**National Quality Forum—Evidence (subcriterion 1a)**

**Measure Number** (*if previously endorsed*)**:** Click here to enter NQF number

**Measure Title**: Delivered Dose of Dialysis Above Minimum

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Click here to enter composite measure #/ title

**Date of Submission**: 2/27/2015

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| **Instructions**  *For composite performance measures:*  *A separate evidence form is required for each component measure unless several components were studied together.*  *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*   * Respond to all questions as instructed with answers immediately following the question. All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed. * If you are unable to check a box, please highlight or shade the box for your response. * Maximum of 10 pages (*incudes questions/instructions*; minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.*** * Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](http://www.qualityforum.org/Measuring_Performance/Submitting_Standards.aspx). |

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| **Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**   1a. Evidence to Support the Measure Focus The measure focus is evidence-based, demonstrated as follows:   * Health outcome: [**3**](#Note3) a rationale supports the relationship of the health outcome to processes or structures of care. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior. * Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4)that the measured intermediate clinical outcome leads to a desired health outcome. * Process: [**5**](#Note5) a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured process leads to a desired health outcome. * Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured structure leads to a desired health outcome. * Efficiency: [**6**](#Note6) evidence not required for the resource use component.   **Notes**  **3.** Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.  **4.** The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) [grading definitions](http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm) and [methods](http://www.uspreventiveservicestaskforce.org/methods.htm), or Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org/publications/index.htm).  **5.** Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.  **6.** Measures of efficiency combine the concepts of resource use and quality (see NQF’s [Measurement Framework: Evaluating Efficiency Across Episodes of Care](http://www.qualityforum.org/Publications/2010/01/Measurement_Framework__Evaluating_Efficiency_Across_Patient-Focused_Episodes_of_Care.aspx); [AQA Principles of Efficiency Measures](http://www.aqaalliance.org/files/PrinciplesofEfficiencyMeasurementApril2006.doc)). |

**1a.1.This is a measure of**: (*should be consistent with type of measure entered in De.1*)

Outcome

Health outcome: Click here to name the health outcome

Patient-reported outcome (PRO): Click here to name the PRO

*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors*

Intermediate clinical outcome (*e.g., lab value*): Kt/V

Process: Click here to name the process

Structure: Click here to name the structure

Other: Click here to name what is being measured

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**HEALTH OUTCOME/PRO PERFORMANCE MEASURE**  *If not a health outcome or PRO, skip to* [*1a.3*](#Section1a3)

**1a.2.** **Briefly state or diagram the path between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.**

N/A

**1a.2.1.** **State the rationale supporting the relationship between the health outcome (or PRO) to at least one healthcare structure, process, intervention, or service (*i.e., influence on outcome/PRO*).**

N/A

*Note: For health outcome/PRO performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.*

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**intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measure**

**1a.3.****Briefly state or diagram the path between structure, process, intermediate outcome, and health outcomes**. Include all the steps between the measure focus and the health outcome.

The measure focus is the measurement of delivered dialysis dose for ESRD hemodialysis and peritoneal dialysis patients to assess adequate dialysis. This leads to improvement in morbidity and mortality as follows: Measure HD and PD adequacy-->Assess value-->Identify problem-->Identify treatment options/adjustments-->Administer the appropriate treatment-->Impact on morbidity and mortality.

**1a.3.1.** **What is the source of the systematic review of the body of evidence that supports the performance measure?**

Clinical Practice Guideline recommendation – ***complete sections*** [***1a.4***](#Section1a4)***, and*** [***1a.7***](#Section1a7)

US Preventive Services Task Force Recommendation – ***complete sections*** [***1a.5***](#Section1a5) ***and*** [***1a.7***](#Section1a7)

Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*) – ***complete sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)

Other – ***complete section*** [***1a.8***](#Section1a8)

*Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.*

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**1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION**

**1a.4.1.** **Guideline citation** (*including date*) and **URL for guideline** (*if available online*):

KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for 2006 Updates: Hemodialysis Adequacy, Peritoneal Dialysis Adequacy and Vascular Access. Am J Kidney Dis 48:S1-S322, 2006 (suppl 1).

http://www.kidney.org/professionals/KDOQI/guidelines\_commentaries

**1a.4.2.** **Identify guideline recommendation number and/or page number** and **quote verbatim, the specific guideline recommendation**.

Adult HD Kt/V Target:

4.1 The minimally adequate dose of HD given 3 times per week to patients with Kr less than 2 mL/min/1.73 m2 should be a spKt/V (excluding RKF) of 1.2 per dialysis session. (A)

Pediatric HD Kt/V Target:

Pediatric HD Kt/V Target:

8.3.1 Children should receive at least the delivered dialysis dose as recommended for the adult population. (A)

Adult PD Kt/V target:

Data from RCTs suggested that the minimally acceptable small-solute clearance for PD is less than the prior recommended level of a weekly Kt/Vurea of 2.0. Furthermore, increasing evidence indicates the importance of RKF as opposed to peritoneal small-solute clearance with respect to predicting patient survival. Therefore, prior targets have been revised as indicated next. 2.1 For patients with RKF (considered to be significant when urine volume is > 100 mL/d): 2.1.1 The minimal "delivered" dose of total small-solute clearance should be a total (peritoneal and kidney) Kt/Vurea of at least 1.7 per week. (B)

2.1.2 Total solute clearance (residual kidney and peritoneal, in terms of Kt/Vurea) should be measured within the first month after initiating dialysis therapy and at least once every 4 months thereafter. (B)

2.1.3 If the patient has greater than 100 mL/d of residual kidney volume and residual kidney clearance is being considered as part of the patient ´s total weekly solute clearance goal, a 24-hour urine collection for urine volume and solute clearance determinations should be obtained at a minimum of every 2 months. (B)

2.2 For patients without RKF (considered insignificant when urine volume is =100 mL/d): 2.2.1 The minimal "delivered" dose of total small-solute clearance should be a peritoneal Kt/Vurea of at least 1.7 per week measured within the first month after starting dialysis therapy and at least once every 4 months thereafter. (B)

Pediatric PD Kt/V target:

“6.3.2.1 The minimal “delivered” dose of total (peritoneal and kidney) small-solute clearance should be a Kt/Vurea of at least 1.8/wk”

“For areas in which no pediatric-specific data exist, the CPGs and CPRs for adult patients should serve as a minimum standard for pediatric patients, but the overall clinical “wellness” of the individual pediatric patient should be the primary factor that influences the quantity and quality of the care provided.”

**1a.4.3.** **Grade assigned to the quoted recommendation with definition of the grade:**

The adult and pediatric hemodialysis guidelines were graded A. The guidelines for adult peritoneal dialysis patients were graded B. The pediatric peritoneal dialysis guidelines were graded CPR. They are based on expert opinion.

**1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: If separate grades for the strength of the evidence, report them in section 1a.7.*)

The rating system defined in the KDOQI Guidelines was used to grade the strength of the Guideline recommendation. KDOQI defined grades as follows:

Grade A: It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is strong evidence that the practice improves health outcomes.

Grade B: It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderately strong evidence that the practice improves health outcomes.

Grade CPR: It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence or on the opinions of the Work Group and reviewers that the practice might improve health outcomes.

**1a.4.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.4.1*)**:**

National Kidney Foundation: DOQI Clinical Practice Guidelines for Hemodialysis Adequacy. Appendix 1. Methods for Evaluating Evidence. Update 2006.

<http://www.kidney.org/professionals/KDOQI/guidelines_commentaries>

**1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?**

Yes **→ *complete section*** [***1a.7***](#Section1a7)

No **→ *report on another systematic review of the evidence in sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)***; if another review does not exist, provide what is known from the guideline review of evidence in*** [***1a.7***](#Section1a7)

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**1a.5.** **UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

**1a.5.1.** **Recommendation citation** (*including date*) and **URL for recommendation** (*if available online*):

N/A

**1a.5.2.** **Identify recommendation number and/or page number** and **quote verbatim, the specific recommendation**.

N/A

**1a.5.3.** **Grade assigned to the quoted recommendation with definition of the grade**:

N/A

**1a.5.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: the* *grading system for the evidence should be reported in section 1a.7.*)

N/A

**1a.5.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.5.1*)**:**

N/A

***Complete section*** [***1a.7***](#Section1a7)

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**1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE**

**1a.6.1.** **Citation** (*including date*) and **URL** (*if available online*):

N/A

**1a.6.2.** **Citation and** **URL for methodology for evidence review and grading** (*if different from 1a.6.1*)**:**

N/A

***Complete section*** [***1a.7***](#Section1a7)

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**1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE supporting the measure**

*If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.*

**1a.7.1.** **What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?**

*\*\*The information in this section applies to the guidelines for the adult hemodialysis and peritoneal dialysis patients.\*\**

**1a.7.2.** **Grade assigned for the quality of the quoted evidence with definition of the grade**:

The adult hemodialysis guidelines were graded A. The guidelines for adult peritoneal dialysis patients were graded B.

**1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.**

The rating system defined in the KDOQI Guidelines was used to grade the strength of the Guideline recommendation. KDOQI defined grades as follows:

Grade A: It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is strong evidence that the practice improves health outcomes.

Grade B: It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderately strong evidence that the practice improves health outcomes.

Grade CPR: It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence or on the opinions of the Work Group and reviewers that the practice might improve health outcomes.

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**: Click here to enter date range

Hemodialysis: 1994 – 2004

Peritoneal dialysis: 1998-2004

**QUANTITY AND QUALITY OF BODY OF EVIDENCE**

**1a.7.5.****How many and what type of study designs are included in the body of evidence**? (*e.g., 3 randomized controlled trials and 1 observational study*)

Hemodialysis: 10. Included RCTs, retrospective and prospective cohort studies.

Peritoneal dialysis: 20

**1a.7.6.** **What is the overall quality of evidence across studies in the body of evidence**? (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*)

Hemodialysis: The body of evidence shows a correlation between delivered dose of HD and patient mortality and morbidity. Thus, this evidence directly supports this measure. Of the 11 studies, 5 measured dialysis dose using spKt/v [1,3,8,9,10], and 3 used URR[4,5,7]. The remaining studies used eKt/V [2,6]. Among the studies using spKt/V, one study was a randomized clinical trial (HEMO study) with 1846 patients, one was a prospective study with 740 patients, and the remaining were retrospective cohort studies with sample sizes of 1771 and 1151. Two of these studies found a significant improvement in mortality with increasing dose of spKt/V. The remaining study compared higher doses of spKt/v to the standard dose (spKt/V =1.2) and found higher doses did not show associated improvement in mortality compared to the standard dose.

1. Eknoyan G, Beck GJ, Cheung AK, et al: Effect of dialysis dose and membrane flux in maintenance hemodialysis. N Engl J Med347:2010-2019, 2002.

2. Depner T, Daugirdas J, Greene T, et al: Dialysis dose and the effect of gender and body size on outcome in the HEMO Study. Kidney Int 65:1386-1394, 2004.

3. Termorshuizen F, Dekker FW, van Manen JG, Korevaar JC, Boeschoten EW, Krediet RT: Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: An analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. J Am Soc Nephrol 15:1061-1070, 2004.

4. Port FK, Wolfe RA, Hulbert-Shearon TE, McCullough KP, Ashby VB, Held PJ: High dialysis dose is associated with lower mortality among women but not among men. Am J Kidney Dis 43:1014-1023, 2004.

5.Port FK, Ashby VB, Dhingra RK, Roys EC, Wolfe RA: Dialysis dose and body mass index are strongly associated with survival in hemodialysis patients. J Am Soc Nephrol 13:1061-1066, 2002.

6. Wolfe RA, Ashby VB, Daugirdas JT, Agodoa LY, Jones CA, Port FK: Body size, dose of hemodialysis, and mortality. Am J Kidney Dis 35:80-88, 2000.

7. Chertow GM, Owen WF, Lazarus JM, Lew NL, Lowrie EG: Exploring the reverse J-shaped curve between urea reduction ratio and mortality. Kidney Int 56:1872-1878, 1999.

8. Leypoldt JK, Cheung AK, Carroll CE, et al: Effect of dialysis membranes and middle molecule removal on chronic hemodialysis patient survival. Am J Kidney Dis 33:349-355, 1999.

9. Salahudeen AK, Dykes P, May W: Risk factors for higher mortality at the highest levels of spKt/V in hemodialysis patients.Nephrol Dial Transplant 18:1339-1344, 2003.

10. Woods HF, Nandakumar M: Improved outcome for haemodialysis patients treated with high-flux membranes. Nephrol Dial Transplant 15:S36-S42, 2000 (suppl 1).

Peritoneal dialysis: The KDOQI panel noted that the body of evidence shows a correlation between total solute clearance for urea and patient mortality and morbidity. Thus, this evidence supports that the delivered dose of dialysis should be measured frequently for assessment of adequate treatment, and treatment should be set accordingly. In particular, of the 20 studies considered in the body of evidence, the results from two randomized clinical trials were used to justify the KDOQI guidelines [2,3]. The results from additional observational studies also supported the KDOQI recommendations [see, e.g. 1,6].

1. Bargman JM, Thorpe KE, Churchill DN: Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: A reanalysis of the CANUSA Study. J Am Soc Nephrol 12:2158-2162, 2001
2. Paniagua R, Amato D, Vonesh E, et al: Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. J Am Soc Nephrol 13:1307-1320, 2002
3. Lo WK, Ho YW, Li CS, et al: Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. Kidney Int 64:649-656, 2003
4. Szeto CC, Wong TY, Leung CB, et al: Importance of dialysis adequacy in mortality and morbidity of Chinese CAPD patients. Kidney Int 58:400-407, 2000
5. Diaz-Buxo JA, Lowrie EG, Lew NL, Zhang SM, Zhu X, Lazarus JM: Associates of mortality among peritoneal dialysis patients with special reference to peritoneal transport rates and solute clearance. Am J Kidney Dis 33:523-534, 1999
6. Rocco MV, Frankenfield DL, Prowant B, Frederick P, Flanigan MJ: Risk factors for early mortality in U.S. peritoneal dialysis patients: Impact of residual renal function. Perit Dial Int 2002 22:371-379
7. Termorshuizen F, Korevaar JC, Dekker FW, van Manen JG, Boeschoten EW, Krediet RT: The relative importance of residual renal function compared with peritoneal clearance for patient survival and quality of life: An analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. Am J Kidney Dis 41:1293-1302, 2003
8. Chung SH, Heimburger O, Stenvinkel P, Qureshi AR, Lindholm B: Association between residual renal function, inflammation and patient survival in new peritoneal dialysis patients. Nephrol Dial Transplant 18:590-597, 2003
9. Jager KJ, Merkus MP, Dekker FW, et al: Mortality and technique failure in patients starting chronic peritoneal dialysis: Results of The Netherlands Cooperative Study on the Adequacy of Dialysis. NECOSAD Study roup. Kidney Int 55:1476-1485, 1999
10. Ates K, Nergizoglu G, Keven K, et al: Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. Kidney Int 60:767-776, 2001
11. Wang AY, Wang M, Woo J, et al: Inflammation, residual kidney function, and cardiac hypertrophy are interrelated and combine adversely to enhance mortality and cardiovascular death risk of peritoneal dialysis patients. J Am Soc Nephrol 15:2186-2194, 2004
12. Szeto CC, Wong TY, Chow KM, Leung CB, Law MC, Li PK: Independent effects of renal and peritoneal clearances on the mortality of peritoneal dialysis patients. Perit Dial Int 24:58-64, 2004
13. Szeto CC, Wong TY, Chow KM, et al: Impact of dialysis adequacy on the mortality and morbidity of anuric Chinese patients receiving continuous ambulatory peritoneal dialysis. J Am Soc Nephrol 12:355-360, 2001
14. Bhaskaran S, Schaubel DE, Jassal SV, et al: The effect of small solute clearances on survival of anuric peritoneal dialysis patients. Perit Dial Int 20:181-187, 2000
15. Rocco M, Soucie JM, Pastan S, McClellan WM: Peritoneal dialysis adequacy and risk of death. Kidney Int 58:446-457, 2000
16. Lo WK, Tong KL, Li CS, et al: Relationship between adequacy of dialysis and nutritional status, and their impact on patient survival on CAPD in Hong Kong. Perit Dial Int 21:441-447, 2001
17. Davies SJ, Phillips L, Russell GI: Peritoneal solute transport predicts survival on CAPD independently of residual renal function. Nephrol Dial Transplant 13:962-968, 1998
18. Perez RA, Blake PG, Spanner E, et al: High creatinine excretion ratio predicts a good outcome in peritoneal dialysis patients. Am J Kidney Dis 36:362-367, 2000
19. Park HC, Kang SW, Choi KH, Ha SK, Han DS, Lee HY: Clinical outcome in continuous ambulatory peritoneal dialysis patients is not influenced by high peritoneal transport status. Perit Dial Int 21:S80-S85, 2001 (suppl 3)
20. Aslam N, Bernardini J, Fried L, Piraino B: Peritoneal dialysis clearance can replace residual renal function. Perit Dial Int 21:263- 268, 2001

**ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE**

**1a.7.7.** **What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence**? (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)

Hemodialysis: Among the studies showing a significant improvement in mortality with increasing dose of spKt/V, relative risks (RR) were presented as spKt/V per increase of 1 unit and spKt/V per 0.1 unit, where spKt/V was analyzed as a continuous measure. The RR per 1 unit increase in spKt/V was 0.76 (95% CI: 0.64, 0.92; p=0.004) [3], and per 0.1 unit increase in spKt/V was 0.95; p<0.05 (no CI given) [8]. The HEMO trial found no significant difference in mortality among patients in the high dose group, with mean = 1.56 and SD=0.09, compared to the low dose group with mean=1.16 and SD=0.08 (RR=0.96; 95% CI: 0.84, 1.10) [1], thus supporting the current target spKt/V of 1.2. However, a subgroup analysis of the HEMO study [2] showed that survival rates in women randomized to the higher dose group were higher than women in the lower dose group (relative risk 0.81; p = 0.02) and this association persisted after adjusting for body size. In the remaining study, findings showed patients receiving the highest dialysis dose (spKt/V>2.4) compared to the standard dose group (spKt/V 1.2-1.3) had an increased risk of mortality (RR=2.5; p<0.05), although this may be suggestive of confounding by indication. No other significant associations between dose groups were found in this study [9]. All but one study showed a benefit for a minimum dose of dialysis when measured as spKt/V.

Peritoneal dialysis: In the adult population, among the studies showing any improvement in mortality in high total clearance versus low total clearance, relative risks ranged from 0.6 to 0.99. In one study, Kt/V was measured as continuous and found a relative risk of 0.94 per 0.1 mL/min increase in Kt/V (95% CI = 0.88, 1.02). The majority of the studies showed a benefit of higher total clearance in PD patients.

**1a.7.8.** **What harms were studied and how do they affect the net benefit (benefits over harms)?**

Hemodialysis: Studies evaluating higher doses of dialysis adequacy did not demonstrate additional benefit at spKt/V doses higher than the current target of 1.2. The increase in mortality at the highest dialysis dose is thought to be due to confounding by indication and does not suggest that higher dialysis dose is associated with increased mortality.

Peritoneal Dialysis: As described above in 1a.7.7, the majority of studies showed a benefit of higher total clearance in PD patients. Furthermore, there is little or no potential harm in assessing total urea Kt/V for PD patients.

**UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE**

**1a.7.9.** **If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review**.

N/A

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**1a.8 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

**1a.8.1** **What process was used to identify the evidence?**

Evidence supporting the adult hemodialysis and peritoneal dialysis targets is listed in 1.a.7.6

The process for obtaining additional sources of evidence is outlined below.

Hemodialysis Kt/V:

The 2010 clinical pediatric dialysis adequacy TEP conducted a literature search, where we retrieved a total of 190 articles using several sources. First, we retrieved 79 articles using a PubMed search of articles with human subjects, published in English since January 1, 2005. The search terms were: [(pediatric OR pediatrics OR children) and (dialysis OR hemodialysis OR peritoneal dialysis) and (adequacy OR "dialysis dose" OR "dose monitoring" OR "residual renal function" OR "urea clearance" OR "solute clearance" OR "phosphate clearance" OR "amino acid clearance" OR "folate clearance" OR "Kt/V" OR "peritoneal equilibration test" OR ("ultrafiltration" and peritoneal)) and NOT (cvvhd OR "continuous veno venous" OR transplant OR "kidney transplant" OR transplantation)].

Second, we reviewed 61 citations from the Kidney Disease Outcomes Quality Initiative Guidelines on pediatric peritoneal dialysis and hemodialysis. Third, we reviewed the tables of contents of the journal Pediatric Nephrology and retrieved two articles from early on-line publishing that had not yet been included in PubMed. Finally, we reviewed the citations in 14 articles previously identified; this found an additional 65 articles for review. Duplicate articles were excluded. A total of 124 articles were found to be relevant for measure development. Four articles listed below [1-4] were determined to be relevant to this specific measure.

In May 2014, an additional review of the literature for new evidence was performed. Additional evidence pertaining to the adult [5-8] and pediatric [9-12] achievement of adequate dialysis (HD) are included in the citations below as a result of that search.

Peritoneal dialysis Kt/V:

The 2013 pediatric PD adequacy TEP reviewed 30-40 studies on peritoneal dialysis adequacy for both the adult and pediatric populations. PD adequacy studies among the pediatric population are largely observational studies; large scale clinical trials do not exist in the pediatric PD population because of the low prevalence of stage 5 CKD among pediatric patients, high transplantation rate, and difficulty of determining measurable study end points. These include studies on solute clearance and clinical outcomes (such as the ADEMEX), the method of measurement of volume in the pediatric population (Morgenstern, et al. JASN 17:285-293, 2006), the importance of measurement of residual renal function (CANUSA study, Bargman JM, et al. JASN 2158-2162, 2001) and the importance of growth as an outcome measure in the pediatric population (Chadha V, et al. PDI 2001), among others.

In May 2014, an additional literature search was performed. Additional evidence related to the adult [15-16] and pediatric [11-14] PD Kt/V measurements are included in the citations below as a result of that search.

**1a.8.2.** **Provide the citation and summary for each piece of evidence.**

Hemodialysis:

1. Lowrie EG, et al. Effect of the hemodialysis prescription of patient morbidity: report from the National Cooperative Dialysis Study. N Engl J Med 305:1176–1181, 1981.

Abstract: This report summarizes morbidity in 151 patients in a cooperative trial designed to evaluate the clinical effects of different dialysis prescriptions. Four treatment groups were divided along two dimensions: dialysis treatment time (long or short), and blood urea nitrogen (BUN) concentration averaged with respect to time (TACurea) (high or low). Dietary protein was not restricted. There was no difference in mortality between the groups. Withdrawal of patients from the high-BUN groups for medical reasons was significantly greater than withdrawal from the lowBUN groups. Hospitalization was also greater in the high-BUN groups, but dialysis treatment time had no significant effects.

The data indicate that the occurrence of morbid events is affected by the dialysis prescription. Increased morbidity appears to accompany prescriptions associated with a relatively high BUN. Conversely, morbidity may be decreased by prescriptions associated with more efficient removal of urea if the dietary intake of protein and other nutrients is adequate. (N Engl J Med. 1981; 305:1176–81.)

1. Owen WF Jr, et al. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med 329:1001–1006, 1993.  
     
    BACKGROUND:

Among patients with end-stage renal disease who are treated with hemodialysis, solute clearance during dialysis and nutritional adequacy are determinants of mortality. We determined the effects of reductions in blood urea nitrogen concentrations during dialysis and changes in serum albumin concentrations, as an indicator of nutritional status, on mortality in a large group of patients treated with hemodialysis.

METHODS:

We analyzed retrospectively the demographic characteristics, mortality rate, duration of hemodialysis, serum albumin concentration, and urea reduction ratio (defined as the percent reduction in blood urea nitrogen concentration during a single dialysis treatment) in 13,473 patients treated from October 1, 1990, through March 31, 1991. The risk of death was determined as a function of the urea reduction ratio and serum albumin concentration.

RESULTS:

As compared with patients with urea reduction ratios of 65 to 69 percent, patients with values below 60 percent had a higher risk of death during follow-up (odds ratio, 1.28 for urea reduction ratios of 55 to 59 percent and 1.39 for ratios below 55 percent). Fifty-five percent of the patients had urea reduction ratios below 60 percent. The duration of dialysis was not predictive of mortality. The serum albumin concentration was a more powerful (21 times greater) predictor of death than the urea reduction ratio, and 60 percent of the patients had serum albumin concentrations predictive of an increased risk of death (values below 4.0 g per deciliter). The odds ratio for death was 1.48 for serum albumin concentrations of 3.5 to 3.9 g per deciliter and 3.13 for concentrations of 3.0 to 3.4 g per deciliter. Diabetic patients had lower serum albumin concentrations and urea reduction ratios than nondiabetic patients.

CONCLUSIONS:

Low urea reduction ratios during dialysis are associated with increased odds ratios for death. These risks are worsened by inadequate nutrition.

1. Gorman G, et al. Clinical outcomes and dialysis adequacy in adolescent hemodialysis patients. Am Journal Kidney Dis; 47: 285-93, 2006.

BACKGROUND:

The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative guidelines recommend that adult hemodialysis (HD) patients receive a minimum dialysis dose by single-pooled Kt/V (spKt/V) of 1.2 or greater. There are no data to support a minimum spKt/V dose for children on HD therapy. We aim to determine the association of spKt/V with mortality and hospitalization in adolescents.

METHODS:

Clinical characteristics of adolescent HD patients aged 12 to 18 years old included in the 2000/2001 End-Stage Renal Disease Clinical Performance Measures Project were linked to US Renal Data System data from October 1, 1999, to October 15, 2001. Hospitalization risks after adjustment for time on dialysis therapy, access, hemoglobin level, albumin level, and height were determined by means of Poisson regression. spKt/V was analyzed by the adult target (< versus > or = 1.2) and by intervals.

RESULTS:

There were 613 patients with 477 patient-years of follow-up, during which there were 14 deaths and 185 hospitalizations covering 1,108 days. After adjustment, patients with an spKt/V less than 1.2 had increased hospitalization risk (1.59; 95% confidence interval, 0.98 to 2.56; P = 0.06) compared with those with an spKt/V of 1.2 or greater. Compared with patients with an spKt/V of 1.2 to 1.4, patients with an spKt/V less than 1.2 had increased adjusted risk for hospitalization (2.46; 95% confidence interval, 1.23 to 4.94; P = 0.01). Increases in spKt/V beyond 1.4 were not associated with improved outcomes.

CONCLUSION:

Applying the current adequacy guideline to adolescent HD patients is justified by the increased hospitalization risk of those who fail to attain an spKt/V of 1.2 or greater. However, attaining an spKt/V in excess of 1.4 was not associated with greater benefit.

1. Fischbach M, et al. Intensified and daily hemodialysis in children might improve statural growth. Pediatr Nephrol 21:1746–1752, 2006.

Abstract: In children conventional hemodialysis does not often improve growth. We determined linear growth in five children on in-center intensified and daily hemodialysis (IDd) regimen, with a mean age of 8 years 7 months at enrollment. Four of five were on growth hormone started for a median of 28.5 months before IDd. IDd was delivered 5 to 6 times weekly, for three hours each session. Mean follow up of IDd was 18.6 months. Dropout from IDd was kidney transplantation (n=4) or transfer to another center (n=1). IDd and free diet improved appetite, thereby protein intake, was above 2 g/kg/BW. Median weekly Kt/V(urea) was 9.1 (8.7 to 10.4). Predialysis phosphorus blood levels were higher at the start (2.04+/-0.34 mmol/L) than at end of IDd (1.39+/-0.41 mmol/L) without need for carbonate of calcium in four of five cases. During conventional dialysis ht SDS decreased from -0.8 to -1.44, which occurred predominantly before rhGH start. Conversion to IDd significantly increased growth velocity to a mean of 13 cm/year (10.3-18) with a mean change of +1.84 ht SDS/year (0.4 to 2.7). This preliminary report suggests the potential efficacy of IDd regimen in promising growth velocity, either directly from a higher dialysis dose or indirectly through an improved nutritional status.

1. Ulusoy S, Güngör E, Gül S et al. Do hemodialysis adequacy data reflect reality? Artif Organs. 2013 Feb;37(2):189-95. doi: 10.1111/j.1525-1594.2012.01537.x. Epub 2012 Oct 9.

Abstract: Hemodialysis (HD) adequacy requires monitoring in line with standards and at appropriate intervals. However, the use of inappropriate or incorrectly applied techniques in the determination of HD adequacy can lead to highly unfortunate results. This study was intended to identify the path to a solution by determining how far HD adequacy in HD centers in our region reflects reality. Three hundred and thirty HD patients from eight centers were included. On the first visit, predialysis and postdialysis blood collection with the centers' own methods being used were observed and errors were recorded. Kt/V1 was calculated from pre- and postdialysis blood specimens taken by the units themselves. On the second visit, one session later, pre- and postdialysis blood samples were collected in line with guidelines by ourselves, the authors, and Kt/V2 was calculated from these samples. The eight units' total Kt/V2 value was significantly lower compared with Kt/V1 (<0.0001). The level of patients in all centers with Kt/V1 <1.2 was 13.5%, and that of patients with Kt/V2 <1.2 was 22.1%. No center, apart from one unit, managed to complete the collection of blood specimens as recommended by the guidelines. With one exception, blood collection for HD adequacy was not performed using proper technique in any center. This simple but easily overlooked situation, HD being regarded as adequate though in fact it is not, may lead to patients not being treated effectively and accurately and to a rise in mortality and morbidity in the long term.

1. Eloot S, Van Biesen W, Vanholder R. A sad but forgotten truth: the story of slow-moving solutes in fast hemodialysis. Semin Dial. 2012 Sep-Oct;25(5):505-9. doi: 10.1111/j.1525-139X.2012.01107.x. Epub 2012 Aug 26.

Abstract: When trying to optimize hemodialysis adequacy, it can be questioned whether one should focus on the dialyzer or on the patient. Another crucial question is whether the currently applied dialysis adequacy parameter, Kt/V(urea) , is a reliable marker. For the small and water-soluble solutes, recent advances in convective strategies and/or new dialyzer designs do not add much removal capacity. Depending on their specific kinetics, generally quite different from those of urea, small solute removal benefits from longer or more frequent dialysis. Clearance of beta-2-microglobulin (β(2) M), a marker of middle molecule removal pattern, is improved with dialysis using more open and permselective membranes, as well as by using high convective volume strategies. Furthermore, longer and more frequent dialyses have highly favorable removal characteristics because they facilitate the retarded transport between plasmatic and extraplasmatic compartments over which these molecules are distributed. As β(2) M may not be representative of other middle molecules, future kinetic analyses of alternative middle molecules will be of the utmost interest. Protein-bound solute clearance is improved by convective techniques, but not by more open dialyzer pores. Knowledge of their kinetics should be helpful in interpreting the observation that frequent (but not longer) dialysis enhances protein-bound solute removal. Hence, further technical improvements in dialyzers will have only a minor impact on dialysis adequacy, as retarded solute movement in the patient plays a decisive role. As urea kinetics is not representative of the kinetics of protein-bound compounds, middle molecules, nor even of other small and water-soluble solutes, it becomes self-evident that urea clearance is a poor predictor of many aspects of dialysis adequacy.

1. Lacson E Jr, Xu J, Suri RS et al. Survival with three-times weekly in-center nocturnal versus conventional hemodialysis. J Am Soc Nephrol. 2012 Apr;23(4):687-95. doi: 10.1681/ASN.2011070674. Epub 2012 Feb 23.

Abstract: Whether the duration of hemodialysis treatments improves outcomes remains controversial. Here, we evaluated survival and clinical changes associated with converting from conventional hemodialysis (mean=3.75 h/treatment) to in-center nocturnal hemodialysis (mean=7.85 h/treatment). All 959 consecutive patients who initiated nocturnal hemodialysis for the first time in 77 Fresenius Medical Care facilities during 2006 and 2007 were eligible. We used Cox models to compare risk for mortality during 2 years of follow-up in a 1:3 propensity score-matched cohort of 746 nocturnal and 2062 control patients on conventional hemodialysis. Two-year mortality was 19% among nocturnal hemodialysis patients compared with 27% among conventional patients. Nocturnal hemodialysis associated with a 25% reduction in the risk for death after adjustment for age, body mass index, and dialysis vintage (hazard ratio=0.75, 95% confidence interval=0.61-0.91, P=0.004). With respect to clinical features, interdialytic weight gain, albumin, hemoglobin, dialysis dose, and calcium increased on nocturnal therapy, whereas postdialysis weight, predialysis systolic blood pressure, ultrafiltration rate, phosphorus, and white blood cell count declined (all P<0.001). In summary, notwithstanding the possibility of residual selection bias, conversion to treatment with nocturnal hemodialysis associates with favorable clinical features, laboratory biomarkers, and improved survival compared with propensity score-matched controls. The potential impact of extended treatment time on clinical outcomes while maintaining a three times per week hemodialysis schedule requires evaluation in future clinical trials.

1. Fissell R, Schulman G, Pfister M, Zhang L, Hung AM. Novel dialysis modalities: do we need new metrics to optimize treatment? J Clin Pharmacol. 2012 Jan;52(1 Suppl):72S-8S. doi: 10.1177/0091270011414576.

Abstract: Delivered dose of hemodialysis has long been an important predictor of mortality. The limitations of conventional hemodialysis treatments have led to a renewed interest in more frequent and longer hemodialysis treatments. As alternative hemodialysis schedules have become more prevalent, a need for modified metrics to measure adequacy has emerged. In addition, there is an interest in finding measures of hemodialysis adequacy that are more reliable in certain subgroups of patients, such as women, ethnic minority groups, or people with small body size. Finally, extended hemodialysis schedules suggest a need for metrics that can measure the clearance of solutes other than urea, such as middle-size molecules, and solutes for which clearance depends on intercompartmental transport across membranes. New metrics to quantify clearance in extended and alternate hemodialysis schedules are needed. As new metrics are developed, it is anticipated that they will also contribute to more accurate assessments of associations between clinical outcomes and delivered dose of dialysis in more intensive, nontraditional hemodialysis schedules. This review provides a historical prospective of dialysis dose and adequacy and describes the need for new metrics from both solute type and dialysis dose prospective as alternative hemodialysis schedules have emerged and become more prevalent.

1. Daugirdas JT. Dialysis dosing for chronic hemodialysis: beyond Kt/V. Semin Dial. 2014 Mar;27(2):98-107.

Abstract: Current views regarding hemodialysis adequacy reach beyond indices of small solute removal such as Kt/V. Nevertheless, new Kt/V-based constructs such as the standard Kt/V, which adjusts not only for dialysis frequency, but which also represents removal of sequestered solutes rather than easily removed urea, continue to be useful. The scaling of dialysis dose to measures of size other than body water results in higher recommended doses of dialysis for children, small patients, and women, compared with the current body water-based scaling approach. Aside from small solute removal, increasing weekly time on dialysis results in slower removal of fluid with better tolerance and with increased removal of phosphorus, although both salt and water and phosphorus control often respond to efforts to reduce intake. The intermediate term benefits of removing larger middle molecules such as beta-2-microglobulin appear to be modest, and the benefits of removal of protein-bound uremic toxins remain to be proved in controlled trials.

1. Kaur A, Davenport A. Hemodialysis for infants, children, and adolescents. Hemodial Int. 2014 Apr 14. doi: 10.1111/hdi.12163. [Epub ahead of print]

Abstract: Children with chronic kidney disease stage 5 requiring dialysis can be treated by peritoneal or hemodialysis. In the United Kingdom nearly twice as many children receive peritoneal dialysis compared with hemodialysis. Technical aspects of pediatric hemodialysis are challenging and include the relative size of extracorporeal circuit and child's blood volume, assessment of adequacy, technical and complications of vascular access. Alternatives to standard hospital-based hemodialysis are also increasingly available. Optimizing nutritional status with the support of specialist pediatric dietitians is key to the management of children receiving hemodialysis. The effects of chronic illness on growth and school achievement, as well as the psychological, emotional, and social development of the child should not be underestimated. This review focuses on the above elements and highlights common pediatric practice in the United Kingdom.

1. Dunne N, Campbell M, Fitzpatrick M, Callery P. Comparison of Kt/V and urea reduction ratio in measuring dialysis adequacy in paediatric haemodialysis in England.J Ren Care. 2014 Jun;40(2):117-24. doi: 10.1111/jorc.12059. Epub 2014 Mar 20.

Background: The National Kidney Foundation-Dialysis Outcomes Quality Initiative (KDOQI) guidelines and the Renal Association recommend the use of either Kt/V or urea reduction ratio (URR) to measure haemodialysis adequacy.   
Objectives: To determine the methods used to measure paediatric haemodialysis adequacy and to assess consistency between calculations of single pool Kt/V (spKt/V) and URR.   
Design: A service evaluation was conducted to establish current practices in measuring dialysis adequacy. A prospective longitudinal study was conducted to compare spKt/V and URR. Participants: Thirty-two children were recruited consisting of 13 males and 19 females in five paediatric dialysis centres.   
Results: Inconsistencies were reported of the method of post-urea sampling with 4 of the 10 centres using the KDOQI recommended sampling method. Five dialysis centres reported using URR and five reported using spKt/V. There were substantial differences between the two measures. Using URR suggested that up to 44% of children did not receive adequate dialysis, whereas measurement by spKt/V suggested no more than 6% of the same dialysis sessions were not adequate.   
Conclusion: One standard measure should be used to assess dialysis adequacy in paediatric centres in England. KDOQI guidelines were not consistently followed in obtaining a post-urea blood sample and this procedure should be standardised.

1. Cadnapaphornchai MA, Teitelbaum I. Strategies for the preservation of residual renal function in pediatric dialysis patients. Pediatr Nephrol. 2014 May;29(5):825-36; quiz 832. doi: 10.1007/s00467-013-2554-0. Epub 2013 Jul 19.

Abstract: In adults with end-stage renal disease (ESRD), the preservation of residual renal function (RRF) has been shown to be associated with decreased mortality and improved control of complications of chronic kidney disease. However, less is known on the benefits of RRF in the pediatric dialysis population. The purpose of this article is to review the clinical significance of RRF and to discuss strategies for the preservation of RRF in children with ESRD.

Peritoneal dialysis:

1. Krediet RT1, Struijk DG. Peritoneal changes in patients on long-term peritoneal dialysis. Nat Rev Nephrol. 2013 Jul;9(7):419-29. doi: 10.1038/nrneph.2013.99. Epub 2013 May 14.

Abstract: Long-term peritoneal dialysis can lead to morphological and functional changes in the peritoneum. Although the range of morphological alterations is known for the peritoneal dialysis population as a whole, these changes will not occur in every patient in the same sequence and to the same extent. Longitudinal studies are therefore required to help identify which patients might develop the changes. Although longitudinal studies using peritoneal biopsies are not possible, analyses of peritoneal effluent biomarkers that represent morphological alterations could provide insight. Longitudinal studies on peritoneal transport have been performed, but follow-up has often been too short and an insufficient number of parameters have been investigated. This Review will firstly describe peritoneal morphology and structure and will then focus on peritoneal effluent biomarkers and their changes over time. Net ultrafiltration will also be discussed together with the transport of small solutes. Data on the peritoneal transport of serum proteins show that serum protein levels do not increase to the same extent as levels of small solutes with long-term peritoneal dialysis. Early alterations in peritoneal transport must be distinguished from alterations that only develop with long-term peritoneal dialysis. Early alterations are related to vasoactive mediators, whereas later alterations are related to neoangiogenesis and fibrosis. Modern peritoneal dialysis should focus on the early detection of long-term membrane alterations by biomarkers--such as cancer antigen 125, interleukin-6 and plasminogen activator inhibitor 1--and the improved assessment of peritoneal transport.

1. Fissell R1, Schulman G, Pfister M, Zhang L, Hung AM. Novel dialysis modalities: do we need new metrics to optimize treatment? J Clin Pharmacol. 2012 Jan;52(1 Suppl):72S-8S. doi: 10.1177/0091270011414576.

Abstract: Delivered dose of hemodialysis has long been an important predictor of mortality. The limitations of conventional hemodialysis treatments have led to a renewed interest in more frequent and longer hemodialysis treatments. As alternative hemodialysis schedules have become more prevalent, a need for modified metrics to measure adequacy has emerged. In addition, there is an interest in finding measures of hemodialysis adequacy that are more reliable in certain subgroups of patients, such as women, ethnic minority groups, or people with small body size. Finally, extended hemodialysis schedules suggest a need for metrics that can measure the clearance of solutes other than urea, such as middle-size molecules, and solutes for which clearance depends on intercompartmental transport across membranes. New metrics to quantify clearance in extended and alternate hemodialysis schedules are needed. As new metrics are developed, it is anticipated that they will also contribute to more accurate assessments of associations between clinical outcomes and delivered dose of dialysis in more intensive, nontraditional hemodialysis schedules. This review provides a historical prospective of dialysis dose and adequacy and describes the need for new metrics from both solute type and dialysis dose prospective as alternative hemodialysis schedules have emerged and become more prevalent.

1. Paniagua R, Amato D, Vonesh E, et al. “Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial.” Journal of the American Society of Nephrology: JASN (2002) 13:1307-20. PMID: 11961019.

Abstract: Small-solute clearance targets for peritoneal dialysis (PD) have been based on the tacit assumption that peritoneal and renal clearances are equivalent and therefore additive. Although several studies have established that patient survival is directly correlated with renal clearances, there have been no randomized, controlled, interventional trials examining the effects of increases in peritoneal small-solute clearances on patient survival. A prospective, randomized, controlled, clinical trial was performed to study the effects of increased peritoneal small-solute clearances on clinical outcomes among patients with end-stage renal disease who were being treated with PD. A total of 965 subjects were randomly assigned to the intervention or control group (in a 1:1 ratio). Subjects in the control group continued to receive their preexisting PD prescriptions, which consisted of four daily exchanges with 2 L of standard PD solution. The subjects in the intervention group were treated with a modified prescription, to achieve a peritoneal creatinine clearance (pCrCl) of 60 L/wk per 1.73 m(2). The primary endpoint was death. The minimal follow-up period was 2 yr. The study groups were similar with respect to demographic characteristics, causes of renal disease, prevalence of coexisting conditions, residual renal function, peritoneal clearances before intervention, hematocrit values, and multiple indicators of nutritional status. In the control group, peritoneal creatinine clearance (pCrCl) and peritoneal urea clearance (Kt/V) values remained constant for the duration of the study. In the intervention group, pCrCl and peritoneal Kt/V values predictably increased and remained separated from the values for the control group for the entire duration of the study (P < 0.01). Patient survival was similar for the control and intervention groups in an intent-to-treat analysis, with a relative risk of death (intervention/control) of 1.00 [95% confidence interval (CI), 0.80 to 1.24]. Overall, the control group exhibited a 1-yr survival of 85.5% (CI, 82.2 to 88.7%) and a 2-yr survival of 68.3% (CI, 64.2 to 72.9%). Similarly, the intervention group exhibited a 1-yr survival of 83.9% (CI, 80.6 to 87.2%) and a 2-yr survival of 69.3% (CI, 65.1 to 73.6%). An as-treated analysis revealed similar results (overall relative risk = 0.93; CI, 0.71 to 1.22; P = 0.6121). Mortality rates for the two groups remained similar even after adjustment for factors known to be associated with survival for patients undergoing PD (e.g., age, diabetes mellitus, serum albumin levels, normalized protein equivalent of total nitrogen appearance, and anuria). This study provides evidence that increases in peritoneal small-solute clearances within the range studied have a neutral effect on patient survival, even when the groups are stratified according to a variety of factors (age, diabetes mellitus, serum albumin levels, normalized protein equivalent of total nitrogen appearance, and anuria) known to affect survival. No clear survival advantage was obtained with increases in peritoneal small-solute clearances within the range achieved in this study.

1. Lo WK, Lui SL, Chan TM, et al. “Minimal and optimal peritoneal Kt/V targets: Results of an anuric peritoneal dialysis patient's survival analysis.” Kidney international (2005) 67:2032-8. PMID: 15840054  
     
    BACKGROUND:

Residual renal clearance has been shown to be much more predictive of survival than peritoneal clearance. There has been little data to support a target level of peritoneal clearance. A retrospective study was therefore conducted to see how the peritoneal Kt/V had affected the survival of anuric patients in our center.

METHODS:

Over a period of 10 years, there were 150 peritoneal dialysis patients with documented anuria. Their survival was analyzed according to their baseline peritoneal Kt/V at the time of documentation of anuria and at the time of their latest altered peritoneal dialysis (PD) prescription (subsequent Kt/V).

RESULTS:

There were 90 females and 42 diabetics. The mean age and duration of dialysis were 57.7 +/- 14.7 and 44.1 +/- 31.3 months, respectively. The 2-year and 5-year survival rates were 88.7% and 66.7%, respectively. We found that patients with baseline peritoneal Kt/V below 1.67 had poorer survival after the documentation of anuria than those above [relative risk (RR) 1.985, P= 0.01], although the baseline Kt/V was not an independent risk factors in the whole group of patients. However, such effect was mainly observed in female patients. The survival was identical between those with Kt/V above or below 1.80 (P= 0.98). Among female patients, the group with baseline Kt/V 1.67 to 1.86 had the best survival, followed by those greater than 1.86 and lowest in those below 1.67 (P= 0.0016). For patients with baseline Kt/V below 1.80, those with subsequent Kt/V above 1.76 had better survival than those below (P= 0.033).

CONCLUSION:

Our data suggested that a negative effect of peritoneal Kt/V on survival is apparent at a level below 1.67 and there exists a limit of its effect at around 1.80. We suggested a minimal Kt/V target of 1.70 and an optimal target at 1.80 in anuric patients based on survival data. Prospective randomized study is required to confirm this finding.

1. Holtta T, Ronnholm K, Jalanko H, Holmberg C. “Clinical outcome of pediatric patients on peritoneal dialysis under adequacy control.” Pediatric Nephrology (2000) 14: 889-97. PMID: 10975294

Abstract: Clinical outcome under adequacy control was studied in 10 pediatric patients under 5 years and 11 patients over 5 years of age on continuous peritoneal dialysis (PD). Outcome was compared between the age groups and with our previous results in patients under 5 years of age. Peritoneal equilibration test and 24-h dialysate collection were performed. Laboratory data, clinical status, and diet were recorded. PD prescription was adjusted for these parameters. The mean weekly urea Kt/V was similar and stable in the two age groups (3.1+/-0.6 vs. 3.2+/-0.4 at baseline). The mean weekly creatinine clearance (C(Cr)) was at baseline significantly lower in the younger age group (58.7+/-11.9 vs. 78.0+/-14.9 l/week per 1.73 m2, P=0.004), but later similar. Urea Kt/V and C(Cr) correlated significantly. Hematological and biochemical parameters were stable, and catch-up growth was observed in 62% of the patients during 9 months of follow-up. The outcome for children under and over 5 years of age did not differ significantly. The clinical outcome in patients under 5 years of age improved under adequacy control, when compared with our previous results in patients of the same age. This suggests a positive effect of adequacy control on clinical outcome.

1. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for 2006 Updates: Hemodialysis Adequacy, Peritoneal Dialysis Adequacy and Vascular Access. Am J Kidney Dis 48:S1-S322, 2006 (suppl 1).
2. Rees L, Feather S, Shroff R. “Peritoneal Dialysis Clinical Practice Guidelines for Children and Adolescents.” British Association of Pediatric Nephrology (2008).
3. White CT, Gowrishankar M, Feber J et al. “Clinical practice guidelines for pediatric peritoneal dialysis.” Pediatric Nephrology: (2006) 21: 1059-66. PMID: 16819641\

Abstract: Peritoneal dialysis (PD) continues to be an important modality of treatment for children with end-stage renal disease. The Canadian Association of Pediatric Nephrologists recognized the need nationally to review the literature on the delivery of PD in children to provide optimal standardized care. This resulted in the development of the Canadian Clinical Practice Guidelines for pediatric PD. Clinical practice guidelines are a useful adjunct to clinical care. The present review includes recommendations for catheter placement and types, requirement for prophylactic omentectomy, initiation and adequacy of dialysis, PD prescription, and solute clearance. It provides physicians with updated evidence-based recommendations that include consideration towards practicality with the major goal of improved and standardized patient care.

1. European Best Practice Guideline Working Group. “European Best Practice Guidelines for Peritoneal Dialysis.” Nephrology Dialysis Transplantation (2005) 20:ix1-ix37.
2. Chadha V, Blowey DL, Warady BA. “Is growth a valid outcome measure of dialysis clearance in children undergoing peritoneal dialysis?” Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis (2001) 21 Suppl 3:S179-84. PMID: 11887816  
      
    OBJECTIVE:

Our study evaluated growth as a clinical outcome measure of peritoneal dialysis (PD) adequacy in children with end-stage renal disease (ESRD).

DESIGN:

This retrospective single-center study was carried out in our tertiary-care medical center.

PATIENTS:

The study enrolled 24 patients who initiated dialysis after January 1, 1995, and who had been on dialysis for a minimum of 1 year.

RESULTS:

The weekly mean total [PD + residual renal function (RRF)] creatinine clearance (C(Cr)) and Kt/V(urea) were 70.3 +/- 18 L per 1.73 m2 and 3.45 +/- 0.73, respectively. Of the 24 patients, 12 (50%) were anuric. The mean height standard deviation score (SDS) changed to -1.78 at the end of 1 year from -1.58 at baseline. Catch-up growth (positive delta height SDS) was observed in 9 patients (37%), 7 of whom (78%) had residual renal function (RRF). In contrast, only 5 of 15 patients (33%) with a negative deltaSDS for height had RRF (p < 0.025). The mean height SDS in patients with RRF improved to -1.64 from -1.78; in patients without RRF, it worsened to -1.90 from -1.37 (p = 0.01). While the weekly total Kt/V(urea) in patients with RRF (3.53) was similar to that in patients without RRF (3.37, p = 0.6), only the native Kt/V(urea) had a significant (but weak) positive correlation with delta height SDS (r2 = 0.17, p = 0.04). In contrast, the total weekly C(Cr) was significantly higher (p = 0.001) in patients with RRF (81.1 L/1.73 m2) as compared with those without RRF (59.5 L/1.73 m2). However, only the native C(Cr)--and not the dialysis C(Cr)--had a significant (but weak) positive correlation with delta height SDS (r2 = 0.17, p = 0.04).

CONCLUSIONS:

These preliminary data provide evidence for a correlation between solute clearance and growth, with RRF exerting a significant influence on that outcome. The Kt/V(urea) data also appear to contradict the presumed equivalence of PD and native clearance in children with ESRD

1. Morgenstern BZ, Wuhl E, Nair KS, Warady BA, et al. “Anthropometric prediction of total body water in children who are on pediatric peritoneal dialysis.” Journal of the American Society of Nephrology: JASN (2006) 17:285-93. PMID: 16319190

Abstract: Accurate estimation of total body water (TBW) is a critical component of dialysis prescription in peritoneal dialysis (PD). Gold-standard isotope dilution techniques are laborious and costly; therefore, anthropometric prediction equations that are based on height and weight are commonly used to estimate TBW. Equations have been established in healthy populations, but their validity is unclear in children who undergo PD, in whom altered states of hydration and other confounding alterations in normal physiology, particularly retarded growth and pubertal delay, may exist. TBW was measured by heavy water (H2O18 or D2O) dilution in 64 pediatric patients who were aged 1 mo to 23 yr and receiving chronic PD in the United States and Germany to establish and validate population-specific anthropometric TBW prediction equations and to compare the predictive power of these equations with formulas that have been established in healthy children. The best-fitting equations are as follows: For boys, TBW = 0.10 x (HtWt)0.68 - 0.37 x weight; for girls, TBW = 0.14 x (HtWt)0.64 - 0.35 x weight. The height x weight parameter also predicts body surface area (BSA). These equations can be simplified, with slightly less precision, to the following: For boys, TBW = 20.88 x BSA - 4.29; for girls, TBW = 16.92 x BSA - 1.81. TBW is predicted without systematic deviations and equally well in boys and girls, North American and European, obese and nonobese, growth-retarded and normally sized, and pre- and postpubertal children. In contrast, previous anthropometric equations that were derived from healthy children systematically overpredicted TBW and were less precise in this pediatric PD population. In summary, a new set of anthropometric TBW prediction equations that are suited specifically for use in pediatric PD patients have been provided.

1. Bargman JM, Thorpe KE, Churchill DN et al. “Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study.” Journal of the American Society of Nephrology (2001) 12(10):2158-62.

Abstract: Studies of the adequacy of peritoneal dialysis and recommendations have assumed that renal and peritoneal clearances are comparable and therefore additive. The CANUSA data were reanalyzed in an effort to address this assumption. Among the 680 patients in the original CANUSA study, 601 had all of the variables of interest for this report. Adequacy of dialysis was estimated from GFR (mean of renal urea and creatinine clearance) and from peritoneal creatinine clearance. The Cox proportional-hazards model was used to evaluate the time-dependent association of these independent variables with patient survival. For each 5 L/wk per 1.73 m(2) increment in GFR, there was a 12% decrease in the relative risk (RR) of death (RR, 0.88; 95% confidence interval [CI], 0.83 to 0.94) but no association with peritoneal creatinine clearance (RR, 1.00; 95% CI, 0.90 to 1.10). Estimates of fluid removal (24-h urine volume, net peritoneal ultrafiltration, and total fluid removal) then were added to the Cox model. For a 250-ml increment in urine volume, there was a 36% decrease in the RR of death (RR, 0.64; 95% CI, 0.51 to 0.80). The association of patient survival with GFR disappeared (RR, 0.99; 95% CI, 0.94 to 1.04). However, neither net peritoneal ultrafiltration nor total fluid removal was associated with patient survival. Although these results may be explained partly, statistically, by less variability in peritoneal clearance than in GFR, the latter seems to be physiologically more important than the former. The assumption of equivalence of peritoneal and renal clearances is not supported by these data. Recommendations for adequate peritoneal dialysis need to be reevaluated in light of these observations.

1. Cho Y1, Johnson DW, Craig JC, Strippoli GF, Badve SV, Wiggins KJ. Biocompatible dialysis fluids for peritoneal dialysis. Cochrane Database Syst Rev. 2014 Mar 27;3:CD007554. doi: 10.1002/14651858.CD007554.pub2.  
     
    BACKGROUND:

The longevity of peritoneal dialysis (PD) is limited by high rates of technique failure, some of which stem from peritoneal membrane injury. 'Biocompatible' PD solutions have been developed to reduce damage to the peritoneal membrane.

OBJECTIVES:

This review aimed to look at the benefits and harms of biocompatible PD solutions in comparison to standard PD solutions in patients receiving PD.

SEARCH METHODS:

We searched the Cochrane Renal Group's Specialised Register (28 February 2013), through contact with the Trials Search Co-ordinator using search terms relevant to this review. Studies contained in the Specialised Register are identified through search strategies specifically designed for CENTRAL, MEDLINE and EMBASE, and handsearching conference proceedings.

SELECTION CRITERIA:

All randomised controlled trials (RCTs) and quasi-RCTs in adults and children comparing the effects of biocompatible PD solutions (neutral pH, lactate-buffered, low glucose degradation product (GDP); neutral pH, bicarbonate (± lactate)-buffered, low GDP; glucose polymer (icodextrin)) in PD were included. Studies of amino acid-based PD solutions were excluded.

DATA COLLECTION AND ANALYSIS:

Two authors extracted data on study quality and outcomes (including adverse effects). The authors contacted investigators to obtain missing information. Summary estimates of effect were obtained using a random-effects model, and results were expressed as risk ratios (RR) and their 95% confidence intervals (CI) for categorical variables, and mean difference (MD) or standardised mean difference (SMD) and 95% CI for continuous variables.

MAIN RESULTS:

Thirty-six eligible studies (2719 patients) were identified: Neutral pH, lactate-buffered/bicarbonate (± lactate)-buffered, low GDP PD solution (24); icodextrin (12). Allocation methods and concealment were generally incompletely reported, and adequate in only ten studies (27.8%). Patients lost to follow-up ranged from 0% to 83.4%. Neutral pH, low GDP versus conventional glucose PD solutionBased on generally sub-optimal quality evidence, the use of neutral pH, low GDP PD solutions was associated with larger urine volumes at the end of the studies, up to three years of therapy duration (7 studies, 520 patients: MD 126.39 mL/d, 95% CI 26.73 to 226.05). Improved preservation of residual renal function was evident in studies with greater than 12 month follow-up (6 studies, 360 patients: SMD 0.31, 95% CI 0.10 to 0.52). There was no significant effect on peritonitis, technique failure or adverse events with the use of neutral pH, low GDP PD solutions. Glucose polymer (icodextrin) versus conventional glucose PD solutionThere was a significant reduction in episodes of uncontrolled fluid overload (2 studies, 100 patients: RR 0.30, 95% CI 0.15 to 0.59) and improvement in peritoneal ultrafiltration (4 studies, 102 patients, MD 448.54 mL/d, 95% CI 289.28 to 607.80) without compromising residual renal function (4 studies, 114 patients: SMD 0.12, 95% CI -0.26 to 0.49) or urine output (3 studies, 69 patients: MD -88.88 mL/d, 95% CI -356.88 to 179.12) with icodextrin use. A comparable incidence of adverse events with the icodextrin (four studies) was reported.

AUTHORS' CONCLUSIONS:

Based on generally sub-optimal quality studies, use of neutral pH, low GDP PD solution led to greater urine output and higher residual renal function after use exceeded 12 months. Icodextrin prescription improved peritoneal ultrafiltration and mitigated uncontrolled fluid overload. There were no significant effects on peritonitis, technique survival, patient survival or harms identified with their use. Based on the best available evidence, the use of these 'biocompatible' PD solutions resulted in clinically relevant benefits without added risks of harm.

1. Cadnapaphornchai MA1, Teitelbaum I. Strategies for the preservation of residual renal function in pediatric dialysis patients. Pediatr Nephrol. 2014 May;29(5):825-36; quiz 832. doi: 10.1007/s00467-013-2554-0. Epub 2013 Jul 19.

Abstract: In adults with end-stage renal disease (ESRD), the preservation of residual renal function (RRF) has been shown to be associated with decreased mortality and improved control of complications of chronic kidney disease. However, less is known on the benefits of RRF in the pediatric dialysis population. The purpose of this article is to review the clinical significance of RRF and to discuss strategies for the preservation of RRF in children with ESRD.

1. Watanabe A1, Lanzarini VV, Filho UD, Koch VH. Comparative role of PET and Kt/V determination in pediatric chronic peritoneal dialysis.Int J Artif Organs. 2012 Mar;35(3):199-207. doi: 10.5301/ijao.5000070.  
     
    INTRODUCTION:

Nutritional state and growth are considered as prognostic markers of chronic peritoneal dialysis (PD) adequacy in pediatric patients. The euvolemia, blood pressure control, and metabolic and electrolytic equilibrium are parameters to be achieved by PD treatment.

OBJECTIVE:

To describe the chronic PD prescription parameters of a cohort of pediatric patients and to compare the obtained hemodynamic, antrophometric and adequacy results with those suggested by the literature.

METHODS:

Retrospective analysis based on clinical records evaluation of 30 pediatric patients undergoing PD for more than 6 months from January 1998 to May 2005.

RESULTS:

In the present study, 17/30 (56.7%) were boys. Chronic kidney disease was secondary to uropathy in 66.7% of the cases. The infusion volume was > 1,000 ml/m2 in 9 patients. The peritoneal membrane was characterized as high (27.8%), high-average (33.3%), low-average (22.2%) and low transporter (16.7%). The weekly urea Kt/V was > 2.1 in all the evaluated patients. Blood pressure parameters above the 95th percentile despite the use of antihypertensive medication were observed in 5/30 patients, four of whom with CKD secondary to glomerulopathy. The initial and final Body Mass Index and weight for height ratio were preserved in 83.3% (25/30) patients.

CONCLUSION:

Elevated indexes of small solutes removal are easily attained in pediatric PD patients and do not imply optimal clinical management do not imply optimal climanagement.

1. Baştuğ F1, Dursun I, Dursun J et al. Could mini-PET be used to instead of 4 h original-PET to assess peritoneal permeability in children on peritoneal dialysis? Ren Fail. 2014 May;36(4):562-6. doi: 10.3109/0886022X.2013.879368. Epub 2014 Jan 23.  
      
    BACKGROUND:

Original peritoneal equilibration test (PET) is an implementation that requires hard work for peritoneal dialysis (PD) staff. Therefore, several authors have attempted to validate short and fast PET protocols, with controversial results. The aim of this study was to evaluate the concordance between the mini-PET and original PET in children.

METHODS:

In 26 stable continuous ambulatory PD patients, we performed an original PET with 2.27% (4 h) and a mini-PET with 3.86% glucose PD fluid (1 h) and compared ultrafiltration (UF) and small solute transports obtained with the two methods.

RESULTS:

Twenty-six children, 14 males, mean age 11.4 ± 5.6 (range 2.5-19 years), were included. Meantime on PD at time of enrollment was 35.2 ± 24.5 months (range 6-84 months). Based on the 4-h creatinine D/P data, the number of the patients within each transport category was as follow: high, 5; average, 18; low, 3. Kappa test showed a significant concordance between original PET and mini-PET (k=0.610). Based on the 4-h glucose D/D0 data, the number of the patients within each transport category was as follow: high, 5; average, 17; low, 4. Kappa test showed a moderate agreement between original PET and mini-PET (0.514, p=0.000). When Pearson correlation analysis between original PET and mini-PET was performed, there were significant positive correlations between original 2.27% PET and mini-PET (r=0.720, p=0.000, r=0.638, p=0.000, respectively). When comparing the numeric results of mini-PET and 4 h of original PET for D/Creatinine, by simple regression analysis, we found statistically significant correlation among PETs.

CONCLUSIONS:

In this study, we showed concordance between the mini-PET and original PET. The 3.86% mini-PET is simple and fast methods to assess free water transport. This also gives information about total UF and small solute transports and it is in good agreement with the original PET.