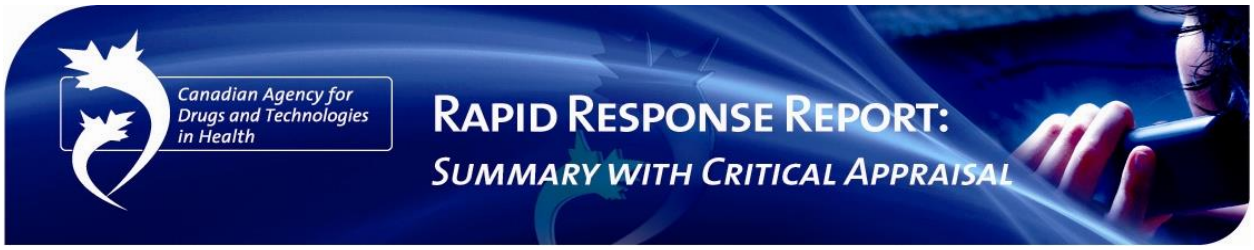


**TITLE: First Initiative Peritoneal Dialysis versus Hemodialysis for the Treatment of Renal Failure: A Review of Clinical Effectiveness and Guidelines**

**DATE:** 08 February 2016

## CONTEXT AND POLICY ISSUES

Hemodialysis (HD) and peritoneal dialysis (PD) are procedures that provide dialytic support for patients with kidney disease, including those with acute kidney failure, who require renal replacement therapy. According to the Kidney Foundation of Canada, in 2010, 59% of people who were being treated for kidney failure in Canada were on dialysis.[1] Although UD and PD are both considered effective options in end stage renal disease (ESRD),[2] HD is the predominant therapy in both maintenance and acute dialysis cases.[1,3] However, PD is slower and is especially indicated for patients who are unable to tolerate hemodialysis because of age, diabetes, vascular access problems, or other complicating cardiovascular conditions.[4] However, peritoneal dialysis is often performed in a continuous fashion so that the weekly solute clearances approach those with hemodialysis.[5] Peritoneal dialysis has been reported to be associated with preserved residual kidney function, reduced infection risk and improved patient contentment, as well as reduced cost and manpower.[3,6] Therefore, the increased use of acute PD as a viable option for the treatment of selected patients with acute kidney injury, particularly those who are hemodynamically compromised or have severe coagulation abnormalities, or when other modalities are not readily available has been advocated.[2,3,6]

It is uncertain whether there is an optimal choice of dialysis modality (HD or PD) in the various conditions for which patients may require dialytic support.[7] In the absence of a randomized trial to address this question and the conflicting findings of observational studies,[6] it is unclear whether one dialysis modality should be preferred over another as a first line approach in patients with acute renal failure, especially given that the need for renal replacement therapy in these patients may be prompted by different conditions necessitating potentially different focuses.

The aim of this review is to summarize available evidence in order to establish whether the choice of the first dialysis modality may impact on the clinical outcomes in patients with renal failure in who dialysis is being initiated for the first time, with a focus on “crash start” dialysis. For

the purpose of this review, "crash start" refers to the situation where the dialysis modality is applied in patients who have renal failure but are naïve to any dialysis.

## RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of peritoneal dialysis versus hemodialysis for the "first initiative" treatment of renal failure in adult patients?

2. What are the evidence-based guidelines regarding optimal first line dialysis for the treatment of renal failure in adult patients?

3. What are the evidence-based guidelines regarding optimal peritoneal dialysis care for the treatment of renal failure in adult patients?

## KEY FINDINGS

There was evidence that the overall survival outcomes associated with PD as initial dialysis modality was, at least, comparable to outcomes associated with HD as initial dialysis modality, with a trend suggesting higher survival rates among patients initiated on PD. Furthermore, there was evidence suggesting that younger patients (< 65 years) may benefit more from PD compared with older patients (> 65 years old). Although PD was associated with significantly lower risk of bacteremia than HD, the rate of mortality due to infections was not statistically significantly different between the two groups. There was no interaction between the initial dialysis modality and gender or diabetes mellitus with regards to mortality. Patients for whom PD was the initial dialysis modality were not associated with impaired prognosis compared with those who had HD as initial dialysis modality. However, patients for whom PD was the initial dialysis modality were more likely to switch modality or to receive kidney transplantations. The literature search for this review did not find any guidelines regarding optimal first line dialysis modality or the optimal peritoneal dialysis care for the treatment of renal failure in adult patients.

## METHODS

### Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. To address research question one, methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and randomized controlled trials. In addition, a focused search for non-randomized studies was conducted wherein main concepts appeared in title or major subject heading and a non-randomized studies filter was applied. To address research questions two and three, methodological filters were applied to limit retrieval to guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and January 8, 2016.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

## Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was performed by a second reviewer based on the inclusion criteria presented in Table 1.

**Table 1:** Selection Criteria

| | |
|---|---|
| **Population** | Adult patients with renal failure who are naïve to any dialysis and who require a 'crash start' or initial start dialysis. |
| **Intervention** | First initiative peritoneal dialysis [a]<br>- Continuous ambulatory ('twin bag')<br>- Automated ('cycler') |
| **Comparator** | Hemodialysis<br>- Nocturnal<br>- Self-care<br>- In-centre |
| **Outcomes** | For Research Question 1:<br>Comparative clinical effectiveness<br>- mortality,<br>- morbidity,<br>- quality of life,<br>- patient satisfaction<br><br>For Research Question 2:<br>Evidence-based guidelines regarding what the optimal 'first initiative'<br>- Patient selection and/or preferred modality (peritoneal dialysis or hemodialysis) for first initiative patients.<br>- Optimal first line treatment or treatment pathways.<br><br>For Research Question 3:<br>Evidence-based guidelines regarding best practices for peritoneal dialysis in adult patients with renal failure |
| **Study Designs** | HTA/Systematic Reviews/Meta-Analyses; Randomized Controlled Trials, Non-randomized Studies; Evidence-based Clinical Practice Guidelines |

[a] This is also known as "crash start" or "initial start" peritoneal dialysis and refers to PD procedure in patients who have renal failure but are naïve to any dialysis. Continuous ambulatory ("twin bag") refers to situations in which the patient is not attached to a machine and can perform some tasks. Automated ('cycler') refers to situations in which the patient is attached to a machine – this would likely happen at night.

## Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2011.

## Critical Appraisal of Individual Studies

All the included studies had non-randomized designs and they were critically appraised using the Downs and Black checklist for measuring study quality.[8] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each

included study were described narratively. The strengths and limitations of the individual studies are summarized in Appendix 3.

## SUMMARY OF EVIDENCE

### Quantity of Research Available

A total of 587 citations were identified in the literature search. Following screening of titles and abstracts, 562 citations were excluded and 25 potentially relevant reports from the electronic search were retrieved for full-text review. Seven potentially relevant publications were retrieved from the grey literature search. Of the 32 potentially relevant articles, 28 publications were excluded for various reasons, while four publications met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

### Summary of Study Characteristics

*Study Design*

All of the included studies[2,9-11] had retrospective observational designs. Two studies[2,9] used propensity-matched analyses to correct for case-mix differences between patients who initiated peritoneal dialysis (PD) and hemodialysis (HD) as first renal replacement therapy. Another study[10] used marginal structural models to analyze outcomes in a cohort of patients who initiated dialysis using either the PD or HD modality. One single-center study[11] with a non-matched control group, in which univariate and multivariate regression were used for analysis.

*Country of Origin*

One study each was conducted in Norway[2] and Germany,[11] while two studies[9,10] were conducted in the United States of America (USA). The Norwegian study[2] and one study from the USA[9] used national databases of their respective countries. Another study from the USA[10] used data from a healthcare organization with a kidney care division operating a large number of facilities (2,225 outpatient facilities as at September 2015) across the USA. The German study[11] analyzed dialysis registry data of patients from a single nephrology centre. Both univariate and multiple logistic regression analyses were used to assess the impact of potential confounder on results.

*Patient Population*

One study[2] analyzed data from 692 matched pairs of adult end-stage renal disease (ESRD) patients who initiated dialysis as first renal replacement therapy from 2005 to 2012. The mean age per modality was 64.6 years and 65.2 years for PD and HD, respectively. The mean body mass index (BMI) was 25.4 kg/m$^2$ for PD and 25.5 kg/m$^2$ for HD, while the mean estimated glomerular filtration rates (eGFR) were 8.8 ml/min/1.73 m$^2$ and 9.0 ml/min/1.73 m$^2$ for the PD and HD modalities, respectively. Another study[9] analyzed data from 1003 matched pairs of ESRD patients who initiated PD or HD as their first dialysis modality between 1 January 2001 and 30 June 2013. The mean age per modality was 57.4 years for PD, and 58.4 years for HD. The study did not report BMI and eGFR data. One study[10] analyzed data from 23,718 incident dialysis patients who initiated dialysis from July of 2001 to June of 2004. Depending on whether patients remained on their initial modality, switched to another modality, or received transplantation, the mean age in the PD group ranged from 47 years to 62 years, while the

mean age in the HD group ranged from 44 years to 64 years. By the same designation, mean BMI ranged from 25.5 to 27.8 kg/m$^2$ in the PD group and 25.1 to 26.3 kg/m$^2$ in the HD group. Data on eGRF not reported in this study.[10] Another study[11] involved patients who started PD or HD in an urgent fashion due to late referral or unexpected deterioration of residual renal function with manifestation of uraemic syndrome or over-hydration. The patients were mainly elderly with mean ages of 72.6 years and 74.1 years for the PD and HD modalities, respectively. Most of the patients (PD, 95%; HD, 89%) were already hospitalized before initiation of dialysis. The study did not report BMI and eGFR data.[11]

*Interventions and Comparators*

In the studies that applied the propensity-matched model[2,9] PD patients were matched in a 1:1 fashion with HD patients, creating 692 pairs of patients with comparable baseline variables in one study,[2] and 1003 matched pair in the other study.[9] In one study,[2] the median follow-up time was 13.0 months in the PD group and 10.0 months in the HD group, while another study[9] had a nine year follow-up period for each modality. In another study[10] 1,358 patients initiated dialysis using PD, while 22,360 initiated dialysis using HD, with a 24 months follow-up period for each modality. In one study,[11] patients received acute unplanned therapy with either PD or HD. Unplanned dialysis initiation was defined as beginning dialysis urgently due to late referral or unexpected deterioration of residual renal function with uraemic syndrome or over-hydration in patients without functional fistula for dialysis and therefore needing a central venous dialysis catheter[11]. The duration of follow-up was six months.

*Outcomes*

Survival was the outcome measure of interest in all the included studies.[2,9-11] In two studies[2,11] both cardiovascular and all-cause mortality were reported. In one study[2] cardiovascular cause of death was defined in accordance with the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) cause of dead (COD) codes as a composite of COD group I–IV including myocardial ischemia and infarction, heart failure, cardiac arrest/sudden death and cerebrovascular accident. The other study[11] did not specify what constituted cardiovascular mortality. This study[11] also reported the risk of infections and the mortality due to infections for PD and HD. In two studies,[2,9] survival analyses were conducted both in terms of the as-treated and the intention-to-treat (ITT) populations. In the as-treated analysis, survival was analyzed on the basis of the modality a patient was on at the time of death, regardless of whether the patient began on a different modality. The ITT analysis attributed death to the initial dialysis modality of the patient regardless of whether the patient switched modalities over the course of the study. In both methods of analysis, patients were censored for the earliest of the following: renal transplantation, dialysis cessation, death, renal recovery, loss to follow-up or study end. In addition, the as-treated analyses censored patients for change in dialysis modality. One study[10] reported modality change, differential transplantation rates, and detailed time-varying laboratory measurements in addition to survival outcomes.

**Summary of Critical Appraisal**

Two studies[2,9] used propensity-matched designs and matching patients in terms of baseline disease burden and demographics to adjust for the case-mix differences between HD and PD patients to resolve the bias due to confounding by indication associated with regular observational studies. They each matched patients on a larger number of variables to ensure improved reliability of the study results. Furthermore, each study[2,12] analyzed survival outcomes

on the basis of both ITT and as-treated population, with both methods yielding similar results to indicate rigorous findings of the studies. Three studies[2,9,10] analyzed data from large, diverse cohorts of patients, thus increasing the potential for their respective study populations to be representative of the general renal failure population requiring renal replacement therapy (RRT), while one study[11] retrospectively analyzed data from a nephrology center. The authors of three studies[2,9,11] declared no competing interests. In one study,[10] an author had received grant support and/or honoraria from a firm that deals in products for renal care including dialysis. However, this is unlikely to bias the outcomes since the company caters for both PD and HD needs.

All of the included studies[2,9-11] were nonrandomized nature, making them susceptible to uncontrolled confounding, measurement errors, and selection bias. Thus, despite improvement over traditional observational studies to adjust for confounding by indication, propensity matched analyses used by two studies[2,9] are unable to properly correct for non-measured potentially confounding variables such as pre-dialysis care, residual renal function, and the kind of physiological dialysis solutions used. For the study that utilized marginal structural models,[10] liability to these limitations and confounding by indication cannot be ruled out. One study[11] had a non-matched control group. Therefore, the potential for biased study results due to imbalances and confounders was high.

The propensity-matched approach, require that only HD patients with similar baseline characteristics as PD patients were included in the study. Therefore, it is unknown if the results from these two studies[2,9] will be generalizable in all patients who require RRT with dialysis. One study[9] included patients who utilized either an arteriovenous fistula or a graft during the first 90 days of study, excluding those who utilized a central venous catheter as vascular access at any time during the first 90 days of dialysis, including patients who initiated dialysis urgently with a catheter. The motivation for the exclusion criterion was to reduce case-mix bias. However, the potential of excluding "crash dialysis patients" from this study[9] cannot be overlooked. In one study,[11] there were significant differences between PD and HD patients at baseline with respect to heart failure (NYHA Stage III–IV), serum creatinine and glomerular filtration rate, and prevalence of malignancy, which could influence the results. Although regression analyses found that these had no significant impact on overall mortality, the possibility that the study was not sufficiently powered to make such detection cannot be ruled out. The study population consisted mainly of elderly patients, and multivariate analysis showed that age at initiation of dialysis was significantly associated with overall mortality risk.[11] Therefore, it is uncertain whether the reported findings will be reproducible in a younger population. All the studies were conducted in countries other than Canada, with one study[2] solely analyzing patient data from the Norwegian Renal Registry, while two[9,10] used analyzed data from the USA, and another study[11] analyzed data from a single nephrology center in Germany.[11] Therefore, the generalizability of the reported findings from these studies to the Canadian context is unknown.

One study[9] had a nine-year follow-up period while two other studies had five-year[2] and two-year[10] follow-up periods, and another study[11] had a six-months of follow-up. It is unknown if these follow-up durations were long enough to predict late complications of any initial dialysis modality.

**Summary of Findings**

*What is the comparative clinical effectiveness of peritoneal dialysis versus hemodialysis for the "first initiative" treatment of renal failure in adult patients?*

Survival

One study[2] found that the initial dialysis modality did not affect all-cause mortality as determined by as-treated analyses, or ITT analyses. The two year hazard ratios (HR) and 95% confidence interval (CI) for the two modalities (PD versus HD) were 0.87 (0.67 to 1.12) for as-treated and 0.93 (0.73 to 1.18) for ITT analyses. Similar results were observed in analyses performed at 5 years with HR (95 % CI) of 0.95 (0.77 to 1.17) for as-treated and 0.99 (0.82 to 1.19) for ITT analyses. Another study[11] found that after six months of therapy, all-cause mortality among incident PD and HD patients with acutely initiated unplanned PD or HD was 30.3% and 42.1% respectively. The difference was not statistically significant ($P = 0.19$). Among PD patients, the proportion of mortality attributed to unknown causes 30% compared to 16.7% among HD patients. The study[11] also found that there was no statistically significant difference ($P = 1.00$) in cardiovascular mortality at the end of six months between incident PD and HD patients with acutely initiated unplanned PD or HD. It is unknown whether the smaller sample size (n=123) with a relatively small incidence of cardiovascular death (six in each group) or the short duration of the study contributed to these observations.

However, two studies[9,10] found that initiating dialysis with PD modality was associated with improved survival outcomes compared with HD. In one study,[9] both the as-treated analyses and ITT analyses at one year resulted in more than twice survival advantage in the PD group compared with HD with the cumulative hazard ratio (CHR) for death (HD versus PD) of 2.38 (95% CI: 1.68 to 3.40; $P<0.0001$) for the as-treated analysis and 2.10 (95% CI: 1.50 to 2.94; $P<0.0001$) for the ITT analysis. At 2 years the CHR was 1.39 (95% CI: 1.06 to 1.82; $P = 0.017$) in the as-treated analysis and 1.26 (95% CI: 0.98 to 1.63; $P = 0.070$) in the ITT analysis. A trend of cumulative risk of death favoring PD was observed for nearly 3 years of follow-up using as-treated analysis and for 2 years using ITT analysis, with no significant differences in outcomes between the modalities thereafter. Among patients initiated on PD modality, as treated analysis found that adjusted survival rates were 95% and 87%, for years 1 and 2, respectively compared with 89% and 83% among patients who initiated HD in the same time period. Similar results were reported from ITT analysis with survival rates of 94% and 86% for PD patients compared with 89% and 83% for HD patients, for years 1 and 2 respectively. Another study[10] found that PD was associated with persistently greater survival compared with HD. Patients who initiated dialysis using the PD modality had 48% lower mortality (i.e., a death hazard ratio [HR] of 0.52; 95% CI: 0.34 to 0.80).

Subgroup outcomes

One study[2] stratified analysis by age and reported that for both two- and five-year follow-up PD was associated with reduced all-cause mortality in patients aged below 65 years. This was not observed in patients older than 65 years. At year-two, the as–treated analysis found that the HR (PD versus HD) was 0.39 (95 % CI: 0.19 to 0.81; $P = 0.011$ for interaction; and HR (95% CI) for the ITT analysis was 0.47 (0.26 to 0.85; $P = 0.009$). Corresponding HR (95% CI) results for analysis at year-five were 0.49 (0.27 to 0.89; $P = 0.010$) for as–treated analysis and 0.58 (0.36 to 0.93; $P = 0.009$) for ITT analysis. The study[2] also found that cardiovascular disease was the cause of death in 49.1 % at year-two, and 48.2 % at year-five as-treated follow-up, with patients younger than 65 years who had initial PD modality associated with lower cardiovascular mortality compared with those who had initial HD modality (HR 0.38, 95 % CI 0.15 to 0.96).

There were no interactions between gender or diabetes mellitus and initial dialysis modality found concerning mortality. PD was not associated with impaired prognosis in any of the pre-

specified subgroups compared to HD. However, multivariate analysis in one study[11] showed that age at initiation of dialysis was significantly associated with overall mortality risk.

Other outcomes

One study[10] found that 6% of those with initial HD compared with 57% of those with initial PD switched modality at least once during their first two years of dialysis, and 6% of the initial PD patients compared with 18% of the initial HD had renal transplantation within the same period. Another study[11] reported that the incidence of bacteremia in incident PD and HD patients treated with acutely initiated unplanned PD or HD was significantly higher in the HD group compared with PD group over the course of the six months (21.1% versus 3.0%, respectively, $P < 0.01$); with the RR (95% CI) for bacteremia (HD vs. PD) estimated to be 0.16 (0.05 to 0.57; $P = 0.005$). However, the overall incidence of mortality due to infection was not significant different between the two groups (17.5% versus 9.1%, respectively, $P = 0.19$).

*What are the evidence-based guidelines regarding optimal first line dialysis for the treatment of renal failure in adult patients?*

The literature search for this review did not find any guidelines regarding optimal first line dialysis modality for the treatment of renal failure in adult patients.

*What are the evidence-based guidelines regarding optimal peritoneal dialysis care for the treatment of renal failure in adult patients?*

The literature search for this review did not find any guidelines regarding optimal peritoneal dialysis care for the treatment of renal failure in adult patients.

**Limitations**

One limitation is that three included studies[2,9,10] retrospectively analyzed data from ESRD patients from the time they initiated dialysis for the first time, and the proportion of such patients who were given "crash start" dialysis is unknown. For the purpose of this review, "crash start" refers to the situation where the dialysis modality is applied in patients who have renal failure but are naïve to any dialysis (see Table 1). Although one study[11] investigated unplanned acute dialysis which must have involved crash start patients, it was a single-center study with uncertainty about sufficient power to detect differences in outcomes between the treatment groups; and because the patients were elderly, it is unknown whether the study results will reproducible in a younger population. In addition, the non-randomized nature of the included studies[2,9,10] makes them liable to biases not accounted for by the various analytical methods. For instance none of the two propensity-matched analysis[2,9] adjusted for potentially confounding variables such as pre-dialysis care, and the kind of physiological dialysis solutions that was used for the selected modality; and one study[9] could not adjust for confounding due to residual renal function and key baseline laboratory values because data regarding these potential confounders were not available at the time dialysis was initiated. In the marginal structural model study[10] uncontrolled confounding (especially confounding by indication), measurement errors, and selection bias were limitations. The potential for such confounders to skew the reported findings in favor of one initial dialysis modality cannot be excluded. The potential for bias due to imbalances and confounders was high for the study[11] in which incident patients had acutely initiated unplanned PD or HD therapy because it was an observational and retrospective study with non-matched control group.

## CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

A propensity matched study[2] found that there was no significant difference in the overall five-year all-cause or cardiovascular mortality between peritoneal dialysis (PD) and hemodialysis (HD) used as initial dialysis modality. However, in analysis stratified by age, PD as initial dialysis modality demonstrated improved survival outcomes in patients younger than 65 years compared to HD. This superior survival outcome associated with PD as initial dialysis modality was not observed in patients older than 65 years. Another propensity matched study[9] found that in the first year of dialysis the cumulative risk of death was more than twice as high among patients for whom HD was the initial dialysis modality compared with patients who used PD as initial dialysis modality. Regardless of the population data used in the analysis – as-treated or intent-to-treat analyses – PD as initial dialysis modality was associated with statistically significant lower cumulative risk of death in this study.[9] A third study[10], which employed marginal structural model analysis also found that over the course of the initial 2 years of dialysis therapy, PD was associated with 48% lower mortality than HD independent of modality switches or differential transplantation rates. The choice of initial dialysis modality had no impact on mortality with regards to gender or diabetes mellitus. Although patients for whom PD was the initial dialysis modality were more likely to switch modality or receive kidney transplantation, PD was not associated with impaired prognosis compared to HD. One single-center retrospective observational study[11] found no significant difference in overall or cardiovascular mortality rates between incident patients with acutely initiated unplanned PD or HD. Although the study[11] found significantly higher risk of bacteremia in HD patients compared to PD patients, the rate of mortality due to infections was not statistically significantly different between the two groups.

The literature search for this review did not find any guidelines regarding optimal first line dialysis modality or the optimal peritoneal dialysis care for the treatment of renal failure in adult patients. However, one guideline[13] prepared for intensive care practice by an expert group of the French Intensive Care Society, with the participation of the French Society of Anesthesia and Intensive Care, the French Group for Pediatric Intensive Care and Emergencies, and the French Dialysis Society, recommended that in critically ill adults patients with acute renal failure who require renal replacement therapy, peritoneal dialysis should probably not be used first-line. The reasoning behind the recommendation was that the time needed to achieve satisfactory metabolic control and adequate volume control means that PD is unsuited to life-threatening situations. Therefore, PD cannot be recommended when other techniques are available. This guideline[13] had no other information about the PD modality which was relevant to this review.

Therefore, overall, evidence from the included studies suggests that the survival outcomes associated with PD as initial dialysis modality is, at least, comparable to outcomes from HD as initial dialysis modality, with a trend suggesting higher survival rates among patients initiated on PD. Furthermore, there is evidence to suggest that younger patients (< 65years) may benefit more from PD compared with older patients (> 65 years old).

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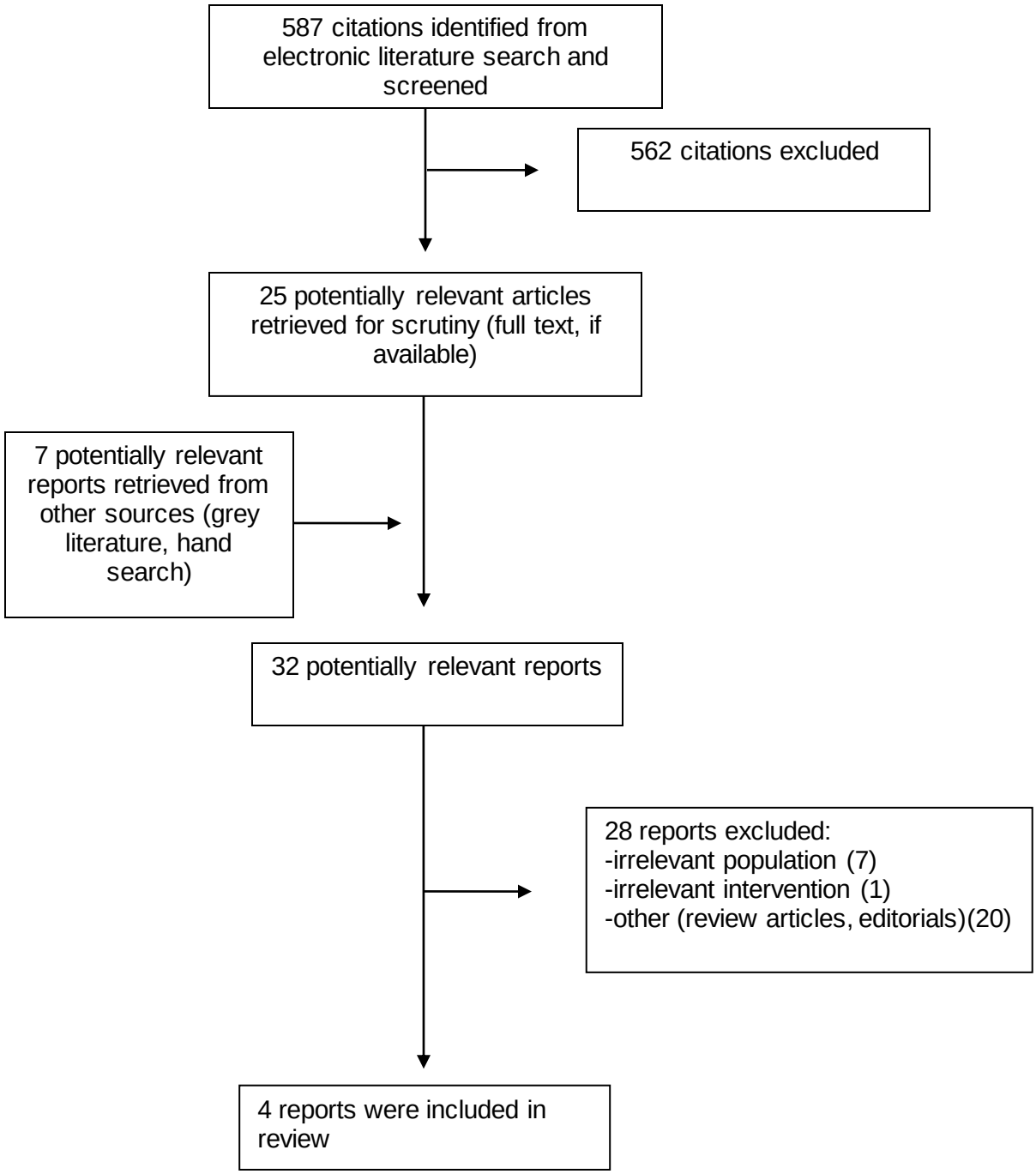
**APPENDIX 1: Selection of Included Studies**



**APPENDIX 2: Characteristics of Included Publications**

**Table A1**: Characteristics of Included Clinical Studies

| First Author, Publication Year, Country, Study Name | Study Design | Patient Characteristics | Intervention(s) | Comparator(s) | Clinical Outcomes |
|---|---|---|---|---|---|
| Waldum-Grevbo, 2015[2]<br><br>Norway | A propensity-matched retrospective study | 692 matched pairs of adult ESRD patients (Mean age was 64.6 ± 15.2 years and 65.3 ± 15 years for the PD and HD modalities respectively) who started dialysis as initial RRT from January 2005 through December 2012.<br>Mean BMI was 25.4 ± 4.2 kg/m$^2$ for PD and 25.5 ± 5.1 kg/m$^2$ for HD, and eGFR were 25.9 ± 5.2 and 8.8 ± 3.1 and 9.0 ± 3.4 ml/min/1.73 m$^2$, for PD and HD respectively. | Peritoneal dialysis, | Hemodialysis | All-cause and cardiovascular mortality |
| | | | Follow-up period was 5 years | | |
| Kumar, 2014[9]<br><br>USA | A propensity-matched retrospective study | 1003 matched pairs ESRD patients who initiated PD or HD as their first dialysis modality between 1 January 2001 and 30 June 2013. The mean age per modality was 57.4 ± 14.2 for PD, and 58.4 ± 13.6 for HD. | Peritoneal dialysis | Hemodialysis | Survival differences /RR of death |
| | | | Follow-up was for 9 years | | |

**Table A1**: Characteristics of Included Clinical Studies

| First Author, Publication Year, Country, Study Name | Study Design | Patient Characteristics | Intervention(s) | Comparator(s) | Clinical Outcomes |
|---|---|---|---|---|---|
| Lukowsky, 2013[10]<br><br>USA | Observational study using marginal structural models | Incident dialysis patients who initiated dialysis in renal care facilities between July of 2001 and June of 2004 and were followed for 24 months. | Peritoneal dialysis | Hemodialysis | Survival differences, modality change, differential transplantation rates over the first 24 months |
| | | | Follow-up was for 2 years | | |
| Koch, 2012[11]<br><br>Germany | Observational cohort study | 123 incident dialysis patients with initiation of unplanned and acute dialysis. The mean age per modality was 72.6 ± 13.4 for PD and 74.1 ± 13.3 for HD. Most of the patients (PD 95%, HD 89%) were already hospitalized before initiation of dialysis. | Peritoneal dialysis | Hemodialysis | Overall mortality, cardiovascular mortality, mortality due to infections, and probability of infection |
| | | | Follow-up for 6 months | | |

ESRD = end stage renal disease; HD = hemodialysis; PD peritoneal dialysis; RR = relative risk; RRT = renal replacement therapy.

**APPENDIX 3: Critical Appraisal of Included Publications**

| **Table A2:** Strengths and Limitations of Randomized Controlled Trials using Downs and Black[6] | |
|---|---|
| **Strengths** | **Limitations** |
| Waldum-Grevbo, 2015[2] | |
| • The propensity-matched design made adjustment to solve the bias due to confounding by indication associated with regular observational studies.<br>• There was < 1% missing data (0.55 %) from the study database, and patient was lost to follow-up, and since analysis included data from only patients who were matched at baseline on a larger number of variables the reliability of the study results likely to be high.<br>• The authors stated that they had no financial or non-financial competing interests to declare | • Despite improvement over traditional observational studies to adjust for confounding by indication, propensity matched analyses is unable to properly correct for non-measured potentially confounding variables such as pre-dialysis care, residual renal function, and the kind of physiological dialysis solutions used.<br>• It is unknown if the follow-up time was long enough to predict late complications of any dialysis modality.<br>• Only HD patients with similar baseline characteristics as PD patients were included in the study. Thus it is unknown if the study results will be generalizable in all patients who require RRT.<br>• The study relies solely on analysis of Norwegian Renal Registry data. Therefore, the generalizability of its results to the Canadian context is unknown. |
| Kumar, 2014[9] | |
| • A propensity-matched study, which matched a large and diverse study population to solve the bias due to confounding by indication.<br>• Survival analyses based on both as-treated and ITT produced similar results indicating rigor of the findings.<br>• The CHR analysis used to directly compared survival between PD and HD patients provide clinicians with a truly prognostic estimate of the cumulative treatment effect of PD vs. HD over time, which is not provided by time-dependent hazard ratios.<br>• In addition, the CHR provides one with the ability to directly compare adjusted survival curves between PD and HD at select times of interest.<br>• All the authors declared no competing interests. | • Patients were included only if they had been members of a particular health care provider organization for at least one year prior to the initiation of dialysis. This suggests selection bias, although the organization provides healthcare across the USA.<br>• All HD patients included in the study utilized either an arterio venous fistula or a graft during the first 90 days of study. HD patients who utilized a central venous catheter as vascular access at any time during the first 90 days of dialysis were excluded from the final analysis. Thus it is unknown whether the results of this study could be replicated when other access catheters are used.<br>• The study excluded HD patients who initiated dialysis urgently with a catheter in an effort to reduce case-mix bias. Thus potential “Crash” dialysis patients may have been excluded from the study.<br>• The study did not have data regarding baseline residual renal function, and baseline laboratory values were limited at the time |

| **Table A2:** Strengths and Limitations of Randomized Controlled Trials using Downs and Black[8] | |
|---|---|
| **Strengths** | **Limitations** |
| | dialysis was initiated. Since these are important confounders, the likelihood of a differential baseline residual renal function and laboratory values skewing the study finding in favor of one dialysis modality cannot be ruled out. |
| Lukowsky, 2013[10] | |
| • The MSM analysis of the study adjusted for many potential confounders including time-varying modality changes and transplant censorship to minimize biases associated with nonrandomized studies.<br>• The study included a large cohort of dialysis patients from the entire USA,<br>• Detailed laboratory measures that were processed in a single laboratory center were included, adjusting | • A nonrandomized study, susceptible to bias due to uncontrolled confounding (especially confounding by indication), measurement errors, and selection bias.<br>• The follow-up period (24 months) is enough to assess the impact of initial dialysis modality on long-term outcomes, including complications.<br>• One of the authors had received grant support and/or honoraria from a firm that deals in products for renal care including dialysis. However, this is unlikely to bias the outcomes since the company caters for both PD and HD needs. |
| Koch, 2012[11] | |
| • Objectives of the study and the details of the intervention were clearly defined<br>• Univariate and multivariate analyses were conducted to assess the influence of potential confounders on the results<br>• The main findings of the study were clearly described with estimates of variability for outcomes, where applicable.<br>• The authors declared no conflict of interest. | • It is uncertain if the study was sufficiently powered to detect differences in outcomes between the treatment groups.<br>• A single centre study conducted over a relatively short period (from March 2005 to June 2010). Therefore, it is uncertain whether the results are generalizable in other settings, or if they would be sustained in the long-term.<br>• Although regression analyses found they had no significant impact on overall mortality, there were some significant differences between PD and HD patients at baseline. However, the possibility that the study was not sufficiently powered to make such detection cannot be ruled out. Areas of baseline differences included:<br>o The prevalence of heart failure (NYHA Stage III–IV) was significantly higher in the PD group compared with the HD group (73 versus 46%in HD group, $P < 0.01$).<br>o HD patients had a significantly higher baseline serum creatinine ($P = 0.046$) with a significantly lower estimated |

| **Table A2:** Strengths and Limitations of Randomized Controlled Trials using Downs and Black[8] | |
|---|---|
| **Strengths** | **Limitations** |
| | glomerular filtration rate (*P* = 0.025).<br>○ HD patients suffered more frequently from malignancy compared with PD patients (26% versus 8%, respectively, *P* = 0.007)<br>• The study population consisted mainly of elderly patients and in multivariate analysis showed that age at initiation of dialysis was significantly associated with overall mortality risk. Therefore, it is uncertain whether the reported findings will be reproducible in a younger population. |

CHR = cumulative hazard ratio; HD = hemodialysis; ITT = intent-to-treat; MSM = marginal structural models; NYHA = New York Heart Association; PD = peritoneal dialysis; RRT = renal replacement therapy; USA = United States of America

**APPENDIX 4: Main Study Findings and Author's Conclusions**

| **Table A3:** Summary of Findings of Included Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| Waldum-Grevbo, 2015[2] | |
| • The as-treated and ITT analyses showed all-cause mortality was not affected by initial dialysis modality. In the as-treated analysis HR (95%) at both year-2 and year-5 were 0.87 (0.67, 1.12) and 0.95 (0.77, 1.17), respectively. The corresponding values using ITT analysis were 0.93 (0.73, 1.18) and 0.99 (0.82, 1.19) for year-2 and year-5, respectively.<br>• Among patients who were younger than 65 years, all-cause mortality was lower with PD compared with HD. The 2 years HR (95% CI) of cardiovascular mortality were 0.39 (0.19, 0.81; *P* for interaction = 0.011) and 0.47 (0.26, 0.85, *P* = 0.009) for as-treated and ITT analyses respectively. The corresponding 5 years HR (95% CI) values 0.49 (0.27, 0.89; *P* = 0.010); and 0.58 (0.36, 0.93, *P* =0.009) for the as-treated and ITT analyses, respectively.<br>• The overall cardiovascular mortality was lower among PD patients younger than 65 years compared with their HD counterparts, with 5 years HR (95% CI) of 0.38 (0.15, 0.96) and 0.28 (0.11, 0.68) in the as-treated and ITT analyses, respectively. | • "In this propensity matched study, PD as initial dialysis modality was not inferior to HD concerning five-year all-cause or cardiovascular mortality in any investigated subgroup of patients in the Norwegian dialysis population. PD as initial dialysis modality conveyed favourable survival compared to HD in patients younger than 65 years. Opposed to the trend of exaggerated use of HD compared to PD, increased use of PD could be advocated according to our data."[2] page 7 |
| Kumar, 2014[9] | |
| • Survival outcomes were more favorable with PD as initial modality compared with HD. The CHR (95% CI) for death at one year (HD vs. PD) was 2.38 (1.68, 3.40; *P*<0.0001) and 2.10 (1.50, 2.94; *P*<0.0001) in the as-treated and intent-to-treat analyses, respectively. The favorable survival outcomes associated with PD as initial modality persisted for nearly 2 years and 3 years of follow-up in the ITT analysis and as-treated analysis respectively, with no differences thereafter.<br>• The CHR (95% CI) values at 2 years were 1.39 (1.06, 1.82, *P* | • "The cumulative risk of death was over two-fold higher over the course of the first year on dialysis among matched incident HD patients compared with incident PD patients in both the adjusted time-dependent as-treated and intent-to-treat analyses." "The results of our analyses demonstrate a statistically significant lower cumulative risk of death associated with PD during the first 2–3 years of dialysis, depending on the method of analysis. "The early survival benefit associated with PD in our study could be attributed |

| Table A3: Summary of Findings of Included Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| = 0.017) and 1.26 (0.98, 1.63, *P* = 0.070) in the as-treated and in the ITT analyses, respectively. | to unmeasured confounding factors resulting in selection bias and early mortality of higher risk HD patients."[9] page 1019 |
| Lukowsky, 2013[10] | |
| • In MSM analyses, peritoneal dialysis was associated with persistently greater survival, with a death HR (95% CI) of 0.52 (0.34, 0.80) HD vs. PD.<br>• In analysis which adjusted for time-varying laboratory measures, PD patients had 48% lower mortality as indicated by death HR (95% CI) of 0.52 (0.34, 0.80)<br>• Among patients with HD as initial dialysis modality 6% had kidney transplant compared with 18% among patients who had PD as initial dialysis modality. Among the patients undergoing HD at day 90, 6% in the HD group switched modality at least once during 2 years, whereas the modality switch rate was 57% among PD patients. | • "Comparing survival of PD and HD among 23,718 incident dialysis patients during their first 2 years of dialysis treatment in a nationally representative cohort using statistical techniques that account for time- varying confounding and differential censorships, we found that incident PD patients had 48% greater survival. These findings, if further confirmed, may have important implications for the choice of dialysis modality and resource allocations in renal replacement therapy programs. Additional research is needed to examine the effect of modality and its changes on the survival of dialysis patients over a longer time period."[10] Page 2 |
| Koch, 2012[11] | |
| • At six months, there was 30.3% all-cause mortality in the PD group compared with 42.1% in the HD group. The difference was not statistically significant (*P* = 0.19). A relatively higher proportion of mortality among PD patients was attributed to unknown causes compared to HD patients (30% versus 16.7%, respectively)<br>• Cardiovascular mortality at the end of six months was 9.1% in PD compared with and 10.5% in HD patients, with no statistically significant difference between the two groups (*P* = 1.00).<br>• The proportion of patients who had bacteremia in the course of the six months study was significantly higher in the HD group compared with PD group (21.1% versus 3.0%, respectively, *P* < 0.01); with the RR (95% CI) for bacteremia (HD vs. PD) estimated to be 0.16 (0.05, 0.57; *P* = 0.005). | • "Dialysis modality (PD versus HD) in an acute unplanned dialysis setting showed, in our population, no significant influence on survival. HD patients had a significantly higher risk of bacteraemia, perhaps due to central venous dialysis catheter. PD seems to be a safe and efficient, at least comparable, alternative to HD in acute unplanned dialysis settings."[11] Page 375 |

| Table A3: Summary of Findings of Included Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| • However, the overall incidence of mortality due to infection was not significant different between the HD and PD groups (17.5% versus 9.1%, respectively, *P* = 0.19). | |

CHR = cumulative hazard ratio; HD = hemodialysis; HR = hazard ratio; ITT = intent-to-treat; MSM = marginal structural models; PD = peritoneal dialysis; RR = relative risk; RRT = renal replacement therapy

## APPENDIX 5: Additional References of Potential Interest

*This guideline was excluded because it has very limited relevant information regarding the use of peritoneal dialysis in adult patients.*

Vinsonneau C, lain-Launay E, Blayau C, Darmon M, Ducheyron D, Gaillot T, et al. Renal replacement therapy in adult and pediatric intensive care : Recommendations by an expert panel from the French Intensive Care Society (SRLF) with the French Society of Anesthesia Intensive Care (SFAR) French Group for Pediatric Intensive Care Emergencies (GFRUP) the French Dialysis Society (SFD). Ann Intensive Care. 2015 Dec;5(1):58.