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ORIGINAL ARTICLE

Propensity score matched mortality comparisons of peritoneal and in-centre haemodialysis: systematic review and meta-analysis

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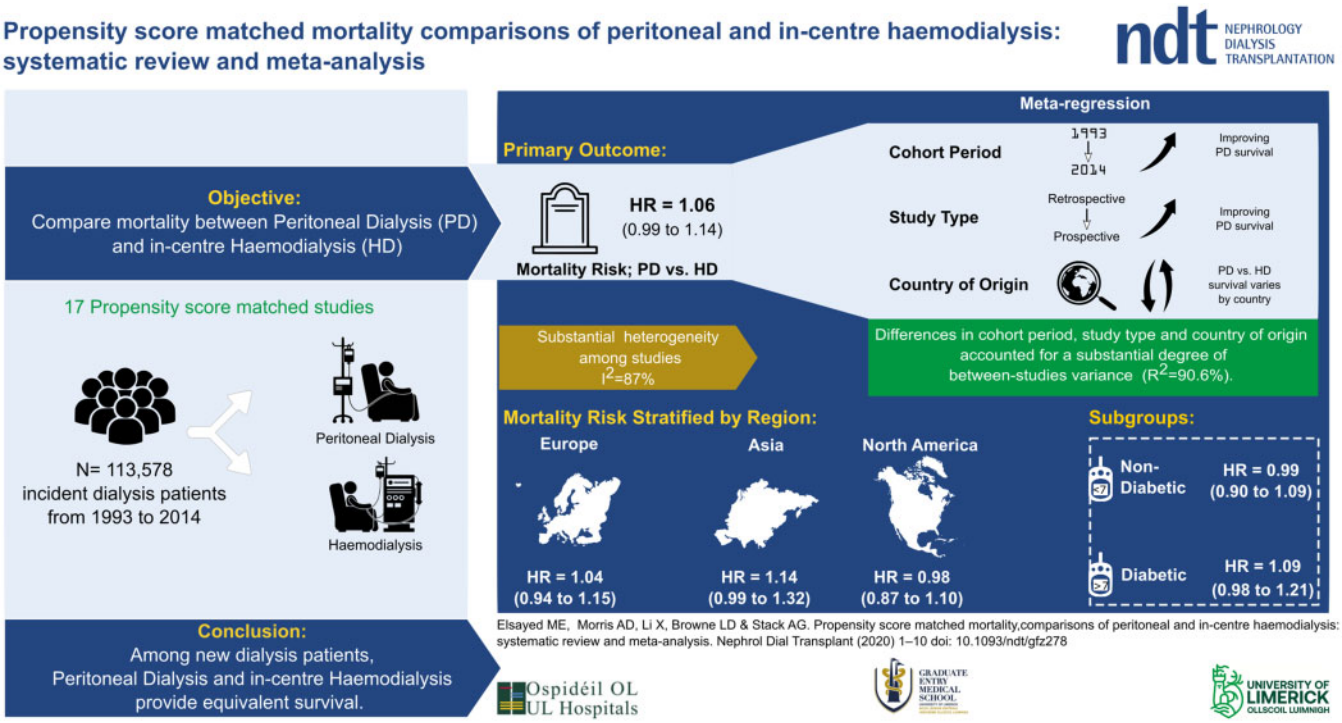

ABSTRACT

Background. Accurate comparisons of haemodialysis (HD) and peritoneal dialysis (PD) survival based on observational studies are difficult due to substantial residual confounding that arises from imbalances between treatments. Propensity score matching (PSM) comparisons confer additional advantages over conventional methods of adjustment by further reducing selection bias between treatments. We conducted a systematic review of studies that compared mortality between in-centre HD with PD using a PSM-based approach.

Methods. A sensitive search strategy identified all citations in the PubMed, Cochrane and EMBASE databases from inception through November 2018. Pooled PD versus HD mortality hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated through random-effects meta-analysis. A subsequent meta-regression explored factors to account for between-study variation.

Results. The systematic review yielded 214 citations with 17 cohort studies and 113 578 PSM incident dialysis patients. Cohort periods spanned the period 1993–2014. The pooled HR for PD versus HD was 1.06 (95% CI 0.99–1.14). There was considerable variation by country, however, mortality risks for PD versus HD remained virtually unchanged when stratified by geographical region with HRs of 1.04 (95% CI 0.94–1.15), 1.14 (95% CI 0.99–1.32) and 0.98 (0.87–1.10) for European, Asian and American cohorts, respectively. Subgroup meta-analyses revealed similar risks for patients with diabetes [HR 1.09 (95% CI 0.98–1.21)] and without diabetes [HR 0.99 (95% CI 0.90–1.09)]. Heterogeneity was substantial ($I^2 = 87\%$) and was largely accounted for by differences in cohort period, study type and country of origin. Together these factors explained a substantial degree of between-studies variance ($R^2 = 90.6\%$).

Conclusions. This meta-analysis suggests that PD and in-centre HD carry equivalent survival benefits. Reported differences in survival between treatments largely reflect a combination of factors that are unrelated to clinical efficacy.

Keywords: haemodialysis, mortality, peritoneal dialysis

INTRODUCTION

Despite observed improvements in survival among patients with end-stage kidney disease (ESKD), the overall risk of death remains alarmingly high for many patients treated with dialysis [1, 2]. Haemodialysis (HD) and peritoneal dialysis (PD) are very different treatment strategies, both technically and mechanistically, and the net benefit of each strategy on health is dependent on the individual clinical efficacy in controlling fluid status and correcting metabolic derangements without contributing to infection risk or cardiovascular disease. For patients approaching ESKD, a full discussion of the potential advantages and disadvantages of PD and HD is an essential component of modern pre-dialysis care programmes. The optimal dialysis modality that confers the greatest survival advantage remains controversial in the absence of evidence from successfully completed randomized controlled trials [3, 4].

To date, comparative studies of survival between PD and in-centre HD have yielded conflicting results and are purely based on observational studies with no randomization of treatment. Substantial systematic differences are found between PD and HD and contribute to substantial selection bias, and many of these characteristics are directly associated with mortality [5–7]. Methodologically, these systematic differences may surpass the ability of conventional methods to adjust for treatment differences and prevent the design and completion of randomized controlled clinical trials. Consequently there is a need for novel and more robust statistical methods to allow more meaningful comparisons [8]. The use of propensity scores, which was introduced in the 1980s, has gained popularity in the last decade (Supplementary data, Figure S1). These are probability scores that are conditioned on treatment assignment. They are most commonly used in matching subjects of different treatment groups to achieve balance in the distribution of measured confounders, allowing direct estimation of causal treatment effects (TEs). They have been shown to outperform conventional regression methods and provide less biased estimates [9–11].

Given the residual uncertainty regarding the optimal survival strategy between HD and PD, we conducted a systematic review and meta-analysis of studies that utilized exclusively a propensity score matching (PSM) approach to compare mortality risks.

MATERIALS AND METHODS

Search strategy, study selection and data synthesis

The protocol of this review was registered and published previously on PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.php? ID=CRD42014014323).

Electronic searches were conducted on the PubMed, Cochrane and EMBASE databases from inception until 30 November 2018 using a sensitive search strategy (Supplementary data, Table S1). Studies were included if they met the following criteria: (i) primary objective to compare mortality risks between PD and in-centre HD, (ii) adult patients with incident ESKD, (iii) PSM as the primary strategy to control for confounding and (iv) published in the English language. Studies that employed propensity score methods other than a matching strategy were not included. In addition, editorials, letters and case reports were also excluded. Two reviewers (M.E.E. and A.D.M.) independently screened and identified studies for inclusion from a web-based platform [12]. In cases of disagreement, a subsequent discussion took place with the resolution of discrepancies by consensus. Data were extracted using a form that was developed prior to article review. The following data were extracted: year of publication, type of study, country of the study, source of the cohort, years of cohort establishment, last year of follow-up, variables used to derive propensity scores, type of matching, number of matched patients and risk of death estimates expressed as hazard ratios (HRs) or relative risks (RRs). Information was retrieved where available on analysis by age group, diabetes and duration on dialysis (vintage), as these factors have previously been shown to modify the impact of modality on mortality [13].

Quality assessment and risk of bias

Risk of bias was examined against the Newcastle–Ottawa Scale for observational studies [14]. This scale awards studies a star-based score that serves as a quick visual assessment tool across three main domains: selection of study groups (up to four stars), comparability of the groups (up to two stars) and ascertainment of the exposure or the outcome of interest (up to three stars). A maximum score of nine stars reflects a study with the highest methodological quality. We also investigated the quality of reporting on PSM methods and the appropriateness of their use. This was assessed on the following domains as proposed by Austin [15]: derivation of propensity scores including choice of variables, reporting and handling of missingness, type of matching methods and definitions, assessment of matching adequacy from appropriate balance diagnostics and adjustment for within-pair correlation in the final model.

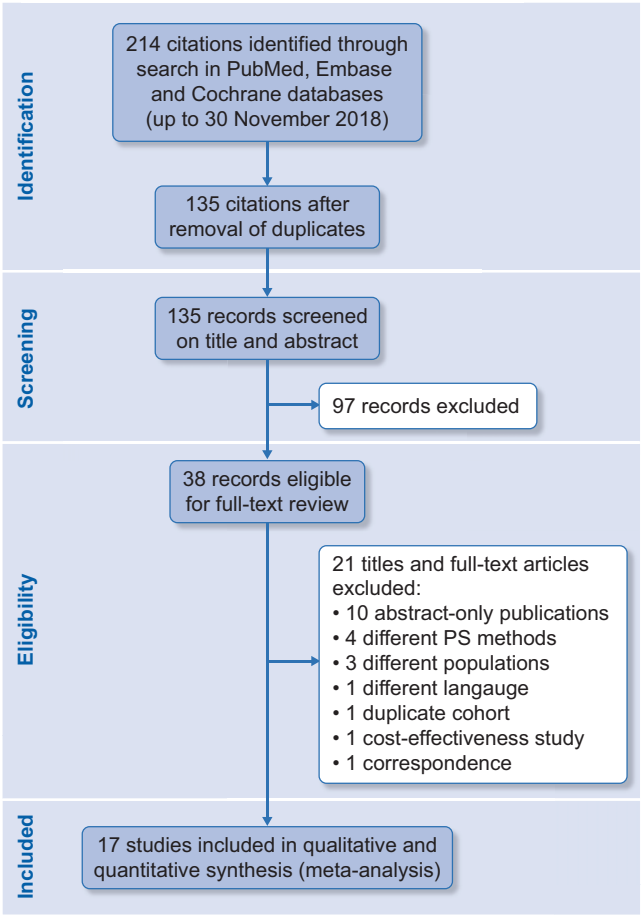

FIGURE 1: PRISMA flow diagram.

Statistical analysis

All analyses were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A random effects meta-analysis model proposed by DerSimonian and Laird [16] was used to calculate the pooled TE estimate. Robustness of outcome was examined through influential sensitivity analysis where a series of meta-analysis models were fitted with one study being omitted at a time. This helped to explore outlier studies that could have largely influenced the results towards a certain direction. Between-studies heterogeneity was assessed using chi-square with a significance level of $P < 0.10$ and I^2 statistic with the following suggested thresholds: low (25–49%), moderate (50–74%) and high (>75%). Random effects meta-regression allowed exploration of factors accounting for between-studies variation. This was performed through regression of the HR of PD versus HD on potential explanatory factors after logarithmic transformation. Since the outcome was on the logarithmic scale (log HR of PD versus HD), factors with a significantly positive coefficient value reflected an increase in HR in relation to the referent factor while factors with a significantly negative coefficient indicated a corresponding decrease in HR. Covariates considered in the meta-regression model included country location, cohort design (classified as retrospective or prospective and the time period of the study. Three chronological periods were defined as follows: historic, when the study population was initiated on dialysis prior to 2000; middle, where cohort recruitment was between 2000 and 2007; and recent, if the cohort began dialysis after 2007. Potential publication bias was assessed by evaluating the study effect using visual inspection of funnel plots and by conducting Egger's regression test. Analyses were conducted using R statistical software (R Foundation, Vienna, Austria).

RESULTS

Search results and characteristics of included studies

The initial search identified 214 citations. After duplicate removal and exclusion on title and abstract screening, 38 citations qualified for a full text review. A further 21 studies were excluded for specific reasons, as shown in Figure 1. Following these exclusions, a total of 17 studies, which were published

Table 1. Characteristics of included studies

	Year of publication	Authors	Country	Source of cohort	Type of study	Start year	End year	Last follow-up	Number of matched HD patients	Number of matched PD patients	Type of primary analysis	Special characteristics
1	2018	Thiery *et al.* [20]	France	REIN registry	Prospective	2006	2008	2013	3088	1105	As treated	–
2	2017	Rigoni *et al.* [21]	Italy	Single centre	Retrospective	2008	2014	2015	279	132	As treated	–
3	2016	Wang *et al.* [27]	Taiwan	NHIRD	Retrospective	2000	2010	2011	975	975	Intention to treat	Patients with previous history of stroke
4	2016	van de Luijtgaarden *et al.* [17]	Europe	ERA-EDTA registry	Prospective	1993	1997	2002	8198	8198	Intention to treat	–
		van de Luijtgaarden *et al.* [17]			Prospective	1998	2002	2007	9610	9610	Intention to treat	–
		van de Luijtgaarden *et al.* [17]			Prospective	2003	2007	2012	9856	9856	Intention to treat	–
5	2016	Lee *et al.* [18]	Korea	Multicentre cohort	Prospective	2008	2013	2015	199	199	Intention to treat	Patients with acceptable controlled diabetes
		Lee *et al.* [18]			Prospective	2008	2013	2015	36	36	Intention to treat	Patients with poorly controlled diabetes
6	2015	Yang *et al.* [26]	Taiwan	NHIRD	Retrospective	1999	2010	2010	244	122	Intention to treat	Patients with ESRD due to APKD
7	2015	Yang *et al.* [28]	Singapore	Single centre	Retrospective	2005	2010	2013	225	225	As treated	–
8	2015	Waldum-Grevbo *et al.* [19]	Norway	Norwegian renal registry	Prospective	2005	2012	2012	682	682	Intention to treat	–
9	2014	Kumar *et al.* [22]	USA	KPSC database	Prospective	2001	2013	2013	1003	1003	Intention to treat	–
10	2014	Kim *et al.* [29]	Korea	HIRA registry	Prospective	2005	2008	2009	7049	7049	Intention to treat	–
11	2014	Contreras *et al.* [23]	USA	USRDS	Prospective	1995	2006	2009	1352	1352	Intention to treat	Patients with SLE
12	2013	Choi *et al.* [30]	Korea	Multicentre	Prospective	2008	2011	2011	278	278	Intention to treat	–
13	2013	Chang *et al.* [31]	Korea	Single centre	Retrospective	2000	2009	2010	212	212	Intention to treat	–
14	2012	Lievense *et al.* [24]	USA	Da Vita database	Prospective	2001	2006	2007	4008	4008	Intention to treat	–
15	2012	Chang *et al.* [32]	Taiwan	NHIRD	Retrospective	1997	2006	2006	4721	4721	Intention to treat	–
16	2010	Weinhandl *et al.* [25]	USA	CMS ESRD database	Retrospective	2003	2003	2006	6337	6337	Intention to treat	–
17	2010	Chou *et al.* [33]	Taiwan	Single centre	Retrospective	1996	2006	2006	78	78	As treated	Patients with positive hepatitis C virus infection

REIN, Renal Epidemiology and Information Network; NHIRD, National Health Insurance Research Database; ERA-EDTA, European Renal Association–European Dialysis and Transplant Association; APKD, adult polycystic kidney disease; KPSC, Kaiser Permanente Southern California; HIRA, Health Insurance Review and Assessment Service; USRDS, United States Renal Data System; SLE, systemic lupus erythematosus; CMS, Centers for Medicare and Medicaid Services.

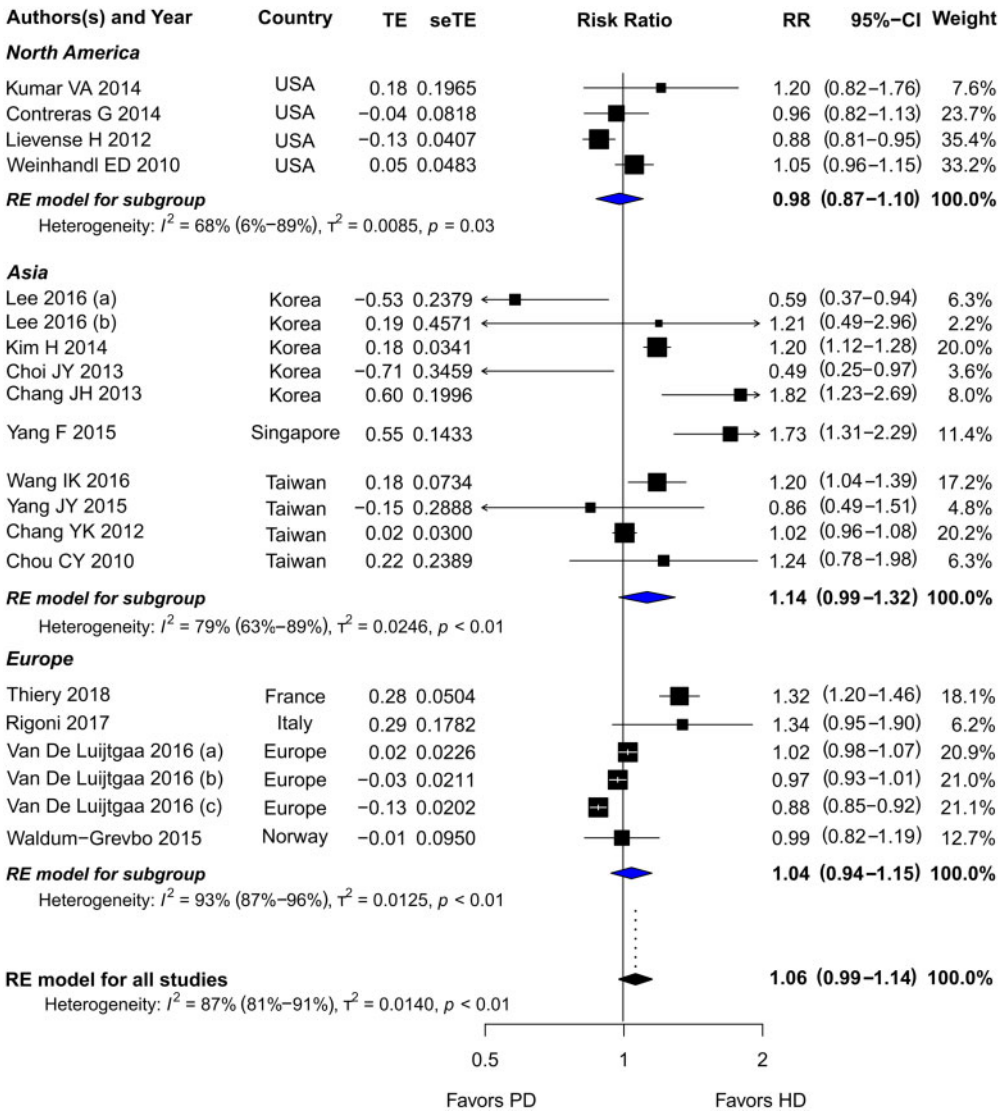

FIGURE 2: Forest plot for meta-analysis of PSM studies comparing mortality risk of PD versus in-centre HD. seTE, standard error of treatment effect.

between 2010 and 2018, contributed to the final meta-analysis. These included 20 historical cohorts, as two studies included >1 cohort [17, 18]. Ten studies were registry-based, three were from multicentre cohorts and the remainder were single-centre studies. There was wide geographical variability, with four studies reporting on European cohorts [17, 19–21], a further four on North American patients [22–25] and nine on dialysis patients from Asian countries. All studies included incident patients who were initiated on dialysis over a period from 1993 to 2014, with six cohorts having patients commencing dialysis before the year 2000 [17, 23, 26, 32, 33]. The total number of dialysis patients was 441715, from which a total of 114 608 patients were matched on propensity scores and contributed to the final analysis. Table 1 describes the characteristics of included studies. Some studies compared mortality risks in populations with specific characteristics, such as those with a previous history of stroke [27], with systemic lupus erythematosus [23], with adult polycystic kidney disease as the cause of ESKD [26] and with chronic hepatitis C [33].

Meta-analysis of mortality risks between PD and in-centre HD

The HR of death for PD versus in-centre HD varied among PSM cohort studies. Overall, 10 studies did not find a significant difference in mortality between PD and in-centre HD [17–19, 21–23, 25, 26, 32, 33], 4 indicated better survival outcome with PD [17, 18, 24, 30] and the remaining studies favoured better survival with in-centre HD [20, 27–29, 31]. The overall pooled HR of death for PD versus HD was 1.06 [95% confidence interval (CI) 0.99–1.14], demonstrating that PD and HD have similar survival rates. Although there was considerable variation in magnitude and direction of the PD/HD HR by country of origin, meta-analyses on studies from the same geographical region (Europe, Asia and North

Table 2. Description of effect modifiers of the association between dialysis modality and risk of death within included studies

	Year of publication	Authors	Subgroup analysis on PSM cohort	Factors defining subgroups	Effect of studied factors with significant results	Vintage effect examined on PSM cohort	Effect of vintage on PD-HD RR
1	2018	Thiery *et al.* [20]	No		–	No	–
2	2017	Rigoni *et al.* [21]	No		–	No	–
3	2016	Wang *et al.* [27]	Yes	Age, sex, diabetes and eight other comorbidities	Higher RR in PD group among women, diabetics and those with four other comorbidities	Yes	No difference in risk in first year. Higher RR in PD group in the second year
4	2016	van de Luijtgaarden *et al.* [17]	Yes	Age and diabetes	Higher RR in PD group in patients ≥65 years old. Diabetes has no effect	No	–
		van de Luijtgaarden *et al.* [17]			Lower RR in PD group among patients <65 years old and non-diabetic patients		–
		van de Luijtgaarden *et al.* [17]			Lower RR in PD group in non-diabetic patients		–
5	2016	Lee *et al.* [18]	No	–	–	No	–
		Lee *et al.* [18]			–	No	–
6	2015	Yang *et al.* [26]	Yes	Age and incident calendar year	No significant effect	No	–
7	2015	Yang *et al.* [28]	Yes	Age, diabetes and cardiovascular disease	Higher RR in PD group with diabetes, cardiovascular disease and non-diabetic patients >65 years old	Yes	No difference in risk in the first year but increased risk of death thereafter in PD group
8	2015	Waldum-Grevbo *et al.* [19]	Yes	Age, sex and diabetes	Lower RR in PD group among patients ≤65 years old	Yes	No change in RR over time
9	2014	Kumar *et al.* [22]	No			Yes	Lower risk of death in PD group in the first 2 years then no difference thereafter
10	2014	Kim *et al.* [29]	Yes	Age, sex, diabetes mellitus and eight other comorbidities	Higher RR in PD group in patients ≥55 years old and those with more than one comorbidity. Diabetes has no effect	Yes	No difference in risk in the first 6 months but increased risk of death thereafter
11	2014	Contreras *et al.* [23]	No			No	–
12	2013	Choi *et al.* [30]	Yes	Age, diabetes and sex	Lower RR in PD group among non-diabetic patients ≤65 years old and non-diabetic females	Yes	No difference in the first year. Lower RR in PD after 18 and 25 months
13	2013	Chang *et al.* [31]	Yes	Age, diabetes and modified Charlson comorbidity score	Higher RR in PD group with diabetes and patients with a modified Charlson comorbidity score >5	No	–
14	2012	Lievense *et al.* [24]	Yes	BMI groups	Lower RR in PD group with baseline BMI of 18.50–29.99 kg/m^2	No	–
15	2012	Chang *et al.* [32]	Yes	Age groups and Charlson comorbidity score	Higher RR in PD group in patients ≥65 years old and patients with high Charlson comorbidity scores	Yes	Higher RR in PD group in the first 3 years in 1997–2001 cohort. No change over time in 2002–2006 cohort
16	2010	Weinhandl *et al.* [25]	Yes	Age, diabetes and cardiovascular disease	Higher RR in PD group in patients ≥65 years old, diabetics and patients with cardiovascular disease	Yes	No difference in RR in the first year. Higher risk in PD group in second and third years
17	2010	Chou *et al.* [33]	No	–		No	

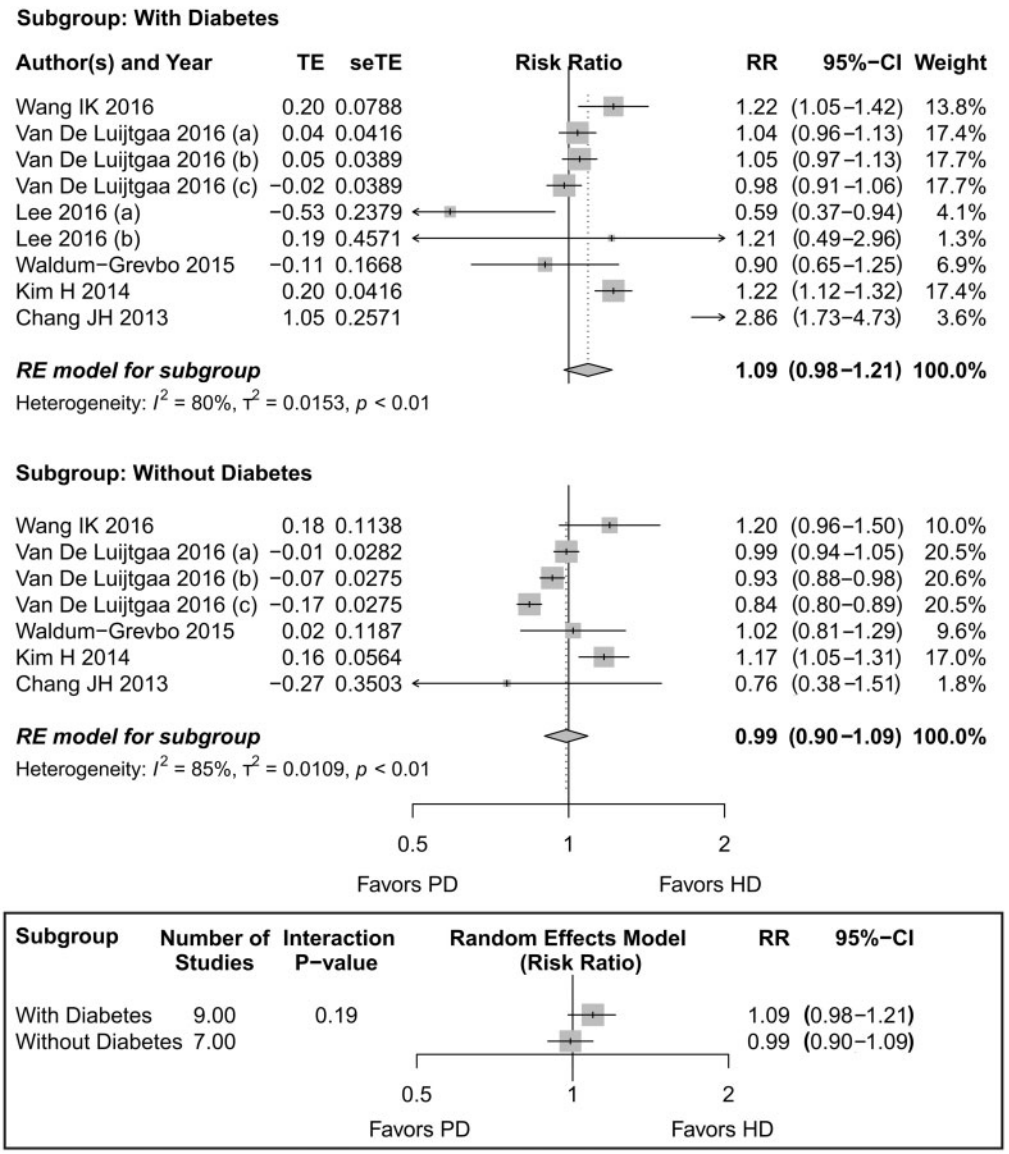

FIGURE 3: Forest plots for meta-analyses of PD versus HD mortality risk by diabetes. seTE, standard error of treatment effect.

American) showed equivalent mortality risks (Figure 2). Subsequent influential sensitivity analyses revealed virtually identical results (Supplementary data, Figure S2). There was a substantial degree of heterogeneity across cohorts, ($I^2 = 87\%$, $P < 0.001$). No significant publication bias was found, as confirmed by the Egger's test (Supplementary data, Figure S4). However, a number of studies fell outside the pseudo 95% confidence limits of the effect size, again confirming substantial heterogeneity.

The multivariate metaregression analysis key factors that contributed to this heterogeneity (Supplementary data, Table S2). Differences in the country of origin, time period during which cohorts were recruited and the type of study design (retrospective versus prospective) explained 90.6% of between-study variance. Further inspection revealed significant improvements in the HR for PD versus HD over time when comparisons were made across cohort periods (Supplementary data, Figure S3).

Effect modifiers of the association between dialysis modality and risk of death

Studies that tested for interactions and explored effect modification of selected variables on the PD/HD mortality relationship are shown in Table 2. The effect of diabetes on the relationship of dialysis modality and mortality was examined in eight studies (10 cohorts). Analyses of four cohorts with diabetes revealed higher mortality for PD than for HD [25, 27, 28, 31]. In three cohort studies without diabetes, mortality risks were significantly lower on PD than HD [17, 30]. A non-significant effect was reported for the other three cohorts [17, 19, 29]. One study looked at the effect of diabetes control among diabetic patients and showed better outcome for PD

patients in the group that had better glycaemic control [18]. Subgroup meta-analyses were conducted in six studies that revealed the pooled HR for PD (versus HD) was 1.09 (95% CI 0.98–1.21) for diabetic patients and 0.99 (95% CI 0.90–1.09) for non-diabetic patients (Figure 3). The interaction term for diabetes and dialysis modality was non-significant.

Age exerted a significant effect in eight cohorts, with five showing worse outcomes for PD among older patients and three studies indicating favourable outcomes among younger patients. Four cohorts showed no age effect. A meta-analysis was not feasible due to differences in chosen age cut-off points and lack of reported estimates.

Eight studies investigated the effect of dialysis vintage on PD/HD mortality. Mortality risks were found to be similar in the first 6–12 months of dialysis initiation in five studies, with four showing higher mortality for PD patients in the subsequent periods [25, 27–29] and one showing a higher risk among HD patients [30]. One study found lower mortality with PD than HD in the first year and similar risks thereafter [22]. Two cohorts reported no evidence of change in mortality risks over time [19, 32].

Risk of bias and appraisal of PSM methods

Studies included in this meta-analysis achieved high scores on the Newcastle–Ottawa Scale ranging from eight to nine stars (Supplementary data, Table S3). In contrast, our analysis revealed that the quality of reporting on PSM varied considerably (Supplementary data, Table S4). With the exception of one study, all studies described the variables that were used to generate the propensity scores. The matching algorithm was clearly stated in 10 studies (58.8%) while the strategy for replacement during the PSM process was explicitly stated in only 3 studies [17, 28, 30]. On evaluating the balance between matched cohorts, most studies applied hypothesis testing and only four (23.5%) used appropriate tests [22, 23, 25, 26]. Three studies adjusted for the paired nature of the matched cohort when estimating HRs [22, 25, 31].

DISCUSSION

To the best of our knowledge, this is the first systematic review and meta-analysis to examine in detail the relative survival benefits of PD compared with in-centre HD based primarily on a propensity-based matching strategy. Previous comparative analysis and systematic reviews of PD/HD mortality were limited due to the inclusion of heterogeneous studies that failed to adequately account for the effect of selection bias [34, 35]. In this carefully constructed meta-analysis of PSM studies, we found overall that the mortality risks were similar for PD and in-centre HD and that the HRs for death remained unchanged in several sensitivity analyses. However, our analysis did uncover significant mortality differences between HD and PD that varied by region, over time and according to the study design. Taken together, these new findings would suggest that while the overall survival of incident patients treated with either PD or HD is similar, reported differences in survival primarily reflect differences in clinical practices within health systems and evolving clinical trends.

The choice of dialysis modality for patients approaching ESKD is determined by a confluence of factors that are associated with the patient, the physician and the prevailing healthcare system and consequently results in fundamental differences between patients selected for PD or HD. Many of these factors have been shown to be independent predictors of survival and adverse outcomes [5–7, 36]. Therefore it has been postulated by many that the observed differences in mortality between dialysis modalities is likely due to selection bias rather than the treatment itself [37]. In order to overcome this specific type of bias, many investigators have advocated the use of PSM to estimate causal TEs rather than conventional regression methods. PSM offers a number of advantages, which make it more appealing than the latter. First, it allows estimation of marginal TEs (average effect of treatment on the population), a feature that is shared with randomized controlled trials. In contrast, conventional regression methods only permit estimation of conditional effects (average effect on the individual) [38]. Second, unlike conventional methods where the outcome is built in with other predictors and confounding variables in the same model, there is clear separation between the design phase and the process of outcome estimation, again in a way that is analogous to randomized experiments [39]. Third, as propensity scores are balancing scores, it is easy to examine the distribution of baseline characteristics, including confounders, between treatment groups. This helps to quantify the extent to which systematic differences are eliminated. In contrast, goodness-of-fit tests are incapable of determining the degree of overlap in the distribution of covariates between treated and untreated groups [8, 40, 41].

This systematic review of more than 114 600 PSM patients found no evidence to support the superiority in survival of one modality over the other. However, quite strikingly, we did find evidence of substantial heterogeneity in mortality risks between PD and HD that mandated further analysis through meta-regression. From these series of analyses, we identified a number of factors that explained a very large proportion of the between-study variability from published studies. First, we identified the 'country of origin' as one of the principal determinants of dialysis modality survival. This perhaps reflects the differences in healthcare systems among countries and consequently differences in funding models and variability in patterns of clinical care. It is likely that the reported disparities in PD utilization rates across the globe as well as underlying financial and reimbursement policies have differentially affected the development of PD as a primary dialysis modality, which in turn has contributed to differences in dialysis outcomes [42–44]. Second, it is also possible that differences in modifiable practice patterns such as vascular access type, PD catheter care and fluid type, PD fluid type, length of dialysis as well as dialysis adequacy influenced mortality, which have been shown to vary internationally [45]. Third, although it might be expected that centres with greater experience with PD therapy might experience better survival than HD, this has not been observed internationally [46, 47]. Indeed, mortality comparisons of PD and HD from studies in East Asia have not confirmed superior results for PD despite the relatively high uptake of PD. Similarly, although epidemiological studies have demonstrated racial differences in survival comparisons of dialysis modalities

[48, 49], we did not find evidence to support effect modification of race on mortality from either Asian or US cohort studies [22, 24–25].

The time span of 21 years (1993–2014) allowed us to investigate temporal trends in patterns of survival between PD and HD, as we postulated that some of the between-study heterogeneity in mortality might be accounted for by changing practice patterns. In these series of analysis, a favourable trajectory in PD versus HD mortality was observed in recent cohorts compared with historic cohorts after accounting for the effects of country and study type (Supplementary data, Figure S3). This period effect may be explained by preferentially greater improvements in PD compared with HD, as evident from published reports from large registries [1, 2, 50, 51]. It may also reflect the advancements in pre-dialysis and in overall dialysis care provision to patients over the past 2 decades [52, 53]. Examples of improved practice patterns include a shift in practice towards preserving residual renal function and peritoneal membrane integrity, the advent of more PD biocompatible fluids, improved dialysis adequacy and increased attention to anaemia, mineral and nutrition parameters and vascular access care [53]. Although several studies have identified diabetes as an effect modifier of the PD/HD mortality relationship, we did not observe evidence of this from our subgroup meta-analysis. Similarly, while age and vintage appeared to have variable effects, it was not possible to reach conclusive results due to a lack of reported estimates.

A key objective of the meta-analysis was to explore the scientific quality and reporting of PSM studies. Our investigations uncovered a series of deficiencies in the reporting of statistical methods, including a description on how the matched pairs were formed. This is noteworthy, as a lack of clarity in the methodology used prevents other researchers from replicating these methods and assessing their appropriateness. Ten studies explicitly described the algorithm used in the PSM analysis. Furthermore, only three studies explicitly mentioned whether the matching process was conducted with or without replacement. This is important, as matching with replacement permits a subject from the control group to contribute to more than one matched set, resulting in multiple matched pairs with the same control subject. This lack of independence needs to be taken into account when estimating TEs [54, 55]. One of the most appealing advantages of using PSM is the ability to assess the degree of balance achieved between matched samples in a transparent fashion. However, the majority appeared not to have done this, at least correctly. Most studies utilized significance hypothesis testing such as *t*-tests to compare the distribution of covariates between matched cohorts. This practice has been strongly discouraged for due to several reasons. First, these tests are dependent on sample size. Therefore a non-significant P-value that is simply due to an underpowered sample could deceivingly indicate a balanced state. Second, while these tests refer to a hypothetical population, balance is an intrinsic characteristic of a matched sample that has no reference to any hypothetical population. This makes the use of significance tests rather irrelevant in determining the degree of established balance. Proper alternatives for balance diagnostics that are independent of sample size are the use of standardized differences and quintile-to-quintile plots [41, 56]. Failure to adequately assess the balance of potential confounders can bias estimates and certainly defies the rationale behind the use of PSM.

Unlike balance diagnostics, there is no consensus on the need to account for the paired nature of matched cohorts when estimating TEs, and indeed more research is needed in this area [38, 55, 57]. In our review, only three studies addressed this point and adjusted the results for within-pair correlation [22, 25, 31]. These deficiencies in reporting and applying PSM methods are similar to those reported in previous reviews that have appraised PSM studies [15, 58–60]. This underscores the need for greater efforts in raising awareness among nephrology researchers and the wider scientific community.

This meta-analysis is not without limitations. Despite advances in the design and analysis of PSM subjects, it is important to emphasize the evidence derived from PSM studies is still inferior to that derived from randomized trials. Estimated propensity scores are dependent on the availability and quality of captured data. Studies usually lack variables that indicate the severity of comorbid diseases, social circumstances such as family support, frailty indicators and perhaps other important factors that could have influenced the choice of modality and outcomes. Also, as many included studies were registry-based, a degree of inherent inaccuracies in coding and record completeness would be expected. Therefore bias arising from unmeasured confounders cannot be eliminated. It is noteworthy that in spite of its advantages, there is not complete consensus on the superiority of PSM versus conventional regression methods and caution must be exercised upon implementation [40, 61]. Finally, the quality of reporting on PSM may have been affected by editing and word limit restrictions, as researchers may have presented more information initially. These points should be weighed against the rigorous systematic approach of this study, the novel focus on mitigating selection bias through achieving methodological uniformity, the inclusion of modern cohorts from various geographical areas, as well as attempts to improve the quality of performing and reporting on PSM methods.

In conclusion, evidence derived from PSM-based comparisons of PD and HD indicates that PD and in-centre HD carry similar survival rates. Differences do exist among subgroups and these depend mainly on the country of origin and the period during which a cohort commenced dialysis. While the quality of reporting and conduct of PSM methods needs to improve in clinical research, they remain a very useful tool in comparing treatment strategies and in assessing causality where randomized clinical trials have proven difficult to implement.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part, except in abstract format.

REFERENCES

1. Pippias M, Kramer A, Noordzij M *et al.* The European Renal Association–European Dialysis and Transplant Association Registry Annual Report 2014: a summary. *Clin Kidney J* 2017; 10: 154–169
2. United States Renal Data System. *2016 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2016
3. ClinicalTrials.gov. Survival on Peritoneal Dialysis (PD) Versus Hemodialysis (HD) in China. https://ClinicalTrials.gov/show/NCT01413074 (1 June 19, date last accessed)
4. Korevaar JC, Feith GW, Dekker FW *et al.* Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: a randomized controlled trial. *Kidney Int* 2003; 64: 2222–2228
5. Stack AG. Determinants of modality selection among incident US dialysis patients: results from a national study. *J Am Soc Nephrol* 2002; 13: 1279–1287
6. Kim HJ, Park JT, Han SH *et al.* The pattern of choosing dialysis modality and related mortality outcomes in Korea: a national population-based study. *Korean J Intern Med* 2017; 32: 699–710
7. Miskulin DC, Meyer KB, Athienites NV *et al.* Comorbidity and other factors associated with modality selection in incident dialysis patients: the CHOICE study. Choices for Healthy Outcomes in Caring for End-Stage Renal Disease. *Am J Kidney Dis* 2002; 39: 324–336
8. Rubin DB. Using propensity scores to help design observational studies: application to the tobacco litigation. *Health Serv Outcome Res Methodol* 2001; 2: 169–188
9. Rubin DB. Estimating causal effects from large data sets using propensity scores. *Ann Intern Med* 1997; 127: 757–763
10. Newgard CD, Hedges JR, Arthur M *et al.* Advanced statistics: the propensity score—a method for estimating treatment effect in observational research. *Acad Emerg Med* 2004; 11: 953–961
11. Martens EP, Pestman WR, de Boer A *et al.* Systematic differences in treatment effect estimates between propensity score methods and logistic regression. *Int J Epidemiol* 2008; 37: 1142–1147
12. Ouzzani M, Hammady H, Fedorowicz Z *et al.* Rayyan—a web and mobile app for systematic reviews. *Syst Rev* 2016; 5: 210–210
13. Collins AJ, Hao W, Xia H *et al.* Mortality risks of peritoneal dialysis and hemodialysis. *Am J Kidney Dis* 1999; 34: 1065–1074
14. Wells GS, O'Connell D, Peterson J *et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Non Randomised Studies in Meta-analyses*. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (1 June 19, date last accessed)
15. Austin PC. A critical appraisal of propensity-score matching in the medical literature between 1996 and 2003. *Stat Med* 2008; 27: 2037–2049
16. Kelley GA, Kelley KS. Statistical models for meta-analysis: a brief tutorial. *World J Methodol* 2012; 2: 27–32
17. van de Luijtgaarden MWM, Jager KJ, Segelmark M *et al.* Trends in dialysis modality choice and related patient survival in the ERA-EDTA registry over a 20-year period. *Nephrol Dial Transplant* 2016; 31: 120–128
18. Lee MJ, Kwon YE, Park KS *et al.* Glycemic control modifies difference in mortality risk between hemodialysis and peritoneal dialysis in incident dialysis patients with diabetes: results from a nationwide prospective cohort in Korea. *Medicine (Baltimore)* 2016; 95: e3118
19. Waldum-Grevbo B, Leivestad T, Reisaeter AV *et al.* Impact of initial dialysis modality on mortality: a propensity-matched study. *BMC Nephrol* 2015; 16: 179
20. Thiery A, Severac F, Hannedouche T *et al.* Survival advantage of planned haemodialysis over peritoneal dialysis: a cohort study. *Nephrol Dial Transplant* 2018; 33: 1411–1419
21. Rigoni M, Torri E, Nollo G *et al.* Survival and time-to-transplantation of peritoneal dialysis versus hemodialysis for end-stage renal disease patients: competing-risks regression model in a single Italian center experience. *J Nephrol* 2017; 30: 441–447
22. Kumar VA, Sidell MA, Jones JP *et al.* Survival of propensity matched incident peritoneal and hemodialysis patients in a United States health care system. *Kidney Int* 2014; 86: 1016–1022
23. Contreras G, Pagan J, Chokshi R *et al.* Comparison of mortality of ESRD patients with lupus by initial dialysis modality. *Clin J Am Soc Nephrol* 2014; 9: 1949–1956
24. Lievense H, Kalantar-Zadeh K, Lukowsky LR *et al.* Relationship of body size and initial dialysis modality on subsequent transplantation, mortality and weight gain of ESRD patients. *Nephrol Dial Transplant* 2012; 27: 3631–3638
25. Weinhandl ED, Foley RN, Gilbertson DT *et al.* Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. *J Am Soc Nephrol* 2010; 21: 499–506
26. Yang JY, Chen L, Chao CT *et al.* Comparative study of outcomes among patients with polycystic kidney disease on hemodialysis and peritoneal dialysis. *Sci Rep* 2015; 5: 12816
27. Wang IK, Liang WM, Lin CL *et al.* Impact of dialysis modality on the survival of patients with end-stage renal disease and prior stroke. *Int Urol Nephrol* 2016; 48: 139–147
28. Yang F, Khin LW, Lau T *et al.* Hemodialysis versus peritoneal dialysis: a comparison of survival outcomes in south-east Asian patients with end-stage renal disease. *PLoS One* 2015; 10: e0140195
29. Kim H, Kim KH, Park K *et al.* A population-based approach indicates an overall higher patient mortality with peritoneal dialysis compared to hemodialysis in Korea. *Kidney Int* 2014; 86: 991–1000
30. Choi JY, Jang HM, Park J *et al.* Survival advantage of peritoneal dialysis relative to hemodialysis in the early period of incident dialysis patients: a nationwide prospective propensity-matched study in Korea. *PLoS One* 2013; 8: e84257
31. Chang JH, Sung JY, Ahn SY *et al.* Hemodialysis leads to better survival in patients with diabetes or high comorbidity, compared to peritoneal dialysis. *Tohoku J Exp Med* 2013; 229: 271–277
32. Chang YK, Hsu CC, Hwang SJ *et al.* A comparative assessment of survival between propensity score-matched patients with peritoneal dialysis and hemodialysis in Taiwan. *Medicine (Baltimore)* 2012; 91: 144–151
33. Chou CY, Wang IK, Liu JH *et al.* Comparing survival between peritoneal dialysis and hemodialysis treatment in ESRD patients with chronic hepatitis C infection. *Perit Dial Int* 2010; 30: 86–90
34. Ross S, Dong E, Gordon M *et al.* Meta-analysis of outcome studies in end-stage renal disease. *Kidney Int* 2000; 57: S28–S38
35. Couchoud C, Bolignano D, Nistor I *et al.* Dialysis modality choice in diabetic patients with end-stage kidney disease: a systematic review of the available evidence. *Nephrol Dial Transplant* 2015; 30: 310–320
36. van de Luijtgaarden MW, Jager KJ, Stel VS *et al.* Global differences in dialysis modality mix: the role of patient characteristics, macroeconomics and renal service indicators. *Nephrol Dial Transplant* 2013; 28: 1264–1275
37. Quinn RR, Hux JE, Oliver MJ *et al.* Selection bias explains apparent differential mortality between dialysis modalities. *J Am Soc Nephrol* 2011; 22: 1534–1542
38. Austin PC. The use of propensity score methods with survival or time-to-event outcomes: reporting measures of effect similar to those used in randomized experiments. *Stat Med* 2014; 33: 1242–1258
39. Rubin DB. The design versus the analysis of observational studies for causal effects: parallels with the design of randomized trials. *Stat Med* 2007; 26: 20–36
40. Wang J, Donnan PT. Propensity score methods in drug safety studies: practice, strengths and limitations. *Pharmacoepidemiol Drug Saf* 2001; 10: 341–344
41. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009; 28: 3083–3107
42. Just PM, de Charro FT, Tschosik EA *et al.* Reimbursement and economic factors influencing dialysis modality choice around the world. *Nephrol Dial Transplant* 2008; 23: 2365–2373
43. Schaefer F, Borzych-Duzalka D, Azocar M *et al.* Impact of global economic disparities on practices and outcomes of chronic peritoneal dialysis in children: insights from the International Pediatric Peritoneal Dialysis Network registry. *Perit Dial Int* 2012; 32: 399–409
44. Jain AK, Blake P, Cordy P *et al.* Global trends in rates of peritoneal dialysis. *J Am Soc Nephrol* 2012; 23: 533–544
45. Robinson BM, Port FK. International hemodialysis patient outcomes comparisons revisited: the role of practice patterns and other factors. *Clin J Am Soc Nephrol* 2009; 4(Suppl 1): S12–S17

46. Mehrotra R, Khawar O, Duong U *et al*. Ownership patterns of dialysis units and peritoneal dialysis in the United States: utilization and outcomes. *Am J Kidney Dis* 2009; 54: 289–298
47. Schaubel DE, Blake PG, Fenton SS. Effect of renal center characteristics on mortality and technique failure on peritoneal dialysis. *Kidney Int* 2001; 60: 1517–1524
48. Rhee CM, Lertdumrongluk P, Streja E *et al*. Impact of age, race and ethnicity on dialysis patient survival and kidney transplantation disparities. *Am J Nephrol* 2014; 39: 183–194
49. Yan G, Norris KC, Yu AJ *et al*. The relationship of age, race, and ethnicity with survival in dialysis patients. *Clin J Am Soc Nephrol* 2013; 8: 953–961
50. Wakasugi M, Kazama JJ, Narita I. Mortality trends among Japanese dialysis patients, 1988–2013: a joinpoint regression analysis. *Nephrol Dial Transplant* 2016; 31: 1501–1507
51. Ryu JH, Kim H, Kim KH *et al*. Improving survival rate of Korean patients initiating dialysis. *Yonsei Med J* 2015; 56: 666–675
52. Port FK, Pisoni RL, Bommer J *et al*. Improving outcomes for dialysis patients in the international dialysis outcomes and practice patterns study. *Clin J Am Soc Nephrol* 2006; 1: 246–255
53. Kendrick J, Teitelbaum I. Strategies for improving long-term survival in peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2010; 5: 1123–1131
54. Hill J, Reiter JP. Interval estimation for treatment effects using propensity score matching. *Stat Med* 2006; 25: 2230–2256
55. Stuart EA. Matching methods for causal inference: a review and a look forward. *Stat Sci* 2010; 25: 1–21
56. Imai K, King G, Stuart EA. Misunderstandings between experimentalists and observationalists about causal inference. *J R Stat Soc A* 2008; 171: 481–502
57. Stuart EA. Developing practical recommendations for the use of propensity scores: discussion of 'A critical appraisal of propensity score matching in the medical literature between 1996 and 2003' by Peter Austin, Statistics in Medicine. *Stat Med* 2008; 27: 2062–2065
58. Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. *J Thorac Cardiovasc Surg* 2007; 134: 1128–1135
59. McMurry TL, Hu Y, Blackstone EH *et al*. Propensity scores: methods, considerations, and applications in the *Journal of Thoracic and Cardiovascular Surgery*. *J Thorac Cardiovasc Surg* 2015; 150: 14–19
60. Weitzen S, Lapane KL, Toledano AY *et al*. Principles for modeling propensity scores in medical research: a systematic literature review. *Pharmacoepidemiol Drug Saf* 2004; 13: 841–853
61. Baser O. Choosing propensity score matching over regression adjustment for causal inference: when, why and how it makes sense. *J Med Econ* 2007; 10: 379–391

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Dialysis after graft loss: a Swiss experience

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ABSTRACT

Background. Patients returning to dialysis after graft loss have high early morbidity and mortality.

Methods. We used data from the Swiss Transplant Cohort Study to describe the current practice and outcomes in Switzerland. All patients who received a renal allograft between May 2008 and December 2014 were included. The patients with graft loss were divided into two groups depending on whether the graft loss occurred within 1 year after transplantation (early graft loss group) or later (late graft loss group). Patients with primary non-function who never gained graft function were excluded.

Results. Seventy-seven out of 1502 patients lost their graft during follow-up, 40 within 1 year after transplantation. Eleven patients died within 30 days after allograft loss. Patient survival was 86, 81 and 74% at 30, 90 and 365 days after graft loss, respectively. About 92% started haemodialysis, 62% with definitive vascular access, which was associated with decreased mortality (hazard ratio = 0.28). At the time of graft loss, most patients were on triple immunosuppressive therapy with significant reduction after nephrectomy. One year after graft loss, 77.5% (31 of 40) of patients in the early and 43.2% (16 out of 37) in the late-loss group had undergone nephrectomy. Three years after graft loss, 36% of the patients with early and 12% with late graft loss received another allograft.