PHILIPPINE CLINICAL PRACTICE GUIDELINES

ON HEMODIALYSIS

FULL DOCUMENT

2018

Clinical Practice Guidelines on Hemodialysis Task Force
Philippine Society of Nephrology & PSN Hemodialysis Committee
Asia-Pacific Center for Evidence-Based Healthcare, Inc.

CLINICAL PRACTICE GUIDELINES FOR HEMODIALYSIS AMONG ADULTS

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ACKNOWLEDGMENT

This project was initiated by the Hemodialysis Committee of the Philippine Society of Nephrology (PSN) and was made possible through the society's financial and administrative support. The PSN did not impose any condition or in any way influence the guideline methods and process nor interfere in the operations and formulation of the final recommendations.

Extensive technical work was provided by the Asia Pacific Center for Evidence Based Healthcare (APCEBH). This ensured that objectivity was maintained in the gathering and processing of the evidence as well as in facilitating and conducting the consensus meeting. This also assured that bias was minimized in the documentation and writing of the final report.

Both the PSN Secretariat and the APCEBH coordinated the tasks among individuals, groups, and committees involved in developing this project, but the Steering Committee of the CPG on Hemodialysis continued to be responsible for the overall direction of the CPG development and accountable for the quality of the output.

This CPG is invaluable for the time and effort spent by the panelists and observers who shared, discussed and poured through evidence and shared their experience. More importantly, it is hoped that this becomes an instrumental first step that can assist physicians of today and those in the years ahead.

DISCLAIMER

This CPG is based on the best available scientific literature at the time of its development and only focuses on Chronic Hemodialysis in adult patients. It is not meant to restrict nephrologists from using sound clinical judgment and considering patients' values and preferences in their practice. Individual patients and their response to various treatments can sometimes be unpredictable and are not guaranteed. Therefore, this CPG must not be used to substitute good judgment in making treatment decisions and tailoring them to the particular needs of the patient.

This CPG can serve to inform policy but it is not meant to serve as a basis for approving or denying financial coverage or insurance claims merely because of nonconformance with recommendations. Neither should the recommendations be considered as legal rules for dictating certain modes of action to the exclusion of others.

ABBREVIATIONS

APCEBH	Asia Pacific Center for Evidence Based Healthcare
CHF	Congestive Heart Failure
CKD	Chronic Kidney Disease
COI	Conflict of Interest
CPG	Clinical Practice Guidelines
CV	Cardiovascular
EBM	Evidence-Based Medicine
ERE	Evidence Review Experts
GFR	Glomerular Filtration Rate
NGT	Nominal Group Technique
PSN	Philippine Society of Nephrology
QOL	Quality of Life
RO	Reverse Osmosis

EXECUTIVE SUMMARY

This Clinical Practice Guideline (CPG) is the first Philippine CPG focusing on hemodialysis among adults. This provides practice recommendations on timing, frequency, and duration of hemodialysis including the frequency of reuse of dialyzers, and the care of the water for dialysis use.

The recommendations are based on the best available evidence at the time of CPG development and are intended for use by nephrologists and other internists as well as the clinical staff of dialysis units nationwide.

The process that was followed for the development of this CPG is called the GRADE Approach – Grading of Recommendations, Assessment, Development and Evaluation. This approach is widely used by guideline developers worldwide and includes the following steps: 1) identification of key questions, 2) retrieval of current evidence, 3) assessment, synthesis of evidence, and drafting of the evidence-based recommendations, 5) identifying the stakeholder panel tasked to sift through the evidence base in consideration of local experience and certain patient groups, 6)

revision and approval of the recommendations by the consensus panel, 7) dissemination and implementation, 8) impact evaluation and 9) updating.

These recommendations are only good until that time when new technology or new evidence surface, and patient or provider preferences change. Revisiting and updating the guidelines will be done every 3 to 5 years.

Summary of the Recommendations

Recommendation 1	Initiation of hemodialysis at eGFR greater than 10 ml/min is not recommended among asymptomatic patients with CKD 5. *(Moderate Quality; Strong Recommendation).*
Recommendation 2	Initiation of hemodialysis in the absence of uremic manifestations is generally not recommended among patients with CKD 5. *(Very Low Quality; Weak Recommendation).*
Recommendation 3	Among CKD 5 patients with CHF, initiating hemodialysis at eGFR <15ml/min may be recommended. *(No Evidence; Weak Recommendation).*
Recommendation 4	Among CKD 5 patients on low-flux hemodialysis, 3 times a week hemodialysis may be recommended. *(Very Low Quality; Weak Recommendation).*
Recommendation 5	Among CKD 5 patients on high-flux hemodialysis, 3 times a week hemodialysis may be recommended. *(No Evidence; Weak Recommendation).*
Recommendation 6	Among CKD 5 patients on low-flux hemodialysis, 4 hours 3 times a week hemodialysis is recommended. No recommendation can be made for 5 hours or longer 2 times a week hemodialysis at this time. *(No Evidence; Weak Recommendation).*
Recommendation 7	Among CKD 5 patients achieving a single-pool Kt/V of at least 1.2 and on dialysis 3x a week, the use of high flux dialyzer may be recommended instead of low flux dialyzer. *(Low Quality; Weak Recommendation).*
Recommendation 8	Among CKD 5 patients on 2x weekly hemodialysis, no recommendation can be made for high-flux over low-flux hemodialysis at this time. *(No Evidence; Weak Recommendation).*
Recommendation 9	Among CKD 5 patients on 3 times a week low flux dialysis, no recommendation can be made to change the 2016 PSN Guideline of not more than 9 reuses. *(Very Low Quality; Weak Recommendation)*
Recommendation 10	No recommendation can be made at this time on testing the total microbial count of RO dialysis water samples taken from point of use per machine once a month versus per machine once a year. *(No Evidence; No Recommendation).*

INTRODUCTION

This document marks the first time that the Philippine Society of Nephrology has taken on the task of formulating clinical practice guidelines pertaining specifically o the practice of Hemodialysis in the Philippine setting. This effort is long overdue, as the burden of chronic kidney disease and end stage renal disease (ESRD) continues to grow, with the number of Filipinos requiring dialysis or transplantation growing by over 30,000 Filipinos every year.

While it is recognized that kidney transplantation is the treatment of choice for ESRD, few are currently able to pursue this option because of medical contraindications, a lack of available organ donors, or a lack of financial resources. For patients without medical contraindications, hemodialysis or peritoneal dialysis serves well as a bridge to transplantation.

Hemodialysis is currently the most common form of renal replacement therapy in the Philippines, and is among the top procedures reimbursed by the Philippine Health Insurance Corporation (at over PhP 7 billion in the year 2015). It exacts a heavy economic burden on patients and their families, as about half of the total health expenditure is still borne out of pocket. With the average monthly income of a Filipino family at PhP 22,250 (FIES Data 2017), and with most patients requiring 104 to 156 hemodialysis sessions per year (or 2 to 3 sessions per week) at an average cost higher than the PhP 2,600 per session for 90 sessions per year covered by Philhealth (Circular No. 022-2015) for its members, it is readily apparent that the economic burden of hemodialysis therapy is tremendous and onerous.

Clinical practice guidelines, insofar as they help us achieve better outcomes for our patients in terms of survival and quality of life, by helping to define the standard of care and reducing variance in practice patterns, and insofar as they help us optimize the allocation of scarce resources – not just financial, but also in terms of the health workforce, infrastructure, and time – are important tools to attain these two ends. Unfortunately, achieving better outcomes and optimizing the allocation of scarce resources are two ends which are always in dynamic tension.

The development of these clinical practice guidelines has been a wide-ranging effort, bringing to the table many members of our professional society and other stakeholders in the practice of Hemodialysis, including representatives of the very people we seek to serve, our patients with ESRD. The entire process of guideline formulation – from the drafting of the questions to be addressed all the way to the final wording of the guideline recommendations, and even beyond this to the identification of evidence gaps that require further research – was overseen by the expert guidance of the Asian Pacific Center for Evidence Based Healthcare.

This document is a work in progress. The recommendations are definite, but it is understood that they shall evolve over time. It shall serve us well to be guided by this document, but at the end of the day the merit of this document will only be known when it has been implemented, and we have assessed the outcomes of our patients after a certain period of its implementation.

GUIDELINE DEVELOPMENT METHODS

Formation of the Working Groups and Consensus Panel

The first task of the PSN Hemodialysis Committee was to create the Steering Committee from its members and entrust it with the direction of the CPG development process. The Steering Committee contacted APCEBH to provide the technical support needed to complete the guidelines. The APCEBH formed teams of Evidence Review Experts (ERE) from APCEBH assisted by PSN fellows-in-training. These teams identified, retrieved, reviewed, and summarized relevant evidence from the medical literature.

The Steering Committee convened a multi-sectoral consensus panel composed of dialysis patients, patient advocates, nurses, nutritionists, transplant surgeons, infectious disease specialists, and nephrologists from the different training institutions in the country.

The Steering Committee members declared their conflicts of interest (COI) and inhibited themselves from voting. Potential members of the consensus panel were screened to minimize possible COI. To ensure independence, each member of the consensus panel was asked to declare their conflicts of interest by completing a conflict of interest form (Appendix B).

Synthesis of the Evidence and Drafting of Recommendations

The Steering Committee drafted ten (10) focused research questions to address priority issues on hemodialysis for CKD 5 patients.

The ERE conducted a systematic search for the best available evidence for each of the questions. The yield from the search was reviewed and articles were considered relevant if they passed the eligibility criteria. Randomized trials or observational studies were appraised for directness, validity, and applicability.

The ERE assessed the quality of evidence according to the GRADE Method as follows:

Observational studies	**Quality of the Evidence**	**Randomized trials**
Extremely strong association and no major threats to validity	High (Further research unlikely to change our confidence in estimate of effect)	No serious flaws in study quality
Strong consistent association and no plausible confounders	Moderate (Further research is likely to have an important impact)	Serious flaws in design or execution or quasi-experimental design
No serious flaws in study quality	Low (Further research is very likely to have an important impact)	Very serious flaws in design or execution
Serious flaws in design and execution	Very low (The estimate of effect is very uncertain)	Very serious flaws and at least one other serious threat to validity
Additional factors that lower quality are: • Important inconsistency of results • Some uncertainty about directness • High probability of reporting bias • Sparse data • Major uncertainty about directness can lower the quality by two levels		
Additional factors that may increase quality are: • All plausible residual confounding, if present, would reduce the observed effect • Evidence of a dose-response gradient		
Factors that may lead to construction of separate evidence summaries and balance sheets for disadvantaged populations: • Evidence of difference in effects in disadvantaged subgroups • Absence of direct evidence for disadvantaged subgroups		

Outcomes across studies that can be combined were synthesized, and evidence summaries and GRADE evidence profiles were prepared for every question. The overall quality of evidence was assessed based on the lowest quality of evidence given to any of the critical outcomes. Benefits and harms were also weighed based on the critical outcomes.

The ERE proposed a strength of recommendation based solely on the level of evidence. A “strong recommendation” is supported by a high or moderate level of evidence, while

a low or very low level of evidence results in a "weak" or "conditional recommendation."

A compilation of the draft recommendations with their corresponding evidence base was then sent to the consensus panel for review prior to the en banc meeting.

Formulation of the Final Recommendations (Consensus Meeting)

The consensus panel was oriented about the consensus process and their mandate to come up with the final recommendations. They were informed that their decision should be based on the following:

1. Quality of evidence
2. Balance between benefits and harms
3. Values and preferences of patients
4. Cost and resource use
5. Other considerations (e.g. local epidemiology, equity, accessibility and feasibility).

The consensus panel decided on the relative importance of each outcome. Each member scored each outcome from 1 to 9 according to perceived importance to decision-making. All outcomes with an average score of 7 or higher were considered critical and should be the basis for the recommendations.

The nominal group technique[i] was used to reach a consensus among the panel members during the en banc meeting. The ERE presented the evidence summaries and the draft recommendation for each question. Each panelist was asked to give their opinions in concise 3 to 4 sentences. Voting was done after each item was thoroughly discussed. Consensus was reached when there was at least 75% agreement. Four (4) draft recommendations were finalized. The rest of the recommendations were finalized after a modified Delphi method.[ii]

The recommendations were presented to all stakeholders in a public forum to obtain feedback especially from those not part of the panel.

Dissemination and Implementation

The plan for implementation and dissemination are as follows:

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[i] *The NGT is a structured 4-step process that includes generating, recording, discussing and voting on ideas to reach a consensus. Ideas are expressed one at a time in a round robin fashion preventing a single person to dominate the discussion.* Resource: Center for Disease Control and Prevention. Evaluation Briefs: Gaining Consensus Among Stakeholders Through the Nominal Group Technique. https://www.cdc.gov/healthyyouth/evaluation/pdf/brief7.pdf. (Accessed 07/08/2018)

[ii] *The modified Delphi method is a way to gather input from participants by use of a questionnaire that contains the unresolved issue and relevant information needed to find consensus or resolve the issue without a face-to-face encounter.* Resource: University of Illinois Extension, College of Agricultural, Consumer and Environmental Sciences. http://www.communitydevelopment.uiuc.edu/sp/Step6/Delphi%20Technique.pdf (Accessed 07/08/2018)

1. Publication in the Philippine Journal of Nephrology.
2. Presentation of the guidelines in major PCP activities like the mid-year convention and chapter post-graduate courses.
3. Distribution of the full guidelines in booklet format.
4. Presentation of the CPG to licensing authority (Department of Health, Local Government Units), third party payors (Philhealth, Health Maintenance Organizations, Philippine Charity Sweepstakes Office and the Department of Social Welfare and Development).
5. Presentation of the guidelines to hemodialysis owners and hemodialysis unit medical directors.
6. Inclusion of the CPG in the Training Manual and in the coverage of the Philippine Board of Nephrology Subspecialty Board Examinations.

FINAL RECOMMENDATIONS

Question 1. Among CKD 5 patients, will initiating hemodialysis at eGFR 5-9 ml/min compared to at 10-14 ml/min lead to better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 1. Initiation of hemodialysis at eGFR greater than 10 ml/min is not recommended among asymptomatic patients with CKD 5. *(Moderate Quality; Strong Recommendation).*

Summary of Evidence

A search was conducted using MEDLINE, clinicaltrials.gov, Cochrane database, TRIP database, published CPGs using terms such as chronic renal insufficiency, chronic kidney disease, chronic renal insufficiency, initiation, hemodialysis, dialysis, mortality, survival, hospitalization, quality of life, cost-effectiveness, randomized controlled trials, clinical studies and meta-analysis. Medical Subject Headings (MEsH) were combined with text words.

There were two (2) publications that report a comparison of early versus late initiation of hemodialysis among CKD 5 patients. In first study[1] called the IDEAL study, patients were randomly assigned either to commence dialysis (peritoneal or hemodialysis) when the estimated GFR was 10.0 to 14.0 ml per minute (early-start group) or to continue to receive routine medical care and commence dialysis when the estimated GFR was 5.0 to 7.0 ml per minute (late-start group).

The second publication[2] was a subgroup analysis of the IDEAL study specifically for those patients initially planned to receive hemodialysis at randomization. There was no significant difference in survival between patients in the early or late-start group (HR ratio with the late-start group as the reference is 0.97 (95% CI: 0.66– 1.41).

The subgroup analysis of the IDEAL study[2] also showed that the occurrence of cardiovascular and infectious events was not influenced by the timing of dialysis. Similarly, the frequency of dialysis treatment-related complications was not different with one exception. Patients in the early- start group were less likely to suffer significant fluid and electrolyte events compared to those in the late- start group (p = 0.02), with 44 events reported in the early- start group versus 73 in the late- start group (hazard ratio = 0.64, 95% CI: 0.44– 0.93).

For the outcome of quality of life, there was one randomized controlled study that showed, no significant difference, as measured by the Assessment of Quality of Life instrument. [3]

For the outcome of cost-effectiveness, there was one study,[3] a companion economic study of IDEAL, which compared total costs of treatment and quality-of life outcomes in the early- and late-start groups. The patients on early initiation of dialysis had increased dialysis costs, increased transport costs, and a trend to higher total treatment costs in comparison to those in whom dialysis has been electively delayed. Results do not provide evidence that planned early start dialysis is cost-effective compared with planned late-start dialysis.

Question 2. Among CKD 5 patients, will initiating hemodialysis when the patient has signs and symptoms of uremia compared to initiating when without uremic signs and symptoms lead to better survival, better quality of life, less hospitalization, or be more cost-effective?

Recommendation 2. Initiation of hemodialysis in the absence of uremic manifestations is generally not recommended among patients with CKD 5. *(Very Low Quality; Weak Recommendation).*

Summary of Evidence

There is conflicting evidence for delaying initiation of hemodialysis (HD) until uremic signs and symptoms appear versus early initiation for the outcome of survival. Early initiation of RRT when CKD 5 patients have no signs and symptoms of uremia showed no significant benefit for the outcome of death over late initiation when patients have developed uremic signs and symptoms based on 1 RCT (low level of evidence) and 1 observational study (very low level of evidence).[1,2] Two other observational studies showed an increased risk for overall mortality with late initiation of hemodialysis.[3,4]

Another observational study (Yamagata 2016) showed an increased risk for death on late initiation of HD for ESRD patients presenting with Congestive Heart Failure and intractable edema (very low level of evidence).[5] However, this study was based on Japan's registry which started in 1988–1989 when dialysis practice may differ from present-day practices. On the other hand, the presence of fluid overload and

hypertension on initiation of HD was not significantly associated with mortality in 1 observational study.[2]

Early initiation of RRT demonstrated no significant benefit on risk for cardiovascular death or death due to infection in 1 RCT (low level of evidence) and 1 observational study (very low level of evidence).[1,3]

Studies were conflicting on the risk for hospitalization among those initiating hemodialysis with uremic signs and symptoms based on 2 observational studies (very low level of evidence). [4-5]

There were no studies found comparing the outcomes of quality of life and cost-effectiveness in the two groups.

Evidence reviewed does not show consistent evidence for benefit on survival or hospitalization with early initiation of HD among CKD patients versus delaying until signs and symptoms of uremia appear.

Cooper 2010 (IDEAL Study)[1] reports a 6-month difference in the initiation of dialysis in those who started late (with uremic symptoms) from those who started early.[1] Initiation of hemodialysis demands an increase in resources and staff to provide the procedure. Dialysis initiation has a major impact on the daily life of the patient and imposes a financial burden to the family. Government support for dialysis patients remains limited in the Philippines. Quality of life and cost-effectiveness of delaying RRT should be determined.

Question 3. Among patients with CKD 5, will initiating hemodialysis among patients with congestive heart failure (CHF) at eGFR 10-14 ml/min compared to at eGFR 5-9 ml/min lead to better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 3. Among CKD 5 patients with CHF, initiating hemodialysis at eGFR <15ml/min may be recommended. *(No Evidence; Weak Recommendation).*

Summary of Evidence

On literature search, there were no studies comparing said outcomes of early versus late initiation of hemodialysis among CKD 5 patients with CHF. However, there was evidence from three cohort studies that show increased risk of mortality among CKD 5 patients who had CHF compared to those without CHF on initiation of dialysis, with a relative risk (RR) of 1.72 (95% CI 1.38, 2.13).[1-3]

Question 4. Among CKD 5 patients on low-flux hemodialysis, will 2 times a week compared to 3 times a week hemodialysis sessions lead to a better quality of life, better survival, less hospitalization or be more cost-effective?

Recommendation 4. Among CKD 5 patients on low-flux hemodialysis, 3 times a week hemodialysis may be recommended. *(Very Low Quality; Weak Recommendation).*

Summary of Evidence

Upon thorough search, there were no randomized controlled trials that compared 2 times a week versus 3 times a week hemodialysis sessions for CKD 5 patients on low flux hemodialysis on the outcomes of quality of life, better survival, less hospitalization and whether either is cost-effective. However, evidence to answer this question was derived from observational studies comparing twice-weekly and thrice-weekly low flux hemodialysis done for 4 hours.

Based on a prospective cohort study, survival rate of patients between the two treatment arms was comparable.[1] Twice-weekly dialysis session group demonstrated no significant difference in all-cause mortality in one cohort study[2] and mortality rate ratio in one retrospective observation analysis[3] when compared to the thrice-weekly dialysis group. The quality of evidence from these three studies is low.

There was an increased risk of cardiovascular disease in the thrice-weekly dialysis group compared to the twice-weekly dialysis group based on a prospective study of low quality.[4]

There was no significant difference in the hospitalization rates between the two groups in a retrospective observational analysis.[3]

Another observational study showed better health-related quality of life scores, but were not significant in the incremental group (1-2x/week dialysis group) for the majority of domains of the Kidney Disease Quality of Life Short Form and Beck's Depression Inventory at 3 months after maintenance HD initiation.[2] Moreover, reassessment of the quality of life scores using the same questionnaires showed no significant difference between the two groups at 12 months of hemodialysis. In this study, 927 patients were initially identified with 822 assigned in the thrice-weekly group while 105 patients were on the incremental group. Propensity score matching of 2:1 was employed with thrice-weekly group having 207 patients while the incremental group had the same number of patients. Quality of life scores were statistically non-significant before and after the propensity score matching.

There was no available cost-effectiveness study comparing twice-weekly versus thrice-weekly low-flux hemodialysis.

Question 5. Among CKD 5 patients on high flux hemodialysis, will 2 times a week compared to 3 times a week hemodialysis sessions lead to better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 5. Among CKD 5 patients on high-flux hemodialysis, 3 times a week hemodialysis may be recommended. *(No Evidence; Weak Recommendation).*

Summary of Evidence

A thorough search was done using the following terms: end-stage renal disease, end-stage kidney disease, end-stage renal failure, hemodialysis, artificial kidney, artificial membrane, high flux hemodialysis, high flux hemodialysis frequency, high flux hemodialysis dose, high flux dialysis dose, high flux dialysis frequency.

There were two clinical trials found, substudies of the HEMO study, which randomized patients into 4 groups – low-flux, high-flux, standard dose, and high-dose hemodialysis, but all were done 3x a week.[1,2] There was no study comparing 3x a week and 2x a week high-flux hemodialysis.

Question 6: Among CKD 5 patients on low flux hemodialysis, will 4 hours 3x a week compared to 5 hours or longer 2x a week lead to better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 6. Among CKD 5 patients on low-flux hemodialysis, 4 hours 3 times a week hemodialysis is recommended. No recommendation can be made for 5 hours or longer 2 times a week hemodialysis at this time. *(No Evidence; Weak Recommendation).*

Summary of Evidence

There were no studies found on literature search that directly answer the question comparing twice weekly (5 hours or more per session) versus thrice weekly (4 hours per session) low-flux hemodialysis. However, what exist in literature are studies that compared the different frequency and duration of high-flux hemodialysis.

An evidence report[1] which formed the basis for the KDOQI Clinical Practice Guideline for Hemodialysis Adequacy[2] included five studies (n = 238) composed of 2 RCTs[3,4] and 3 Controlled Clinical Trials[5,6,7] that altered both frequency and duration of high-flux hemodialysis sessions.

Pooled analysis of two RCTs (n = 138) that compared longer duration and more frequent sessions (5 to 7 times per week) versus conventional hemodialysis (three times per week; 4 hours/session) showed no significant difference in all-cause mortality (RR 2.18, 95% CI 0.33, 14.48; I^2 = 0%; very low quality of evidence). [3,4] One CCT (n = 35) also showed similar results (RR 1.69, 95% CI 0.40, 7.19; very low quality of evidence).[5] One

RCT (n = 87) showed no significant difference in all-cause hospitalizations between treatment groups (HR 1.42, 95% CI 0.69, 2.90; very low quality of evidence).[4]

One RCT reported no significant difference in change in EuroQol 5-D index from baseline between groups (0.05, 95% CI -0.07-0.17).[3] There were no studies on cost-effectiveness.

Question 7. Among CKD 5 patients achieving a single-pool Kt/V of at least 1.2 and on dialysis three times a week, will using a high flux dialyzer instead of low flux dialyzer lead to a better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 7. Among CKD 5 patients achieving a single-pool Kt/V of at least 1.2 and on dialysis 3x a week, the use of high flux dialyzer may be recommended instead of low flux dialyzer. ***(Low Quality; Weak Recommendation).***

Summary of Evidence

On thorough search of medical literature, four (4) clinical trials were found that examined the effect of a high flux dialyzer compared to a low flux dialyzer in CKD 5 patients who achieved a single-pool Kt/V of at least 1.2 and on dialysis three times a week in terms of survival. All the studies were conducted in developed countries particularly in Europe and the USA.[1-4] One of the four trials assessed quality of life[5] while another did a cost-effectiveness study on a subgroup of participants.[6]

Among CKD 5 patients achieving a single-pool Kt/V of at least 1.2 and on dialysis three times a week, high flux dialyzer showed no added benefit in decreasing all-cause mortality compared to low flux dialyzer with a relative risk (RR) of 0.93 (95% CI 0.86 to 1.01) in 4 randomized controlled clinical trials involving a total of 3911 participants. However, from the same trials, high flux dialyzer appears to be beneficial in decreasing cardiovascular related mortality with a RR of 0.82 (95% CI 0.71 to 0.95).[1-4]

No benefit was found in the infection-related deaths with a RR of 0.91(95%CI 0.72 to 1.16) and the rate of hospitalization with a RR of 0.89 (95% CI 0.89 to 2.36) from 2 randomized controlled clinical trials involving 2439 participants.[2,4] One of the above studies assessed the health-related quality of life of 1,813 participants annually for 3 years using the Index of Well-Being (IWB) and the Kidney Disease Quality of Life - Long Form (KDQOL-LF) questionnaire. Only Sleep scores and Patient satisfaction scores under Symptom/Problem domain showed benefit among those on high-flux dialyzer, with average effects of +2.25 (SE 0.95) and +2.12 (SE 0.88) respectively. A trend towards sleep benefit was suggested at the 2nd and 3rd year of follow-up. No added benefit was noted in all other scores including Index of Well-Being, Physical component summary score and Mental component summary score.[5] A follow-up study aiming to compare HRQOL differences between old (i.e. >70 years) and young patients found better-preserved multidimensional quality of life in older patients at baseline and no substantial change in multidimensional QOL at 3 years.[7]

Question 8: Among CKD 5 patients on 2 x a week hemodialysis, does low flux compared to high flux hemodialysis lead to better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 8. Among CKD 5 patients on 2x weekly hemodialysis, no recommendation can be made for high-flux over low-flux hemodialysis at this time. *(No Evidence; Weak Recommendation).*

Summary of Evidence

There were no studies found on literature search directly comparing low flux versus high flux among patients receiving twice a week hemodialysis only. The CONTRAST study enrolled patients receiving either 3 times compared to 2 times a week hemodialysis, but the latter group only comprised 6% of the total number of patients in the trial (n = 714).[1] No subgroup analysis were performed as well.

Currently there is no data on the comparative effects of 2 times a week low flux and high hemodialysis with high flux on quality of life, survival, hospitalization and even cost.

Question 9. Among CKD patients on 3 times a week low-flux dialysis, does 6th dialyzer reuse compared to 10th dialyzer reuse lead to better quality of life, better survival, less hospitalization or be more cost-effective?

Recommendation 9. Among CKD 5 patients on 3 times a week low flux dialysis, no recommendation can be made to change the 2016 PSN Guideline of not more than 9 reuses. *(Very Low Quality; Weak Recommendation)*

Summary of Evidence

After a thorough search of Medline and Cochrane Databases through Pubmed, a Google Scholar search, and hand searching through references of relevant studies, fourteen (14) studies were eventually deemed eligible for inclusion but the focus was on reuse versus single use only.[1-14] One systematic review was also retrieved for assessment.[15] Two additional studies were also retrieved that looked into costing of reuse versus single use.[16,17] Unfortunately, no evidence was gathered comparing 6th dialyzer reuse versus 10th dialyzer reuse on stage 5 CKD patients on 3 times a week low-flux dialysis.

The studies on reuse versus single use were the available studies that were assessed and the quality ranged from very low to low owing to the fact that most were observational and subject to potential confounders.

The studies also varied in their conclusions with some studies showing that dialyzer reuse compared to single use was associated with an increase in mortality[3,4,11]

sometimes depending on type of dialyzer used as 2 studies analyzed data based on dialyzer type.[3,4] On the other hand, 9 studies showed no significant difference between reuse and single use with some studies showing data also analyzed based on dialyzer type.[1,4-6-10,12-14] There was one study that showed single use compared to reuse was associated with higher mortality with an OR of 2.94 (1.56, 5.55).[13] All information on mortality outcome is consistent with the conclusion of a systematic review done in 2012 with almost the same set of articles.[15]

Hospitalization as reported by 3 studies[6,7,10] showed conflicting results as well. One of these studies indicated hospitalization associated dialyzer reuse compared to single use.[7] The other looked at free-standing and hospital-based dialysis units, with the free-standing units showing hospitalization associated dialyzer reuse while the hospital-based dialysis units showed no significant difference between reuse compared to single use.[6] As for the study by Collins (2004), there was no significant difference in hospitalization risk among the reuse group versus single use group.[10]

There was one multiple crossover study on dialyzer reuse that had random allocation to order of treatment.[2] It reported no differences for symptoms of pruritis, cramps, nausea, headache, chest pain, backache or fatigue and thus dialyzer reuse was found to have neither clinical advantages nor disadvantages.

Two studies were retrieved that looked at cost effectiveness - one was an economic evaluation of hemodialyzer reuse compared to single conventional use[16] and the other looked at total direct cost of conventional single use and mechanical reuse of dialyzers.[17] Both studies came to the conclusion that moderate savings will be incurred by reusing hemodialyzers, although the economic evaluation by Manns (2012) emphasized that whether the savings will be large or minimal will depend on local circumstances.[16] The more current study by Qureshi (2016) stipulated that reuse of dialyzer is still cost-effective especially for patients living in resource constrained settings.[17] A local study on costing may further strengthen this conclusion.

Currently there is no data to support whether 6th reuse is better, inferior or equivalent compared to 10th reuse for CKD patients on 3 times a week low flux dialysis. The studies gathered were on reuse versus single use with reuse showing neither benefit nor harm, but may incur savings depending on the local situation.

Question 10. Will testing the total microbial count of RO dialysis water samples taken from point of use per machine once a month compared to per machine once a year lead to better quality of life, better survival, less hospitalization, or be more cost-effective?

Recommendation 10. No recommendation can be made at this time on testing the total microbial count of RO dialysis water samples taken from point of use per

machine once a month versus per machine once a year. ***(No Evidence; No Recommendation).***

Summary of Evidence

There were no studies found after a thorough literature search that directly answer the question. There were no studies that looked at the specified outcomes. What exist in literature are accepted standards for microbial count of dialysis water published by the International Standards Organization (ISO) or the American National Standards Institute (ANSI) and the Association for the Advancement of Medical Instrumentation (AAMI). It should be understood these dialysis water and fluid standards evolved from municipal water standards. Epidemiologic data were used and each AAMI standard or recommended practice is a consensus from a collective committee of health care professionals and industry representatives.[1]

Currently there is no data to support that testing the total microbial count of RO dialysis water samples taken from point of use per machine once a month versus per machine once a year lead to better quality of life, better survival, less hospitalization, or be more cost-effective.

Summary of the Issues and Information per Recommendation

Recommendation	Issues and Information
1. Initiation of hemodialysis at eGFR greater than 10 ml/min is not recommended among asymptomatic patients with CKD 5. (Moderate Quality; Strong Recommendation)	There are 2 studies that reported a comparison of early versus late initiation hemodialysis among CKD 5 patients. There was no significant difference in survival, hospitalization and quality of life between patients in the early or late-start groups. Results do not provide evidence that planned early start dialysis is cost-effective compared with late start.
2. Initiation of hemodialysis in the absence of uremic manifestations is generally not recommended among patients with CKD 5. (Very Low Quality; Weak Recommendation)	The studies showed conflicting evidence for delaying initiation of hemodialysis until uremic signs and symptoms appear versus early initiation. Two studies showed no significant benefit, while 2 other studies showed an increased risk in overall mortality with late initiation.
3. Among CKD 5 patients with CHF, initiating hemodialysis at eGFR <15ml/min may be recommended. (No Evidence; Weak Recommendation)	There are no studies directly comparing hemodialysis initiated at eGFR 10-14 ml/min versus initiation at eGFR 5-9 ml/min among CKD 5 patients with CHF. The evidence derived from 3 cohort studies compared CKD 5 patients with CHF to CKD 5 patients without CHF. The studies showed a higher risk of death among those with CHF. Initiation of hemodialysis at eGFR greater than 10 ml/min is not recommended among asymptomatic patients with CKD 5, but in practice, physicians would often start hemodialysis among patients with CHF at a higher eGFR.

4. Among CKD 5 patients on low-flux hemodialysis, 3 times a week hemodialysis may be recommended. (Very Low Quality; Weak Recommendation)	There are no randomized controlled trials that compared 2 times versus 3 times a week low-flux hemodialysis for CKD 5 patients. The 3 observational studies that were assessed had risk of bias issues and imprecise estimates for mortality, hospitalization, and quality of life. Cardiovascular disease was significantly higher in the 3 times a week group, but the study that showed this had risk of bias issues. as well.
5. Among CKD 5 patients on high-flux hemodialysis, 3 times a week hemodialysis may be recommended. (No Evidence; Weak Recommendation)	There are no studies comparing 2 times a week versus 3 times a week high-flux hemodialysis. There are 2 clinical trials that randomized patients into 4 groups – low-flux, high-flux, standard dose, and high-dose hemodialysis, but all hemodialysis were done 3 times a week.
6. Among CKD 5 patients on low-flux hemodialysis, 4 hours 3 times a week hemodialysis is recommended. No recommendation can be made for 5 hours or longer 2 times a week hemodialysis at this time. (No Evidence; Weak Recommendation)	There are no studies that directly compared twice weekly (5 hours or more per session) versus thrice weekly (4 hours per session) low-flux hemodialysis among CKD 5 patients. Studies on more frequent and longer duration of high-flux hemodialysis versus conventional hemodialysis howed no significant difference in mortality, hospitalization, and quality of life.
7. Among CKD 5 patients achieving a single-pool Kt/V of at least 1.2 and on dialysis 3x a week, the use of high flux dialyzer may be recommended instead of low flux dialyzer. (Low Quality; Weak Recommendation)	The studies showed no significant differences in all-cause mortality, death from infection, and hospitalization rates between high-flux versus low-flux hemodialysis. There was a significantly lower rate of cardiovascular death in the high-flux group.
8. Among CKD 5 patients on 2x weekly hemodialysis, no recommendation can be made for high-flux over low-flux hemodialysis at this time.	There are no studies directly comparing 2 times a week low-flux versus 2 times a week high-flux hemodialysis. Although the CONTRAST study enrolled patients receiving 3 times a week compared to 2 times a week hemodialysis, only 6% of the total number of patients in the study were actually in the 2 times a week group. No subgroup analysis was performed on this group.
9. Among CKD 5 patients on 3 times a week low flux dialysis, no recommendation can be made to change the 2016 PSN Guideline of not more than 9 reuses. (Very Low Quality; Weak Recommendation)	There are no studies directly comparing 6^{th} reuse versus 10^{th} reuse among CKD 5 patients on low-flux hemodialysis. The studies were on reuse versus single use. There is conflicting evidence among the observational studies, but more studies showed no significant difference on the outcomes of mortality and hospitalization between reuse and single use.
10. No recommendation can be made at this time on testing the total microbial count of RO dialysis water samples taken from point of use per machine once a month versus per machine once a year. Change to status quo- One test per machine once a year. (No Evidence; No Recommendation)	There are no studies that directly answer the question and looked at the specified outcomes. The information comes from accepted standards for microbial count of dialysis water by the International Standards Organization (ISO) or American National Standards Institute (ANSI), and the Association for the Advancement of Medical Instrumentation (AAMI). These standards evolved from municipal water standards.

FUTURE IMPLICATIONS

The guideline development process revealed important knowledge gaps that can be taken on by the Society or interested advocacy groups as a research project. These research projects can also focus on obtaining information on important clinical outcomes that include, but are not limited to, survival, hospitalization, adverse events and quality of life.

The group identified research gaps in the following:

1. Effect of early or late initiation of hemodialysis among patients with mild uremic symptoms.
2. Effect of twice weekly versus thrice weekly low-flux hemodialysis on clinically important outcomes.
3. Effect of twice weekly versus thrice weekly high-flux hemodialysis on clinically important outcomes.
4. Comparisons on frequency of low-flux dialysis per week and its effect on clinically important outcomes.
5. Effect of twice weekly low-flux versus twice weekly high-flux hemodialysis on clinically important outcomes.
6. Effect of thrice weekly low-flux versus thrice weekly high-flux hemodialysis on clinically important outcomes.
7. Comparisons on duration (4 hours versus 5 hours) of dialysis and its effect on clinically important outcomes.
8. Data on the number of dialyzer reuse and its effect on clinically important outcomes. Comparisons between 6^{th}, 8^{th}, and 10^{th} reuse or even up to 15^{th} reuse and its effect on clinically important outcomes.
9. Effect of early or late initiation of hemodialysis among those with CHF.
10. Data comparing water analysis done per month versus per year or per month versus per machine.

REFERENCES PER RECOMMENDATION

Recommendation 1. Initiation of hemodialysis at eGFR greater than 10 ml/min is not recommended among asymptomatic patients with CKD 5.

1. Cooper B, Branley P, Bulfone L, Collins J, Craig J, Fraenkel M et al. A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis. New England Journal of Medicine. 2010;363(7):609-619.
2. Collins J, Cooper B, Branley P, Bulfone L, Craig J, Fraenkel M et al. Outcomes of Patients with Planned Initiation of Hemodialysis in the IDEAL Trial. Hemodialysis. 2011;:1-9.
3. Harris A, Cooper B, Li J, Bulfone L, Branley P, Collins J et al. Cost-Effectiveness of Initiating Dialysis Early: A Randomized Controlled Trial. American Journal of Kidney Diseases. 2011;57(5):707-715.

Recommendation 2. Initiation of hemodialysis in the absence of uremic manifestations is generally not recommended among patients with CKD 5.

1. Cooper B, Branley P, Bulfone L, et al. A randomized, controlled trial of early versus late initiation of dialysis. N Engl J Med 2010;363:609-19.

2. Rivara MB, Chen CH, Nair A, Cobb D, Himmelfarb J, Mehrota R. Indication for Dialyaia Initiation and Mortality in Patients with Chronic Kidney Failure. AJKD (2017) 69:41-50.
3. Li WY, Wang YC, Shang JH, Lin SH, Wu KD, Chen YM. Comparison of Outcomes Between Emergent-start and Planned-start Peritoneal Dialysis in Incident ESRD patients: a Prospective Observational Study. BMC Nephrol. 2017; 18:359.
4. Chen YM, Wang YC, Hwang SJ, Lin SH, Wu KD. Patterns of Dialysis Initiation Affect Outcomes of Incident Hemodialysis Patients. Nephron. 2016; 132: 33-42
5. Yamagata K, Nakai S, Iseki K, Tsubakihara Y, The Committee of Renal Data Registry of the Japanese Society fot Dialysis Therapy. Therapeutic Apheresis and Dialysis. 2012; 16(2):111-120.

Recommendation 3. Among CKD 5 patients with CHF, initiating hemodialysis at eGFR <15ml/min may be recommended.

1. Bradbury BD, Fissell RB, Albert JM, Anthony MS, Critchlow CW, Pisoni RL, Port FK, Gillespie BW. Predictors of Early Mortality among Incident US Hemodialysis Patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS)**.** *Clin J Am Soc Nephrol* 2: 89–99, 2007.
2. Harnett JD, Foley RN, Kent GM, Barre PE, Murray D, Parfrey PS. Congestive heart failure in dialysis patients: Prevalence, incidence, prognosis and risk factors. *Kidney International*, Vol. 47 (1995), pp. 884—890
3. Yamada S, Ishii H, Takahashi H, Aoyama T, Morita Y, Kasuga H, Kimura K, Ito Y, Takahashi R, Toriyama T, Yasuda Y, Hayashi M, Kamiya H, Yazawa Y, Maruyama S, Matsuo S, Matsubara T, Murohara T. Prognostic Value of Reduced Left Ventricular Ejection Fraction at Start of Hemodialysis Therapy on Cardiovascular and All-Cause Mortality in End-Stage Renal Disease Patients. *Clin J Am Soc Nephrol* 5: 1793–1798, 2010

Recommendation 4. Among CKD 5 patients on low-flux hemodialysis, 3 times a week hemodialysis may be recommended.

1. Elamin S, Abu-Aisha H. Reaching target hemoglobin level and having a functioning arteriovenous fistula significantly improve one year survival in twice weekly hemodialysis. Arab J Nephrol Transplant. 2012;5(2):81–86.
2. Park JI, Park JT, Kim YL, et al. Comparison of outcomes between the incremental and thrice-weekly initiation of hemodialysis: a propensity-matched study of a prospective cohort in Korea. Nephrol Dial Transplant. 2016 (0): 1-9.
3. Mukherjee T, Devi G,Geetha S, Anchan NJ, Sankarasubbaiyan S.A comparison of practice pattern and outcome oftwice-weekly and thrice-weekly hemodialysis patients.Indian J Nephrol 2017;27:185-9.
4. Cheng Y, Tu W, Xiao Q. et al. Risk of cardiovascular disease inpatients on thrice-weekly versus twice-weekly hemodialysis. Int J Cardiol (2014), http://dx.doi.org/10.1016/j.ijcard.2014.04.052.

Recommendation 5. Among CKD 5 patients on high-flux hemodialysis, 3 times a week hemodialysis may be recommended.

1. Eknoyan G, Beck GJ, Cheung A et al. Effect of Dialysis Dose and Membrane Flux in Maintenance Hemodialysis. N Eng J Med 2002;347(25),2010-19.
2. Cheung AK, Sarnak MJ, Yan G et al. Cardiac diseases in maintenance hemodialysis patients: results of the HEMO study. Kidney International, 2004; 65, 2380-89.

Recommendation 6. Among CKD 5 patients on low-flux hemodialysis, 4 hours 3 times a week hemodialysis is recommended. No recommendation can be made for 5 hours or longer 2 times a week hemodialysis at this time.

1. Slinin Y, Ishani A, Greer N, MacDonald R, Olson C. An Evidence Report for the Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines and Recommendations for Hemodialysis Adequacy. Accessed 25 February 2018 from https://www.kidney.org/sites/default/files/HD-Adequacy-ERT-Report_20150204.pdf

2. Slinin Y, Greer N, Ishani A, MacDonald R, Olson C. 2015. Timing of Dialysis Initiation, Duration and Frequency of Hemodialysis Sessions, and Membrane Flux: A Systematic Review for a KDOQI Clinical Practice Guideline. Am J Kidney Dis. 66(5):823-836
3. Culleton B, Walsh M, Klarenbach SW, et al. Effect of frequent nocturnal hemodialysis versus conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. JAMA. 2007;298(11):1291-1299.
4. Rocco MV, Lockridge RS Jr, Beck GJ, et al; for the Frequent Hemodialysis Network (FHN) Trial Group. The effects of frequent nocturnal home hemodialysis: the Frequent Hemodialysis Network Nocturnal Trial. Kidney Int. 2011;10(80):1080-1091.
5. Lindsay RM, Leitch R, Heidenheim AP, Kortas C. The London Daily/Nocturnal Hemodialysis Study—study design, morbidity, and mortality results. Am J Kidney Dis. 2003;42:5-12.
6. Chan CT, Floras JS, Miller JA, Richardson RMA, Pierratos A. Regression of left ventricular hypertrophy after conversion to nocturnal hemodialysis. Kidney Int. 2002;61:2235-9.
7. Fagugli R, Pasini P, Pasticci F, Ciao G, Cicconi B, Buoncristiani U. Effects of short daily hemodialysis and extend standard hemodialysis on blood pressure and cardiac hypertrophy: a comparative study. J Nephrol. 2006;19:77-83.

Recommendation 7. Among CKD 5 patients achieving a single-pool Kt/V of at least 1.2 and on dialysis 3x a week, the use of high flux dialyzer may be recommended instead of low flux dialyzer.

1. Asci, G., Toz, H., Ozkahya, M., Duman, S., Demirci, M., Cirit, M., et al. (2013). The Impact of Membrane Permeability and Dialysate Purity on Cardiovascular Outcomes. *J Am Soc Nephrol 25*, 1014-1023.
2. Eknoyan, G., Beck, G., Cheung, A., Daugirdas, J., Greene, T., Kusek, J., et al. (2002). Effect of Dialysis Dose and Membrane Flux in Maintenance Hemodialysis. *N Engl J Med*, Vol 347 No. 25 2010-2018.
3. Grooteman, M., van den Dorpel, M., Bots, M., Penne, E., van der Weerd, N., Mazairac, A., et al. (2012). Effect of Online Hemodiafiltration on All-Cause Mortality and Cardiovascular Outcomes. *J Am Soc Nephrol 20*, 1087-1096.
4. Locatelli, F., Martin-Malo, A., Hannedouche, T., Loureiro, A., Papadimitriou, M., Wizemann, V., et al. (2009). Effect of Membrane Permeability on Survival of Hemodialysis Patients. *J Am Soc Nephro 20l*, 645-654.
5. Unruh, M., Benz, R., Greene, T., Yan, G., Beddhu, S., DeVita, M., et al. (2004). Effects of hemodialysis dose and membrane flux on health-related quality of life in the HEMO study. *Kidney International*, 355-366.
6. Levesque, R., Marcelli, D., Cardinal, H., Caron, M., Grooteman, M., Bots, M., et al. (2015). Cost-Effectiveness Analysis of Hig-Efficiency Hemodiafiltration versus Low-Flus Hemodialysis based on the Canadian Arm of the CONTRAST study. *Appl Health Econ Health Policy*, Online.
7. Unruh, M., Newman, A., Larive, B., Dew, M., Miskulin, D., Greene, T., et al. (2008). The influence of age on changes in health-related quality of life over three years in a cohort undergoing hemodialysis. *JAGS, 56:* 1608-1617.

Recommendation 8. Among CKD 5 patients on 2x weekly hemodialysis, no recommendation can be made for high-flux over low-flux hemodialysis at this time.

1. Grooteman, M., van den Dorpel, M., Bots, M., Penne, E., van der Weerd, N., Mazairac, A., et al. (2012). Effect of Online Hemodiafiltration on All-Cause Mortality and Cardiovascular Outcomes. *J Am Soc Nephrol 20*, 1087-1096.

Recommendation 9. Among CKD 5 patients on 3 times a week low flux dialysis, no recommendation can be made to change the 2016 PSN Guideline of not more than 9 reuses.

1. Held PJ, Pauly MV, Diamond L: Survival analysis of patients undergoing dialysis. JAMA 1987; 257: 645–650.
2. Churchill DN, Taylor DW, Shimizu AG, Beecroft ML, Singer J, Barnes CC, Ludwin D, Wright N, Sackett DL, Smith EKM: Dialyzer re-use – a multiple crossover study with random allocation to order of treatment. Nephron 1988; 50: 325-331.

3. Held PJ, Wolfe RA, Gaylin DS, Port FK, Levin NW, Turenne MN: Analysis of the association of dialyzer reuse practices and patient outcomes. Am J Kidney Dis 1994; 23: 692–708.
4. Feldman HI, Kinosian M, Bilker WB, Simmons C, Holmes JH, Pauly MV, Escarce JJ: Effect of dialyzer reuse on survival of patients treated with hemodialysis. JAMA 1996; 276: 620–625.
5. Collins AJ, Ma JZ, Constantini EG, Everson SE: Dialysis unit and patient characteristics associated with reuse practices and mortality: 1989–1993. J Am Soc Nephrol 1998; 9:2108–2117.
6. Feldman HI, Bilker WB, Hackett MH, Simmons CW, Holmes JH, Pauly MV, Escarce JJ: Association of dialyzer reuse with hospitalization and survival rates among U.S. hemodialysis patients: do comorbidities matter? J Clin Epidemiol 1999; 52: 209–217. (a)
7. Feldman HI, Bilker WB, Hackett M, Simmons CW, Holmes JH, Pauly MV, Escarce JJ: Association of dialyzer reuse and hospitalization rates among hemodialysis patients in the US. Am J Nephrol 1999; 19: 641–648. (b)
8. Ebben JP, Dalleska F, Ma JZ, Everson SE, Constantini EG, Collins AJ: Impact of disease severity and hematocrit level on reuse associated mortality. Am J Kidney Dis 2000; 35: 244–249.
9. Port FK, Wolfe RA, Hulbert-Shearon TE, Daugirdas JT, Agodoa LY, Jones C, Orzol SM, Held PJ: Mortality risk by hemodialyzer reuse practice and dialyzer membrane characteristics: results from the USRDS dialysis morbidity and mortality study. Am J Kidney Dis 2001; 37: 276–286.
10. Collins AJ, Liu J, Ebben JP: Dialyser reuse associated mortality and hospitalization risk in incident medicare haemodialysis patients, 1998–1999. Nephrol Dial Transplant 2004; 19: 1245–1251.
11. Lowrie EG, Li Z, Ofsthun N, Lazarus JM: Reprocessing dialysers for multiple uses: recent analysis of death risks for patients. Nephrol Dial Transplant 2004; 19: 2823–2830.
12. Fan Q, Liu J, Ebben JP, Collins AJ: Reuse-associated mortality in incident hemodialysis patients in the United States, 2000 to 2001. Am J Kidney Dis 2005; 46: 661–668.
13. Chuang FR, Lee CH, Chang HW, Lee CN, Chen TC, Chuang CH, Chiou TT, Wu CH, Yang CC, Wang IK: A quality and cost-benefit analysis of dialyzer reuse in hemodialysis patients. Ren Fail 2008; 30: 521–526.
14. US Renal data system. USRDS 2011 annual data report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2011.
15. Galvao TF, Silva MT, Araujo MEA, Bulbol WS, Cardoso ALMP. Dialyzer Reuse and Mortality Risk in Patients with End-Stage Renal Disease: A Systematic Review. Am J Nephrol 2012;35:249–258.
16. Manns BJ, Taub K, Richardson RM, Donaldson C. To reuse or not to reuse? An economic evaluation of hemodialyzer reuse versus conventional single-use hemodialysis for chronic hemodialysis patients. Int J Technol Assess Health Care. 2002 Winter;18(1):81-93.
17. Qureshi R, Dhrolia MF, Nasir K, Imtiaz S, Ahmad A. Comparison of total direct cost of conventional single use and mechanical reuse of dialyzers in patients of end-stage renal disease on maintenance hemodialysis: A single center study. Saudi J Kidney Dis Transpl [serial online] 2016 [cited 2018 Feb 22];27:774-80.

Recommendation 10. No recommendation can be made at this time on testing the total microbial count of RO dialysis water samples taken from point of use per machine once a month versus per machine once a year.

1. ANSI/AAMI RD 52:2004. Dialysate for Hemodialysis. p1-53.
2. New AAMI Water Quality Standard for Hemodialysis. ANSI/AAMI 13959:2014.

APPENDIX A. PANEL COMPOSITION AND AFFILIATION

Steering Committee
Ricardo A. Francisco, Jr., MD, MHA, FPCP, FPSN - Veterans Memorial Medical Center
Irmingarda P. Gueco, MD, MBA, FPCP, FPSN - The Medical City
Noel M. Castillo, MD, FPCP, FPSN - The Medical City
Helen T. Ocdol, MD, MMHoA, FPCP, FPSN - St. Luke's Medical Center

Panelists
Training Institutions
Florencio T. Ong, MD, FPCP, FPSN - Chinese General Hospital
Filoteo C. Ferrer, MD, FPCP, FPSN - Makati Medical Center
Roberto C. Tanchanco, MD, MBA, FPCP, FPSN - The Medical City
Elizabeth Angelica L. Roasa, MD, FPCP, FPSN - University of Santo Tomas Hospital
Corazon R. Macaraeg, MD, FPCP, FPSN - Veterans Memorial Medical Center

Specialty Society / Colleges (Physicians)
Hilda M. Sagayaga, MD, FPCS - Philippine Society of Transplant Surgeons
Rachelle C. Dela Cruz, MD, FPPS - Pediatric Nephrology Society of the Philippines
Maria Rhona G. Bergantin, MD - Philippine Society for Microbiology and Infectious Diseases
Catherine T. Yu, MD - Philippine Society for Microbiology and Infectious Diseases

Specialty Society / Colleges (Allied Medicine)
Raquel Z. Tejada, RN, CRNS - Renal Nurses Association of the Philippines
Juvy M. Sy, RND - Nutrition and Dietetics Association of the Philippines

Dialysis Patients and their Support Groups
Benita S. Padilla, MD, FPCP, FPSN - Human Organ Preservation Effort (HOPE)
Mr. Reynaldo Abacan - Dialysis PH Support Group, Inc.
Ms. Marimel Lamsin - Kidney Transplant Association of the Philippines, Inc. (KITAP)

PSN Chapters
Joseph Michael P. Abcede, MD, FPCP, FPSN - Southern Tagalog Chapter
Ofelia D. Datu, MD, FPCP, FPSN - Nothern Luzon Chapter
Rommel P. Bataclan, MD, FPCP, FPSN - Central Luzon Chapter
Maria Lorna Yap-Wong, MD, FPCP, FPSN - Bicol Chapter
Agnes M. Villaflor, MD, FPCP, FPSN - Western Visayas Chapter
Glynis S. Tingzon, MD, FPCP - Western Visayas Chapter
Ma. Socorro J. Maravilla, MD, FPCP, FPSN - Negros Island Region
Margarita S. Abalon, MD, FPCP, FPSN - Mindanao Chapter

PSN Past Presidents (w/o dialysis unit as owner or medical director)
Benjamin A. Balmores, Jr., MD, FPCP, FPSN
Delia V. Bayog, MD, FPCP, FPSN
Nenita A. Collantes, MD, FPCP, FPSN

APPENDIX B. EVIDENCE REVIEW EXPERTS & ASSOCIATES

Evidence Review Experts – Supervisory Committee

Evelyn O. Salido, MD, MSc (Clinical Epidemiology) - Asia Pacific Center for Evidence Based Healthcare & University of the Philippines, College of Medicine
Lia Aileen P. Villanueva, MD, MSc (Clinical Epidemiology) - Asia Pacific Center for Evidence Based Healthcare & University of the Philippines, College of Medicine
Leonila F. Dans, MD, MSc (Clinical Epidemiology) - Asia Pacific Center for Evidence Based Healthcare & University of the Philippines, College of Medicine
Maria Vanessa V. Sulit, RN, MSc (Clinical Epidemiology) - Asia Pacific Center for Evidence Based Healthcare

Evidence Review Experts

Aldrich Ivan Lois D. Burog, MD
Ma. Lucila M. Perez, MD - St. Luke's College of Medicine William H. Quasha Memorial
Carol Stephanie Chua Tan, MD - Philippine General Hospital
Marc Andrew O. Perez, MD - Region 1 Medical Center
Janice S. Garcia, MD - University of Santo Tomas Hospital
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Howell Henrian G. Bayon, CSP-PASP – St. Luke's Medical Center, Global
Arlene C. Crisostomo, MD - St. Luke's Medical Center

Evidence Review Experts' Associates

Natividad A. Almazan, MD, MSc (Clinical Epidemiology) - St. Luke's Medical Center
Lorraine Grace B. Almelor-Sembrana, MD
Arginino Romeo V. Dorado, MD - Makati Medical Center
Mark Rodriguez, MD - Chong Hua Hospital, Cebu
Kristine Mae V. Alava, MD - University of Santo Tomas Hospital

APPENDIX C. DECLARATION OF CONFLICTS OF INTEREST

DECLARATION OF INTERESTS
PSN Hemodialysis Guideline Panel

DECLARATION

With regard to my voluntary service as member of the Guideline Panel for the Hemodialysis for Chronic Kidney Disease Clinical Practice Guideline of the Philippine Society of Nephrology, I hereby declare that:

☐ I have no pecuniary or other personal interest, direct or indirect, in any matter that raises or may raise a conflict with my duties as member of the Guideline Panel.

☐ I have pecuniary or other personal interest, direct or indirect, in certain matter that raises or may raise a conflict with my duties as member of the Guideline Panel.
I have the following potential conflict(s) of interest to report: *(check all that apply)*

- ○ I receive royalties, licensing fees, patents from any product or device related to the use of hemodialysis for chronic kidney disease. (This includes patents, the rights for which have been turned over to an institution, but from which the individual benefits).
- ○ I receive honoraria, grant support, stock or equity, gifts or other payments directly received from pharmaceutical company/ies.
- ○ I serve as an officer, board member or employee of a device, pharmaceutical or diagnostic product related to use of hemodialysis for chronic kidney disease.
- ○ I serve on speakers bureau labeled as promotional and/or when any associated presentation is content-restricted in any way, including, but not limited to the requirement to use only company-provided material:
  a. paid for by any mechanism other than an unrestricted educational grant to a CME-approved entity; and/or
  b. product-specific
- ○ I am a director or owner of a hemodialysis facility or have shares in a hemodialysis facility.
- ○ I represent a commercial healthcare-related entity (with a product or device related to the use of hemodialysis for chronic kidney disease) before FDA advisory committees.

The following relationships are allowed:

1. advisory/consultancies when research-related will be considered as a research activity, even if the company with which you have the relationship, has products related to the guideline. Thus, work with a pharmaceutical or device company involving study design or service on a Data Service Monitoring Board WILL be allowed.
2. serving as an investigator on a research study
3. presentations at national or international meetings provided that:
   a. presentations are non-promotional and there should be no involvement of industry in presentation content. There should be complete intellectual independence with regard to presentation content.
   b. there is NO direct payment by industry to an individual for his/her participation (any industry support of speaker expenses must be through a third-party organization, institution, CME or other educational provider.

1 of2

DECLARATION OF INTERESTS
PSN Hemodialysis Guideline Panel

Please elaborate on the potential conflict arising from the above situation with regards to the transaction concerned (e.g. nature of service/ transaction, if affiliated person involved, the identity of the affiliated person and your relationship with that person):

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.....
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.....

I hereby confirm that the disclosure made above are complete and correct to the best of my information and belief. I agree that if I become aware of any information that might indicate that this disclosure is inaccurate or that I have not complied with the conflict of interest policy, I will notify [the chair of the Guideline committee] immediately.

Signature

Name & Designation

Date

APPENDIX D. EVIDENCE BASE