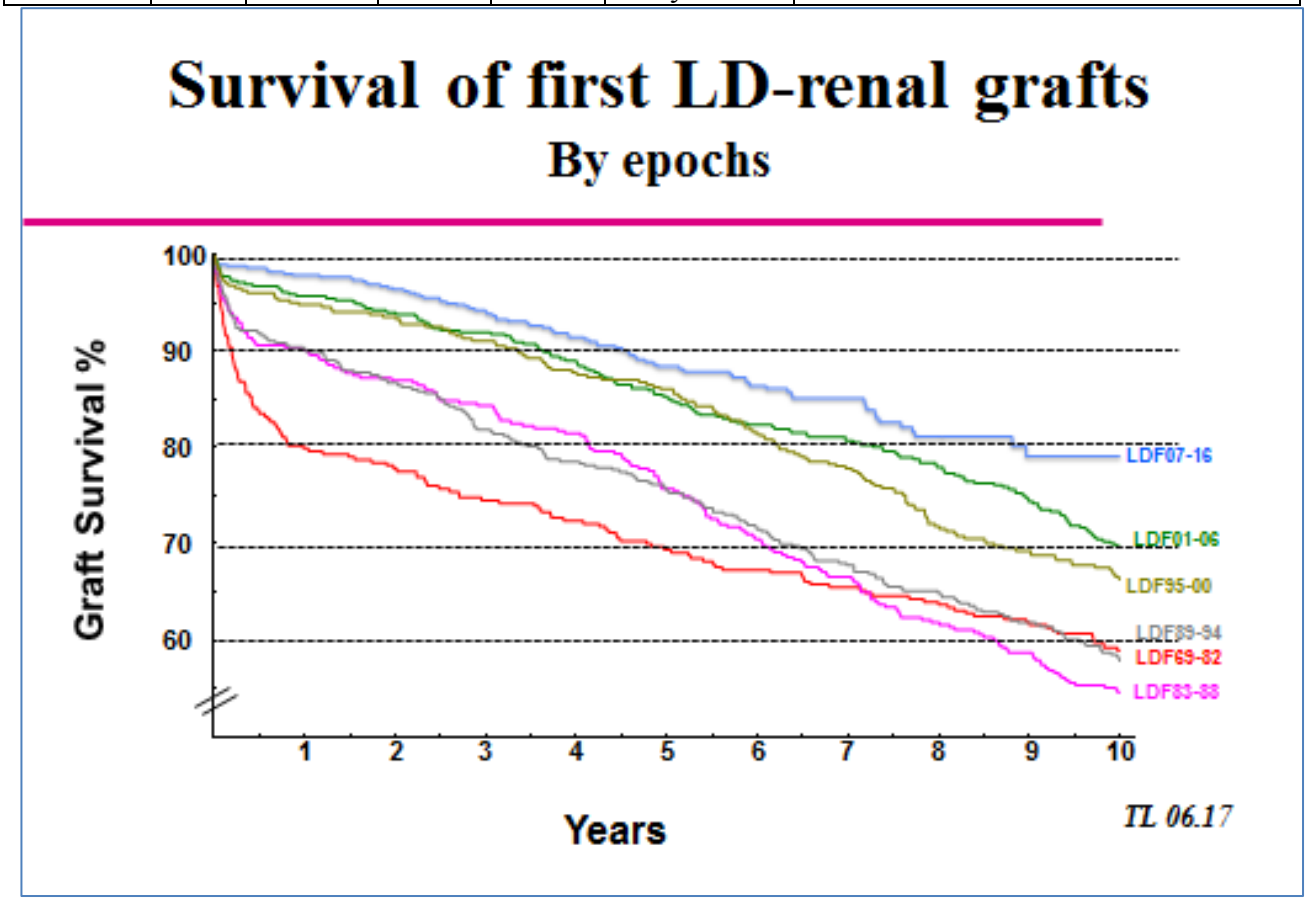
The following two Kaplan-Meier plots show the 10-year survival of first renal grafts from respectively living donors and deceased donors from selected epochs.

a: Living donor grafts:

In the period 1969-82, immunosuppression consisted of only azathioprine + prednisolone. The source of living donor grafts in the period was only close relatives, either fully HLA-matched or mismatched for one HLA-haplotype. Following the introduction of cyclosporine in 1983, also relatives mismatched for both HLA-haplotypes as well as biologically nonrelated donors (mostly spouses or in-laws) were accepted.

The following table shows that in spite of an increasing proportion of non-related donors and increasing recipient (R-age) and donor (D-age) mean age, the graft survival has improved markedly over time. It may be noted, however, that in the pre-CyA-group which had a high proportion of early graft losses, the observed half-life (i.e. the time by which half of the grafts had been lost) was higher than in the two following periods. The annual follow-up reports also confirm that long-time survivors without calcineurin-inhibitors in general have lower blood pressure and higher eGFR. The indicated half-life for the 2007-16-group is estimated by projection.

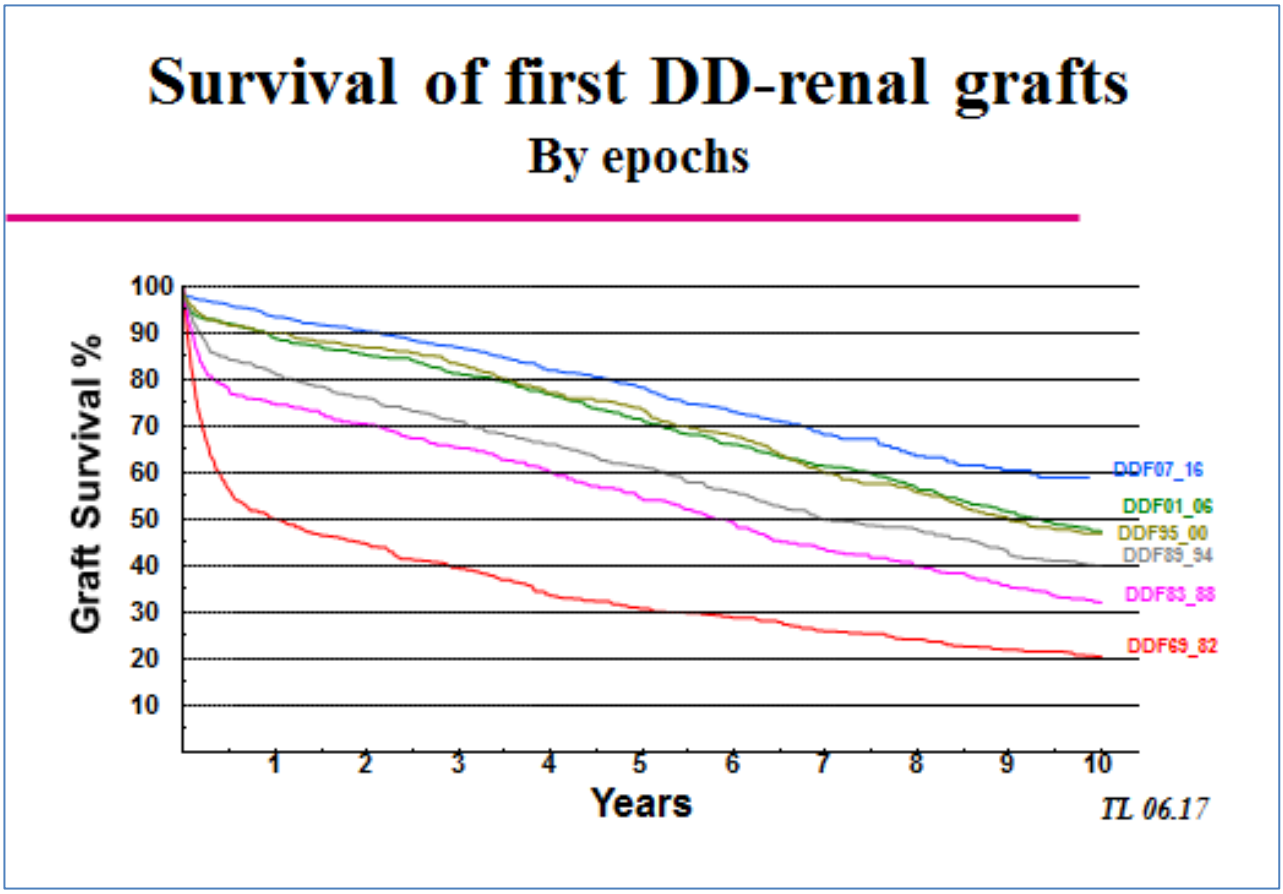
Period	N	Related	R-age	D-age	'Half-life'	Immunosuppression (main)
1969-82	332	100 %	34.6	46.7	13 y.	Aza + Pred
1983-88	382	91 %	39.9	49.0	11 y.	CyA + Pred ± Aza
1989-94	456	81 %	42.2	47.9	12 y.	CyA + Pred + MMF or Aza
95-2000	399	77 %	43.0	48.1	15 y.	CyA + Pred + MMF
2001-06	484	72 %	43.8	47.0	15 y.	CyA or Tac + Pred + MMF
2007-16	661	66 %	45.7	49.1	'20 y.'*	Tac + Pred + MMF + Basiliximab



b: Deceased donor grafts:

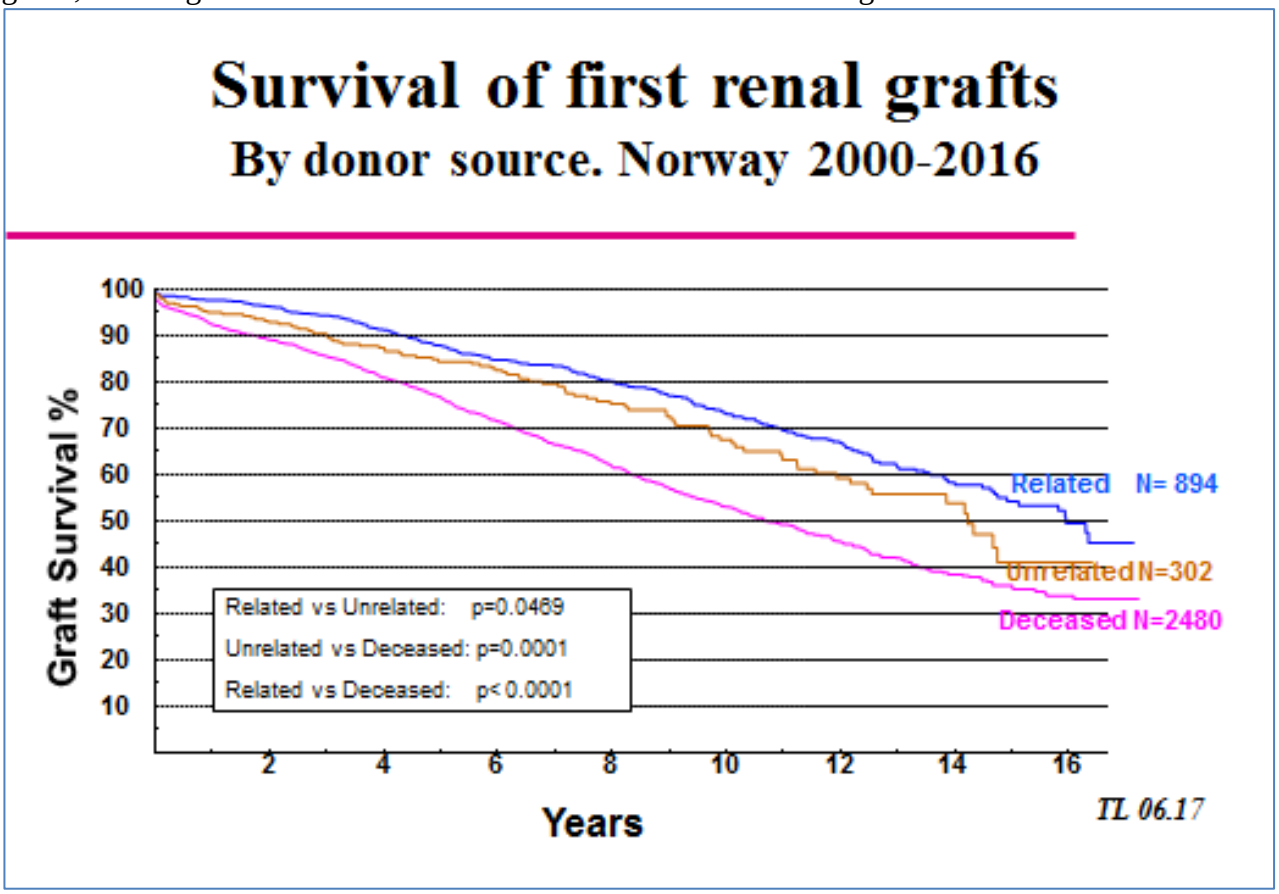
The immunosuppressive protocols for recipients of deceased donor grafts have gone through similar changes, and similarly both recipient and donor age has increased. Half-life was poor in the pre-CyA era, but has improved gradually since, Again; the half-life estimation for the latest period is by projection.

Period	N	R-age	D-age	'Half-life'	Immunosuppression (main)
1969-82	587	47.4	35.1	1 y.	Aza + Pred
1983-88	457	51.0	35.4	6 y.	CyA + Pred ± Aza
1989-94	529	54.8	42.3	7 y.	CyA + Pred + MMF or Aza
95-2000	598	54.7	43.4	9 y.	CyA + Pred + MMF
2001-06	707	56.3	46.2	9 y.	CyA or Tac + Pred + MMF
2007-16	1663	56.1	51.5	'13 y.'*	Tac + Pred + MMF + Basiliximab

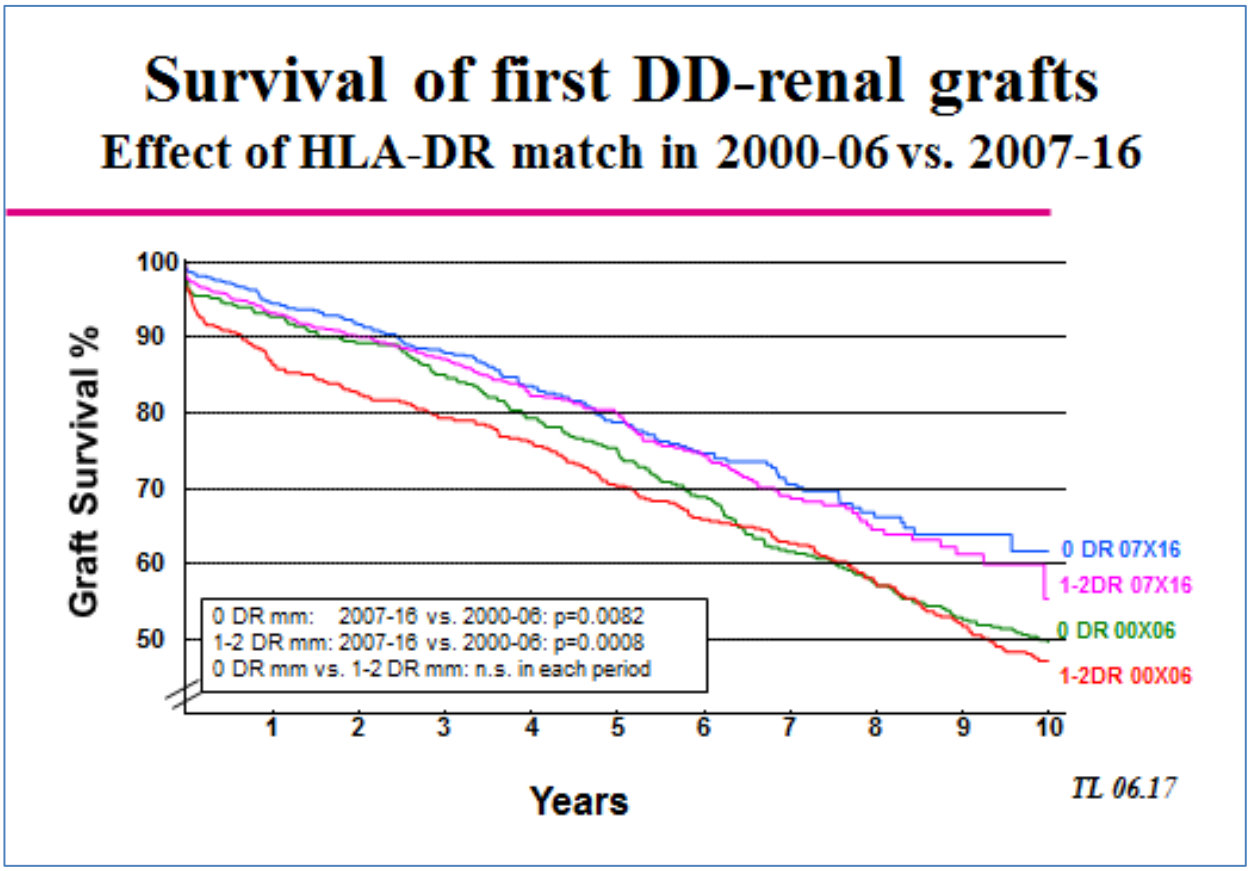


c: Transplants performed since Jan. 2000:

Also in the new millennium, grafts from living donors have a better survival than deceased donor grafts, further grafts from a related donor do somewhat better than grafts from unrelated donors.



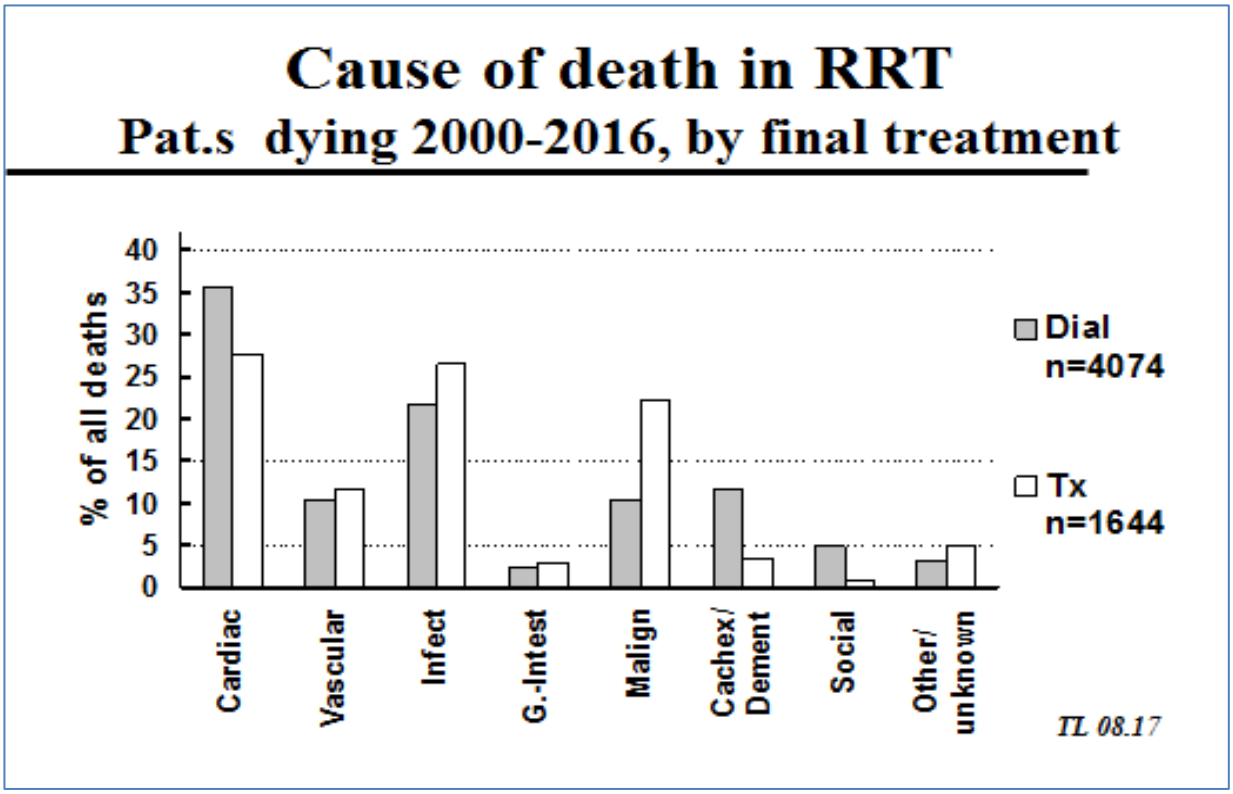
The effect of **HLA-matching** on the survival of grafts from deceased donors has been disputed over the years. From our Norwegian data we have repeatedly reported a significant beneficial effect of matching for HLA-DR, but not for HLA-A&B. When the first-graft data in the new millennium were analysed, the DR-matched group still did better for the first 4-5 post-transplant years. However, the introduction of basiliximab induction as standard in 2007 led to improved survival for both the DR-matched and the DR-mismatched grafts, after this, we see no significant influence of DR-matching in the group of first DD-grafts..



Death in RRT:

A total of 411 patients in renal replacement therapy died during 2016, i.e. 7.6% out of the 5389 persons at risk. Among these, 68% were males and 32% females. Median age at death was 75 years, mean 73 years, and the range 33-96 years. Median time from start of RRT until death was 56 months, with a range spanning from 15 days to 48 years.
The final mode of treatment was HD for 227 patients and PD for 51, while 133 died with a more or less well-functioning graft. One patient died within two months after graft loss, thus 134 deaths were termed "Tx-related". Dialysis treatment was terminated and followed by death in 69 patients; in 26 of those the patient had decided to refuse further treatment.
Cardiac complications (33%) were the most frequent causes of death, followed by infections (27%), and malignant tumours (12%).

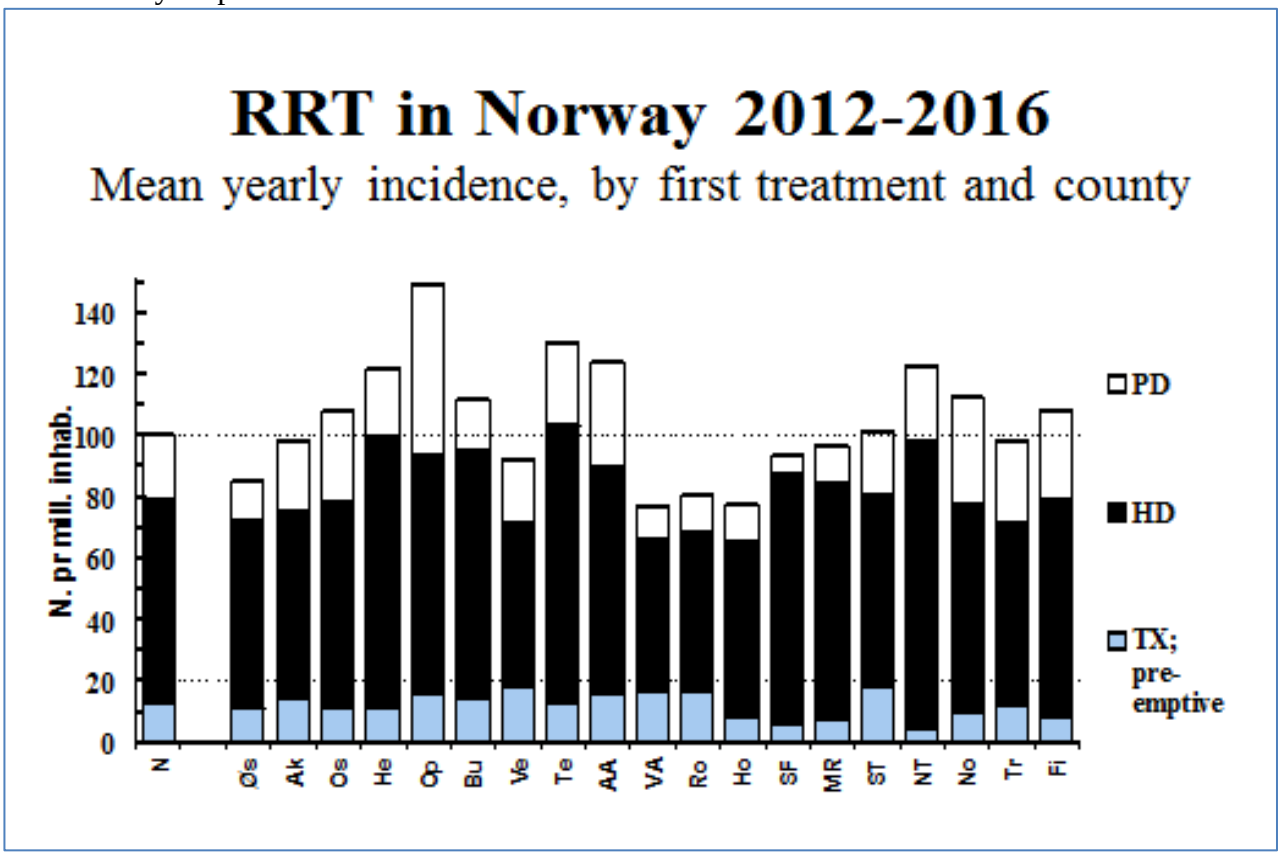
For comparison, the following figure shows main causes of death in all patients dying in RRT during the period 2000-2016 according to final treatment mode. In the group "Social" are included patients who refused further treatment as well as (a few) suicides.



Regional differences within Norway.

Incidence:

The 25 Norwegian centres differ in size and their use of the different treatment modes (HD, PD or pre-emptive transplant). Further the number of new RRT-patients varies considerably from year to year. To make up for the annual variations and the overlapping centre coverage, patients were grouped by county of domicile at RRT-start and the incidences were calculated as a yearly mean for the five-year period 2012-2016:



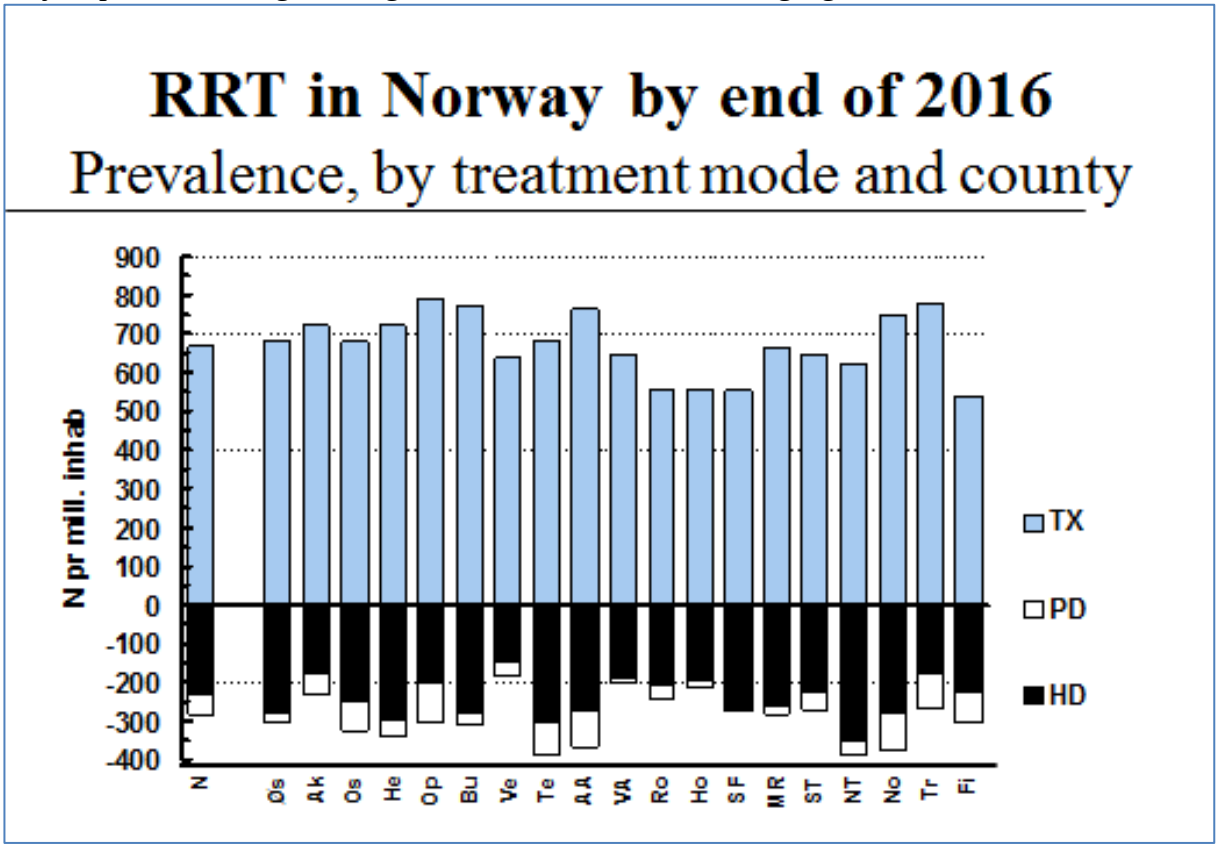
As appears, the mean annual incidence of RRT-start varied from 76 to 149 pr. million, with Vest-Agder having the lowest and Oppland the highest mean incidence. With the rather small population in most counties, figures may be expected to change from year to year, but over years there has been a lower incidence in the southwest/west-coast counties. Analysis of county-wise age groupings, diagnosis groupings, differences in acceptance for permanent dialysis, or late referral rates, has failed to explain the marked variations in incidence.

There is national consensus that pre-emptive transplantation is preferable. Looking solely at 2016-data (see Appendix), this was achieved in only 11 % of all. In the individual counties the numbers are small, but this figure ranged from 0 % to 25 % (Sogn-og-Fjordane). For the 5y-period, 12.5% of patients starting RRT were pre-emptively transplanted, within counties ranging from 4 to 21% (highest in Vest-Agder).
Efforts are also done to increase the use of PD. Still in some counties PD is rarely used, in others up to 62 % (Oppland) of new patients in 2016 had this as first treatment mode. 61% received HD as first treatment mode, in the counties this ranged from 29 % to 93 %.

The proportion of the new dialysis patients in 2016 who started RRT without having been known by the renal unit for at least 4 months was 20 %, with wide variations between centres; from 0 % and up to 43 %. In the majority of these cases the diagnosis would imply that renal failure has developed gradually over years. These figures seem not to have improved significantly over the years; thus in most counties it still seems to be need for improved co-operation with the primary health service, in order to achieve more in-time referrals.

Prevalence:

Again, the data demonstrate great differences between the counties. In all counties the majority of patients have a functioning graft, constituting from 62% to 77% of the total RRT-population. The dialysis prevalence ranges from 187 to 387 per mill. inhabitants in the counties, indicating considerable differences in workloads and costs. In order to illustrate this cost-difference, the dialysis prevalence is given negative numbers in the following figure:



In some counties, three out of four dialysis patients are not considered candidates for a new graft, in others this applies to one out of three. But counties with high dialysis prevalence do not necessarily have a high prevalence of 'non-transplantable' patients.

Concluding remarks:

Although the 2016 incidence is somewhat higher than in the recent years, the tendency still is that the incidence of RRT in Norway is levelling off, in line with that seen in other European countries. The transplantation rate also in 2016 was a little lower than that of previous years; still the transplant population increased by 1.4 %, while the dialysis population increased by 6.1 % compared to end of 2015, and the number of recorded HD-sessions increased by 2.8 %. Due to the still improving survival rate both in dialysis and transplantation, further increased prevalence of RRT-patients can be expected over the coming years.

Registry data are also regularly used by Norwegian nephrologists as basis for scientific papers, congress presentations and PhD-theses. A list of publications has since 2012 been presented on www.nephro.no along with the annual reports; during 2016 a total of 18 papers and two PhD-theses have been more or less based upon data from the registry.
Data delivered to the ERA-EDTA Registry in Amsterdam are included in their reports and publications; some data are also forwarded to the USRDS-reports (the chapter of "International Comparisons").

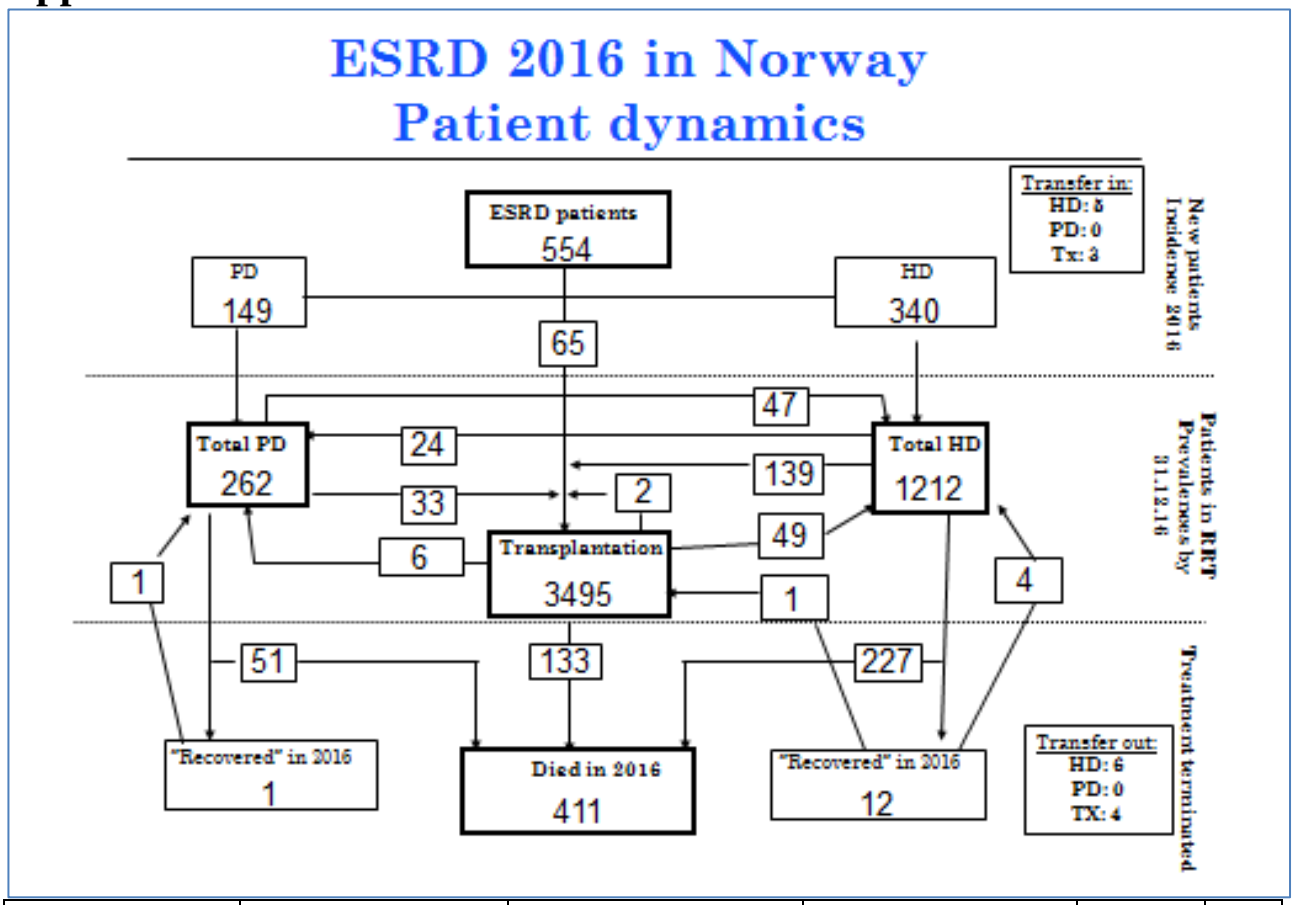
The registry has received status as a National Medical Quality Registry by the proper National authorities. Consequently, as of 01.01.2016 the RRT-registry has been merged with the Norwegian Renal Biopsy Registry into "Norsk Nyreregister" (The Norwegian Renal Registry). In order to ensure that data from the old and the new databases were consistent, the old database was kept updated throughout 2016. This made it possible to make another annual report in the same format as in preceding years. The present report will surely be the last annual report made in the present format and by the undersigned author.

Regardless of status, the cooperation with all Norwegian nephrologists, demanding their steady efforts to keep the registry updated, has always been, and will always be, a prerequisite for keeping a complete and reliable registry.

The author will take this opportunity to thank all collaborating colleagues for their cooperation through all these years, making the registry to what it has become.

Report completed 17.08.2017
Torbjørn Leivestad M.D. Ph.D.

Appendix:



		New pat in RRT 2016				Pat. in RRT by 1/1.2017				Dialyses etc. 2016			Died 2016		
	Satellites	HD/HDF	PD	Preemptive Tx	Total	HD/HDF	PD	Graft	Tot	HD total	PI.exch	Other	Dial.pat	Tx-pat.	Not tx-candidate
Tromsø	7	14	6	3	23	42	18	136	196	**6495**	11	0	8	6	34
Harstad		3	2	1	6	9	4	46	59	**1570**	0	0	4	1	9
Bodø	8	18	16	2	36	62	23	166	251	**10781**	8	0	5	5	65
Levanger	6	12	1	0	13	49	5	82	136	**8184**	1	27	10	3	25
Trondheim	4	16	10	7	33	73	15	222	310	**11551**	113	652	13	10	39
Kristiansund N	2	7	0	0	7	28	0	34	62	**4230**	0	0	5	0	17
Ålesund	1	11	2	1	14	41	5	131	177	**6561**	61	0	12	4	30
Førde	2	6	0	2	8	28	1	58	87	**4764**	6	16	3	1	22
Bergen	4	26	7	3	36	85	9	266	360	**13207**	45	57	26	12	50
Stord		3	0	1	4	11	0	18	29	**1639**	0	0	2	1	5
Haugesund	2	3	4	2	9	29	7	58	94	**4831**	15	35	6	1	15
Stavanger		19	3	3	25	74	10	209	293	**11118**	19	49	13	10	43
Kristiansand S	1	10	1	2	13	39	3	128	170	**6374**	0	0	9	4	28
Arendal		10	5	1	16	29	10	81	120	**3942**	14	123	11	5	21
Telemark	3	15	4	2	21	52	14	120	186	**8214**	20	30	17	3	39
Tønsberg		10	9	6	25	32	10	150	192	**4234**	83	32	15	9	20
Hønefoss	1	14	0	2	16	33	0	55	88	**4216**	0	0	5	3	21
Drammen	1	17	7	2	26	49	12	166	227	**7383**	56	32	16	8	17
Bærum		10	0	0	10	25	0	41	66	**3952**	0	0	10	2	16
Lillehammer	3	9	21	3	33	38	20	148	206	**6055**	21	0	15	7	32
Elverum	1	18	3	3	24	56	8	123	187	**8338**	0	95	16	7	35
Østfold	2	16	5	3	24	81	7	198	286	**12766**	17	0	12	8	37
AHUS		29	18	10	57	123	39	338	500	**18155**	0	0	21	13	70
Ullevål		43	25	3	71	112	42	344	498	**17796**	27	0	21	8	72
RH		1	0	3	4	12	0	177	189	**2920**	128	103	2	3	2
SUM		***340***	***149***	***65***	***554***	***1212***	***262***	***3495***	***4969***	***189276***	*645*	*1251*	***277***	***134***	***764***
# Pr. mill inhab.		*64,9*	*28,5*	*12,4*	*105,8*	*231,4*	*50,0*	*667,4*	*948,9*	*ie. +2,8 %*					*145,9*
% of total		*61,4*	*26,9*	*11,7*	*100,0*	*24,4*	*5,3*	*70,3*	*100,0*	*from 2015*					*51,8*