



# Dialysis withdrawal in The Netherlands between 2000 and 2019: time trends, risk factors and centre variation

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## ABSTRACT

**Background.** Dialysis withdrawal is a common cause of death in dialysis-dependent patients. This study aims to describe dialysis withdrawal practice in The Netherlands, focussing on time trends, risk factors and centre variation.

**Methods.** Data were retrieved from the Dutch registry of kidney replacement therapy patients. All patients who started maintenance dialysis and died in the period 2000–2019 were included. The main outcome was death after dialysis withdrawal; all other causes of death were used for comparison. Time trends were analysed as unadjusted data (proportion per year) and the year of death was included in a multivariable logistic model. Univariable and multivariable analyses were performed to identify factors associated with withdrawal. Centre variation was compared using funnel plots.

**Results.** A total of 34 692 patients started dialysis and 18 412 patients died while on dialysis. Dialysis withdrawal was an increasingly common cause of death, increasing from 18.3% in 2000–2004 to 26.8% in 2015–2019. Of all patients withdrawing, 26.1% discontinued treatment within their first year. In multivariable analysis, increasing age, female sex, haemodialysis as a treatment modality and year of death were independent factors associated with death after dialysis withdrawal. Centre variation was large (80.7 and 57.4% within 95% control limits of the funnel plots for 2000–2009 and 2010–2019, respectively), even after adjustment for confounding factors.

**Conclusions.** Treatment withdrawal has become the main cause of death among dialysis-dependent patients in The Netherlands, with large variations between centres. These findings emphasize the need for timely advance care planning and

improving the shared decision-making process on choosing dialysis or conservative care.

**Keywords:** advance care planning, end-stage renal disease, end of life, kidney failure, mortality

## INTRODUCTION

Although dialysis is generally a life-prolonging treatment in patients with kidney failure, its treatment burden can be high. The dialysis population is rapidly ageing and, in the elderly, the survival benefit is more limited [1]. Concurrently, the impact on patients' health-related quality of life and functional status is large [2, 3]. The alternative of conservative care is generally offered and discussed before initiation of dialysis when kidney failure progresses. Once dialysis treatment has been initiated the question may arise whether treatment continuation remains beneficial, e.g. when quality of life decreases and/or comorbidity progresses. Treatment cessation is a common cause of death in chronic dialysis-dependent patients and age is a risk factor for dialysis withdrawal [4–10]. Previous studies have reported widely variable discontinuation rates, ranging from 7% to 31% [4, 11]. Although the designs and definitions vary between these studies, large differences exist, both between countries and periods of time. When comparing countries, large intercultural differences exist in the acceptability of the cessation of life-prolonging treatment, such as maintenance dialysis, for both patients and their physicians [12–14]. Two previous studies reported increasing rates of dialysis withdrawal over time within their regions: Ellwood *et al.* [4] in Canada and Chan *et al.* [8] in Australia and New Zealand. Studies from Europe, however,

## KEY LEARNING POINTS

### What is already known about this subject?

- Dialysis withdrawal is a common cause of death for chronic dialysis-dependent patients but reported withdrawal rates show large variations between individual studies. Although study designs and definitions vary, intercultural differences in the acceptability and applicability of dialysis discontinuation appear to play a key role.
- Age is a risk factor for withdrawal and the dialysis population is ageing. Two previous studies from Australia/New Zealand and Canada showed that withdrawal rates were increasing but these are dated or included only haemodialysis (HD) patients. Additionally, it is unknown if the same trend is seen in the European dialysis population.
- Dutch nephrologists experience treatment cessation as both formally and informally allowed and patient autonomy is considered fundamental in Western medicine, possibly resulting in higher withdrawal rates for patients in The Netherlands.

### What this study adds?

- Dialysis withdrawal has become the most common cause of death in The Netherlands with nearly one-third of patients dying after treatment withdrawal in 2019.
- Treatment withdrawal is associated with increasing age, female sex, HD as a treatment modality (compared with peritoneal dialysis) and year of death.
- Large variations between individual dialysis centres were found, even after adjusting for confounding factors, indicating significant variations in clinical practice. Variation between centres is increasing over time.

### What impact this may have on practice or policy?

- As survival after dialysis withdrawal is often short and withdrawal is increasingly common, physicians and their patients should discuss advance care planning early. Advance care planning has been shown to improve end-of-life care and patient and family satisfaction.
- Further studies are needed to improve our understanding of the large variations that exist between individual dialysis centres.
- International research collaboration is needed to further investigate withdrawal practices between countries.

are limited and none describe time trends. In large parts of the Western world, including The Netherlands, patient autonomy is considered fundamental in medicine and Dutch treating physicians experience treatment cessation as both formally and informally allowed [14]. In particular, in older and/or frail patients, conservative care is often, if not always, discussed, reflected by national guidelines and multiple large Dutch study initiatives in the last decade [15–20]. However, it is unknown if and/or to what extent these premises influence discontinuation rates and whether there is significant practice variation between Dutch hospitals. Hence the aim of this study was to describe dialysis withdrawal practices in The Netherlands over a long period of time, focussing on time trends, risk factors and centre variation for dialysis withdrawal.

## MATERIALS AND METHODS

### Study design

We performed a retrospective analysis of patients included in the REgistratie Nierfunctievervangende NEderland (RENINE), the Dutch national registry of all patients on Dialysis withdrawal in the Netherlands between 2000 and 2019

maintenance kidney replacement therapy, defined as the requirement of dialysis for at least 28 days or ever receiving a kidney transplant. It has a nationwide coverage of 100% of all centres offering dialysis treatment and >95% of all prevalent dialysis patients consent to participate in the registry [21]. In the RENINE, basic patient characteristics (i.e. sex, age and primary renal diagnosis), dialysis characteristics {i.e. modality [haemodialysis (HD) or peritoneal dialysis (PD)], location (in-centre or home dialysis), date of initiation, switching or termination of treatment} and date and cause of death are registered by treating physicians.

### Study population

All patients of all ages who initiated maintenance dialysis from 1 January 2000 to 31 December 2019, gave consent for registration in the RENINE and died within this period were included. Since the primary aim of this study was cause of death on dialysis, data for patients in whom dialysis was stopped due to kidney transplantation or recovery of kidney function were excluded. As all data were analysed anonymously, no additional informed consent for this study was required.

## Outcome parameters

The main study outcome was death by dialysis withdrawal, as registered by the treating physician. Dialysis withdrawal included the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) codes for ‘patient’s refusal of further treatment’, ‘dialysis withdrawal for medical reasons’ and ‘dialysis withdrawal for any other reason’ [22]. As the code for ‘dialysis withdrawal for medical reasons’ was added to the Dutch Renal Registry in 2010, we combined it with the code for ‘dialysis withdrawal for any other reason’. All other causes of death were used for comparison, including deaths with unknown aetiology, as cessation of dialysis treatment was deemed likely to be known to the treating physician. All causes of death were grouped into seven categories: cardiac disease, cerebrovascular disease, infection, malignancy, treatment withdrawal, other causes of death and death of uncertain aetiology [23]. For additional analyses, treatment withdrawal was further divided into early (i.e. within the first year after dialysis initiation) and late withdrawal (i.e. after the first year of treatment).

## Determinants

Age was assessed as age at death, except when comparing early versus late withdrawal, as age increases with treatment duration: here age at the start of dialysis was used. Primary renal diagnoses are registered in the RENINE using the ERA-EDTA coding system and for this study reduced to its four most prevalent diagnoses: renal vascular disease, glomerulonephritis, diabetes mellitus and all other diagnoses (including unknown aetiology) [22]. The group with the largest number of patients was used as the reference category. Dialysis vintage was defined as the total consecutive duration of the last dialysis treatment, regardless of changes in dialysis modality and/or location. If patients switched dialysis modality or location (i.e. in-centre to home dialysis or vice versa), only the last used modality or location before death was used for analyses, as its association with the decision to withdraw treatment was deemed the strongest. Home dialysis encompassed both home HD and PD. For year of death, four cohorts of 5 years (2000–2004, 2005–2009, 2010–2014 and 2015–2019) were created.

## Statistical analyses

Main analyses include assessment of time trends, risk factors and centre variation. First, time trends for dialysis withdrawal were analysed as unadjusted data (proportion per year) and year of death was ultimately included in a multivariable logistic model. Second, variables associated with cessation of dialysis were analysed as univariable analyses. All variables deemed clinically related to dialysis cessation (predefined as age, sex, primary renal diagnosis, dialysis modality and dialysis vintage) were then included in a multivariable logistic model. The location of dialysis was not included, as it was assumed to show collinearity with treatment modality. Finally, to assess practice variation between centres, individual centres were compared using funnel plots with 95% control limits [24]. Satellite locations of main centres, if present, were allocated to their main centre. To assess centre variation over time, we analysed the period 2000–2009 and 2010–2019 separately using two funnel

plots. As patient populations and the proportion of treatment modalities used varied between centres, adjustment was applied for the five factors most strongly associated with dialysis withdrawal in the multivariable analysis.

Descriptive statistics were expressed as numbers and percentages. Continuous data were expressed as means with standard deviations (SDs) for normally distributed data and medians with interquartile ranges (IQRs) for non-normally distributed data. Continuous determinants were categorized to account for non-linear associations. Risks were displayed as odds ratios (ORs) with 95% confidence intervals (CIs). Nominal data were compared using chi-squared tests and continuous data using either *t*-tests or Mann–Whitney *U*-tests for normally and non-normally distributed data, respectively. A *P*-value <0.05 was considered statistically significant. All analyses were performed using SPSS version 26 (IBM, Armonk, NY, USA) and funnel plots were created using Stata version 16.1 (StataCorp, College Station, TX, USA).

## RESULTS

A total of 34 692 patients in 62 centres started maintenance dialysis, of which 20 389 (58.8%) died within the study period. Of these deceased patients, 1961 (9.6%) received a kidney transplant after dialysis and prior to their death. Likewise, 16 patients (0.1%) were lost to follow-up (i.e. unknown if they were still on dialysis, transplanted or on conservative care) between dialysis and death. Both these groups were excluded, resulting in a cohort of 18 412 patients for analysis. Baseline characteristics of the study population are shown in Table 1. There were no missing values for any of the baseline characteristics.

During the whole study period, 4073 (22.1%) patients died after dialysis withdrawal, most commonly due to patient’s refusal of further treatment (Table 2). Of all patients withdrawing from dialysis, 1062 (26.1%) died within their first year of treatment. Patients who withdrew early (i.e. within the first year) did not statistically significantly differ from patients who withdrew late (i.e. after the first year) in terms of age at dialysis initiation, sex, dialysis modality and dialysis location but did in terms of primary renal diagnosis (Supplementary data, Table S1).

## Time trends

The proportion of patients who died due to dialysis withdrawal increased from 13.5% in 2000 (or 18.3% for 2000–2004) to 31.2% in 2019 (or 26.8% for 2015–2019), making it the most common cause of death (Figure 1). Death due to unknown aetiology was the most common cause of death in 2000 and it was the second most common cause of death in 2019. All other causes of death remained stable over time or became less prevalent. The mean age at dialysis initiation increased from  $67.0 \pm 11.7$  years to  $71.3 \pm 10.8$  years for the cohorts 2000–2004 and 2015–2019, respectively. The mean age at treatment withdrawal increased from  $73.6 \pm 11.2$  to  $74.6 \pm 10.2$  years for the cohorts 2000–2004 and 2015–2019, respectively. Time trends for ERA-EDTA codes for dialysis withdrawal are shown in Table 3. ‘Treatment withdrawal due to patient’s refusal of further treatment’ remained stable at ~60% of all dialysis withdrawal cases.

**Table 1. Characteristics of the total study cohort and comparison of patients dying after dialysis withdrawal versus patients with all other causes of death**

Characteristics	Study cohort (N = 18 412)	Dialysis withdrawal (n = 4073)	Other causes of death (n = 14 339)	P-value <sup>a</sup>
Age at death (years), mean ± SD	72.5 ± 11.4	75.5 ± 10.7	71.6 ± 11.4	<0.001
Sex (male), n (%)	11 400 (61.9)	2339 (57.4)	9061 (63.2)	<0.001
Primary renal diagnosis, n (%)				0.016
Renal vascular disease	5671 (30.8)	1334 (32.8)	4337 (30.2)	–
Glomerulonephritis	1262 (6.9)	258 (6.3)	1004 (7.0)	–
Diabetes mellitus	3923 (21.3)	841 (20.6)	3082 (21.5)	–
Others/unknown aetiology	7556 (41.0)	1640 (40.3)	5916 (41.3)	–
Dialysis vintage (months), median (IQR)	25.6 (39.8)	29.1 (44.6)	24.6 (38.5)	<0.001
Modality (HD versus PD), n (%)	15 757 (85.6)	3625 (89.0)	12 132 (84.6)	<0.001
Year of death, n (%)				<0.001
2000–2004	2478 (13.5)	454 (11.1)	2024 (14.1)	–
2005–2009	4673 (25.4)	907 (22.3)	3766 (26.3)	–
2010–2014	5566 (30.2)	1186 (29.1)	4380 (30.5)	–
2015–2019	5695 (30.9)	1526 (37.5)	4169 (29.1)	–
Location (in-centre versus home <sup>b</sup> ), n (%)	15 548 (84.4)	3582 (87.9)	11 966 (83.5)	<0.001

<sup>a</sup>Comparison between death by dialysis withdrawal versus other causes of death. There were no missing values for any of the variables.

<sup>b</sup>Includes both PD and in-centre HD.

**Table 2. Overall causes of death of the study cohort**

Cause of death	n	Total (%)	Subgroup (%)
Cardiac disease	3672	19.9	–
Cerebrovascular disease	660	3.6	–
Infection	2643	14.4	–
Malignancy	1394	7.6	–
Treatment withdrawal	4073	22.1	–
Patient refused further treatment	2517		61.8
Treatment withdrawn due to medical reasons or treatment ceased due to any other reason	1556		38.2
Other	2067	11.2	–
Uncertain aetiology	3903	21.2	–
Total	18 412	100.0	100.0

### Risk factors

In univariable analyses, factors that were statistically significantly associated with a higher likelihood of death due to dialysis withdrawal when compared with other causes of death were older age, female sex, increasing dialysis vintage, HD (as compared with PD) and more recent year of death (Table 3). All primary renal diagnosis groups (glomerulonephritis, diabetes mellitus and other diagnoses) were associated with having a lower likelihood of death due to dialysis withdrawal when compared with renal vascular disease. Finally, a multivariable logistic model was created using age, sex, primary renal diagnosis, dialysis vintage, dialysis modality and year of death (Table 4). After adjustment, primary renal diagnosis and dialysis vintage were no longer statistically significantly associated with dialysis withdrawal. Year of death was statistically significantly associated with dialysis withdrawal for the cohort 2015–2019 only. All other factors did not show major changes between univariable and multivariable analysis.

### Centre variation

Both the total number of patients (range 1–875) and proportion of patients who died due to dialysis withdrawal (range 0–41.2%) showed large variations between centres (unadjusted data for 2000–2019). Figure 2A and B showed adjusted data using funnel plots. After adjustment for age, sex, dialysis vintage, modality and year of death—the five factors most associated with dialysis withdrawal in the multivariable analysis—46 of 57 centres (80.7%) were within, 5 (8.8%) were above and 6 (10.5%) were below the 95% control limits for the 2000–2009 cohort (Figure 2A). For the 2010–2019 cohort, 35 of 61 (57.4%) were within, 12 (19.7%) were above and 14 (23.0%) were below the 95% control limits (Figure 2B). Hence centre variation increased between 2000–2009 and 2010–2019.

### DISCUSSION

This study shows that dialysis withdrawal is an increasingly common phenomenon in The Netherlands, even after adjustment for relevant confounding factors. With nearly one-third of deaths attributed to dialysis withdrawal in 2019, the proportion has more than doubled in 20 years, making dialysis withdrawal the most common cause of death by a large margin. Moreover, our study shows that increasing age, female sex, use of HD as a treatment modality and year of death are associated with dialysis withdrawal. Finally, our study shows that withdrawal rates differ significantly between dialysis centres, again even after adjustment for relevant confounders, likely indicating large practice variations between centres rather than variations in the patient case mix. Furthermore, this centre variation increased between 2000–2009 and 2010–2019.

The (unadjusted) rate of dialysis withdrawal increased substantially during our study period: 13.5% in 2000 to 31.2% in 2019 or, for 5-year strata, 18.3% in 2000–2004 to 26.8% in 2015–2019. These results are in line with the findings by two

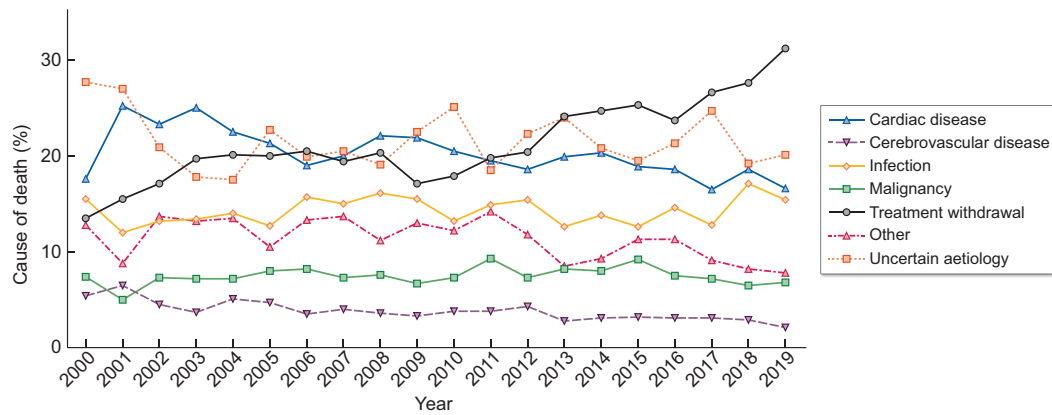


FIGURE 1: Causes of death (grouped) per calendar year of death. Proportion of each cause of death per calendar year, unadjusted data.

Table 3. ERA-EDTA codes for treatment withdrawal per 5-year strata

Reason for withdrawal	2000–2004 (n = 454)	2005–2009 (n = 907)	2010–2014 (n = 1186)	2015–2019 (n = 1526)
Patient refused treatment, n (%)	286 (63.0)	579 (63.8)	766 (64.6)	886 (58.1)
Treatment withdrawn due to medical reasons or treatment ceased due to any other reason <sup>a</sup> , n (%)	168 (37.0)	328 (36.2)	420 (35.4)	640 (41.9)

<sup>a</sup>Displayed as a combined group as the ERA-EDTA code ‘dialysis withdrawal for medical reasons’ was added to the Dutch Renal Registry in 2010.

Table 4. Association between patient and dialysis characteristics and death by dialysis withdrawal versus any cause of death

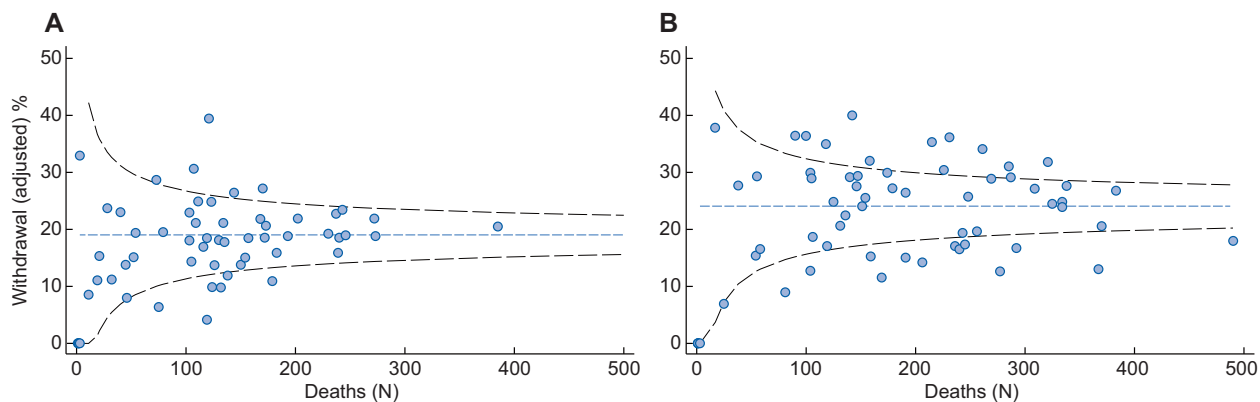
Characteristics	Univariable analyses	Multivariable analysis
Age at death (years)		
<60	(Reference)	(Reference)
60–64	1.00 (0.82–1.14)	0.98 (0.82–1.18)
65–69	1.12 (0.96–1.32)	1.09 (0.93–1.29)
70–74	<b>1.45 (1.25–1.68)</b>	<b>1.41 (1.22–1.64)</b>
75–79	<b>1.89 (1.64–2.16)</b>	<b>1.82 (1.58–2.09)</b>
>80	<b>2.77 (2.37–3.08)</b>	<b>2.53 (2.21–2.89)</b>
Sex (female versus male)	<b>1.27 (1.19–1.37)</b>	<b>1.28 (1.19–1.38)</b>
Primary renal diagnosis		
Renal vascular disease	(Reference)	(Reference)
Glomerulonephritis	<b>0.84 (0.72–0.97)</b>	1.02 (0.87–1.19)
Diabetes mellitus	<b>0.89 (0.80–0.98)</b>	1.11 (1.00–1.23)
Others	<b>0.90 (0.83–0.98)</b>	1.05 (0.96–1.14)
Vintage		
0–6 months	(Reference)	(Reference)
6–24 months	1.01 (0.91–1.13)	0.98 (0.87–1.09)
2–4 years	<b>1.18 (1.05–1.32)</b>	1.07 (0.95–1.20)
>4 years	<b>1.36 (1.22–1.52)</b>	1.08 (0.96–1.21)
Modality (HD versus PD)	<b>1.47 (1.32–1.64)</b>	<b>1.30 (1.17–1.46)</b>
Year of death		
2000–2004	(Reference)	(Reference)
2005–2009	1.07 (0.95–1.22)	0.95 (0.84–1.08)
2010–2014	<b>1.21 (1.07–1.36)</b>	0.99 (0.87–1.12)
2015–2019	<b>1.63 (1.45–1.83)</b>	<b>1.30 (1.15–1.47)</b>

Results shown as ORs with 95% CIs. Statistically significant risks in bold. All factors shown were included in the multivariable logistic model.

previous studies from non-European countries: Ellwood *et al.* [4] described an increase in treatment withdrawal as cause of death from 7.9% to 19.5% between 2001 and 2009 in Canada.

These proportions are similar to our data for those years. Our study additionally shows that in the past decade, withdrawal rates increased even further. Chan *et al.* [8] reported an increase in dialysis withdrawal as the cause of death in 11–32% of patients between 1997–2000 and 2013–2016, respectively, in New Zealand and Australia. Again, these percentages are comparable to ours, albeit slightly higher, possibly explained by their study only including patients on HD, as PD was associated with lower discontinuation rates in our study. The withdrawal rate in the last year of our study cohort (31.2% in 2019) is one of the highest reported to date, partially explained by it being the most recent data.

The increasing withdrawal rates over time could be explained by changes in the dialysis population, most notably age: in 20 years, the mean age at dialysis initiation in our study population increased from 67.0 to 71.3 years. Concurrently, the survival for elderly patients on maintenance dialysis improved: the 1-year crude mortality in The Netherlands decreased from 19% to 16% for incident dialysis patients >65 years of age between 2010–2014 and 2015–2018, respectively [21]. A comparable decrease was seen for 3-year mortality. As a result, more older patients will be exposed to long-term dialysis and its associated high treatment burden. Interestingly, even after adjustment for confounding factors, including age, withdrawal in the last 5 years of the study period became significantly more frequent. While dialysis withdrawal increased, the breakdown in withdrawal on patients’ request or medical or other grounds remained stable over time, as shown in Table 3. It is likely that the increase in dialysis withdrawal results from both patients’ behavioural changes and changes in the medical conditions of an ageing



**FIGURE 2:** (A) Funnel plot for dialysis withdrawal variance between centres, 2000–2009. Each dot represents one participating centre. Data shown are dialysis withdrawal as a percentage of total causes of death, adjusted for age at death, sex, dialysis vintage, dialysis modality and year of death. The horizontal line represents the mean, dotted lines above and below this line represent the 95% control limits. (B) Funnel plot for dialysis withdrawal variance between centres, 2010–2019. Each dot represents one participating centre. Data shown are dialysis withdrawal as a percentage of total causes of death, adjusted for age at death, sex, dialysis vintage, dialysis modality and year of death. The horizontal line represents the mean, dotted lines above and below this line represent the 95% control limits.

dialysis population. However, changes in the ERA-EDTA codes for treatment withdrawal per 2010 could also have played a role. Another influencing factor could be the increasing number of kidney transplantations: from 2000–2004 to 2015–2019, the mean number of kidney transplants in The Netherlands increased from 597 to 945 per year (an ~60% increase) [25]. Meanwhile, the mean prevalent dialysis population increased from 5076 to 6337 patients (an ~25% increase). As patients eligible for transplantation are often younger and less frail, the risk profile of the population remaining on dialysis increases, possibly increasing withdrawal rates. In our analyses we were able to adjust for age but not for frailty. Finally, legalization of active euthanasia in The Netherlands in 2001 could have influenced the acceptability of treatment withdrawal [26]. Although active euthanasia and cessation of life-sustaining treatment, such as maintenance dialysis, are fundamentally different, this legislation might have increased the willingness of patients, but also their healthcare providers, to discuss treatment and withdrawal of treatment at the end of life.

We identified and confirmed several factors associated with dialysis withdrawal in our study population: age, female sex, use of HD as a treatment modality and year of death. Many studies also showed that age is associated with dialysis withdrawal, as increasing age is often accompanied by increased frailty and dependency, worsening of comorbidities and decreasing life expectancy in general [4–10]. Female sex is also an identified risk factor [4, 6, 7, 10, 27]. Possibly this is partially the result of men dying more often of other causes, such as cardiovascular disease, but could also be a result of psychological factors and/or gender inequality in some countries. Our study shows that, compared with PD, HD is a risk factor for dialysis withdrawal. This was previously described by several authors and is likely a result of patient selection: frail patients and/or patients requiring emergency dialysis are more often started on HD [11, 27]. A previous study also showed that, on average, treatment satisfaction is higher in patients treated with PD than those treated with HD, possibly resulting in lower withdrawal rates [28].

Both primary renal diagnosis and dialysis vintage were associated with dialysis withdrawal in univariable analysis but not in multivariable analysis. Likely this is the result of a strong correlation with age: patients with renal vascular disease (used as reference category) are typically significantly older than patients with other diagnoses and patients age with increasing treatment duration. Multiple studies also did not find any association between renal diagnoses and withdrawal rates, although grouping of diagnoses differs between studies [4, 5, 29]. With increasing dialysis duration, several (non-age and non-uraemia related) challenges can arise, e.g. vascular access problems in HD. However, multiple studies also did not find an (independent) correlation between dialysis vintage and withdrawal rates [5, 7, 10, 30].

Finally, our data show a remarkable variation in withdrawal rates between centres. This result is both in line with a previous study showing large regional differences within the USA and one study reporting widely varying unadjusted withdrawal rates between seven dialysis units in Scotland [6, 7]. These differences could be due to varying patient profiles between centres, differences in offering conservative care as an alternative to dialysis treatment, varying patient and healthcare provider beliefs on (the acceptability of) dialysis withdrawal, variations in the practice of engaging in end-of-life discussions or a reflection of subjective reporting of treatment cessation as the (main) cause of death. By adjusting for several patient factors, including age as the factor most associated with dialysis withdrawal, we tried to limit the effect of the varying case mix between centres. The variation in withdrawal rates between centres is increasing over time, contrary to what one would expect, as Dutch guidelines in the last few years (2016 for the guideline on kidney replacement therapy and 2017 for the palliative care guideline) tried to harmonize the dialysis initiation and cessation practices. Due to small numbers, we did not assess centre variation per year and likely it will take some time for clinicians to adapt their practices. Nevertheless, further qualitative research is needed to clarify these differences and explore the views on and reporting of treatment cessation by the treating physicians in these centres.

The main limitations of this study are its retrospective nature and its lack of a pre-defined definition of dialysis withdrawal, which is a common problem in studies reporting on dialysis withdrawal practices. A systematic review from 2013 found seven different definitions in 7 studies; the remaining 16 studies did not report any definition at all [31]. Using well-defined codes for determining the cause of death during the whole 20-year follow-up period partially limits this problem and showed that most withdrawals were patient initiated. Another possible limitation could be the limited data on patient characteristics, as important factors, such as comorbidities and frailty, are not yet registered nationally in The Netherlands. This could have influenced the effect of factors where patient selection comes into play, such as dialysis modality and location of dialysis. Finally, using incident dialysis patients only possibly resulted in some selection of causes of death shortly after the start of the study period.

The main strength of our study is the use of a large dataset, including nearly all (>95%) patients on maintenance dialysis in The Netherlands. The observed significant variations in withdrawal practices between individual centres further emphasizes the limited usefulness of studies with a smaller number of centres, while this nationwide study generates a generalizable result for all Dutch patients. Also, the uniform collection and reporting of data for >20 years enables us to describe reliable time trends.

The clinical implications of our study are 2-fold: first, recognizing the high number of treatment withdrawals—26% withdrew within the first year after dialysis initiation—could help physicians improve the shared decision-making process on starting dialysis or not. Conservative care could be a viable option for selected patients instead of starting and early withdrawal from dialysis. When and how to best inform patients on dialysis or conservative care remains an ongoing debate in nephrology [19]. The effect of active counselling regarding conservative care on early dialysis withdrawal deserves further study. Early treatment withdrawal might be expected to decrease when patients are actively counselled on conservative care. In our study, however, we observed an increase in dialysis withdrawal at times when conservative care is more openly and frequently discussed. Second, as international guidelines advise, treatment withdrawal can be a good option and should be discussed in certain scenarios, e.g. when a patient's life expectancy is short and/or quality of life is low [32]. The increasing withdrawal rates emphasize the need for timely advance care planning, as the impact on patients and their relatives can be great and life expectancy after withdrawal is generally short [33]. Advance care planning for patients with kidney failure has been shown to improve end-of-life care and patient and family satisfaction [34, 35]. By not only improving when and how to start dialysis, but also when and how to cease treatment, better individualized patient care can be achieved.

In conclusion, dialysis withdrawal has become the main reported cause of death in The Netherlands among dialysis-dependent patients during 2000–2019, with large variations between centres. These findings emphasize the need for timely advance care planning and urge treating healthcare professionals

to inform their patients when choosing to start dialysis or not. Further studies are needed to further clarify withdrawal practices between countries and centres.

## SUPPLEMENTARY DATA

Supplementary data are available at [ndt](https://ndt.oxfordjournals.org/) online.

## FUNDING

No additional funding for this study was received.

## AUTHORS' CONTRIBUTIONS

All authors were involved in the study design, data interpretation and drafting of the manuscript. M.O. performed the analyses under supervision of T.H. T.H. created the funnel plots. All authors approved the final version.

## CONFLICT OF INTEREST STATEMENT

W.B. received grant support from Zilveren Kruis Insurance, outside the submitted work. All other authors declare they have no competing interests.

## DATA AVAILABILITY STATEMENT

The data underlying this article were provided by the Nefrovisie Foundation under licence and will be shared on request to the Nefrovisie Foundation.

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