AJKD
Narrative Review

Practice-Based Versus Patient-Level Outcomes Research in Hemodialysis: The DOPPS (Dialysis Outcomes and Practice Patterns Study) Experience

Friedrich K. Port, MD, MS

When randomized controlled trials are unavailable, clinicians have to rely on observational studies. However, analyses using observational data to evaluate specific treatments and their associations with outcomes often are biased through confounding by clinical indication for the treatment of interest. Given the rich observational data and limited clinical trial data available in the dialysis population, successfully accounting for this bias can lead to substantial knowledge generation. In recent decades, much has been learned about statistical methods for observational data, including the fact that even extensive adjustments may not always overcome this bias, particularly when unmeasured confounders exist. In this article, examples based on the international DOPPS (Dialysis Outcomes and Practice Patterns Study) are used to demonstrate the value of practice-based instrumental variable analyses. This methodology leverages the marked differences in practice patterns among dialysis facilities and uses the reasonable assumption that patients are assigned to a dialysis facility without consideration of its specific treatment pattern in order to minimize bias in analyses relying on observational data. Examples using the dialysis facility as an instrument that are reviewed in depth in this article include studies of dialysate sodium concentration, systolic blood pressure targets, and treatment time, demonstrate the value of this methodology to produce advanced knowledge. However, practice-based analyses have potential limitations. Specifically, observation of sufficiently large differences in practice patterns is required and these analyses should consider that the treatment of interest may be associated with other facility treatment practices. These examples from the DOPPS hopefully will stimulate advances in methodologies and critical clinical work toward improving patient care by identifying beneficial treatment practices applicable to dialysis, chronic kidney disease, and beyond.
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INDEX WORDS: Confounding by indication; dialysate sodium; predialysis blood pressure; dialysis treatment time; instrumental variable analyses; observational studies; international dialysis.

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INTRODUCTION

Because randomized clinical trials are rare, particularly in nephrology,[1] much of clinical knowledge continues to be based on observational studies. Observational study methodologies have markedly improved over the last several decades. In this review, I show a progression witnessed over 40 years in the analyses of mortality outcomes in observational studies from registries and multicenter studies with prospective data collection. I also emphasize the additional knowledge gained from multicenter studies by using practice-based analyses beyond the typical analytic approach of case-mix–adjusted Cox models. Practice-based analyses may compare uniform versus individualized prescriptions or use instrumental variable analyses in 2 stages, while also adjusting for other practice indicators.

THE EARLY YEARS OF THE US RENAL DATA SYSTEM

When I arrived as a faculty member at the University of Michigan 40 years ago, in the mid-1970s, I became involved in the oldest statewide registry in the United States of patients treated for end-stage renal disease (ESRD). Our analyses were among the first to deal with time-to-treatment bias when comparing outcomes for dialysis patients and transplant recipients, in that the latter typically represented dialysis survivors.[2-4]

Based on prior experience in analyzing ESRD data from the Centers for Medicare & Medicaid Services (CMS) and the Michigan Kidney Registry, Dr Philip J. Held and I were jointly awarded the first US Renal Data System (USRDS) contract from the National

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Institutes of Health in 1988. Setting the stage for research to come, one of the first USRDS articles titled "How Good Are the Data?" focused on ensuring complete ascertainment of mortality and other outcomes. After expanding USRDS data to include specialized data collection from randomly selected national samples of dialysis facilities and their patients, subsequent research could include more detailed description of both national practices and variation among individual dialysis facilities. This design led to evaluation of outcomes by mode of dialysis,[5] dialysis dose,[6] and numerous other analyses, all of which, due to the breadth of comorbid condition and laboratory data, could include statistical adjustment for patient characteristics and other factors.

INTERNATIONAL COMPARISONS AND THE BIRTH OF THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY

Our early study comparing survival data for patients with ESRD in the USRDS with data from registries in Europe (the European Dialysis and Transplant Association) and Japan (the Japanese Society for Dialysis Therapy) was led by Dr Held and demonstrated for the first time that survival was substantially shorter in the United States than in Europe and Japan.[7] The shorter survival in the United States was seen in virtually all age groups regardless of diabetes status.[7]

Many US nephrologists assumed that these mortality differences could be explained by more thorough ascertainment of deaths in the United States than in the European or Japanese registries. However, if mortality truly was higher in the United States, this finding would suggest a critical need to study ways to improve care and outcomes for patients with ESRD in the United States. Recognizing this opportunity, Amgen funded our proposed study, the DOPPS (Dialysis Outcomes and Practice Patterns Study), in 1996 to focus on practice patterns and outcomes in the United States, Japan, and several of the larger European countries. Led by Drs Held, Wolfe, and myself, the DOPPS randomly selected national samples of dialysis facilities and patients within facilities in each country; used a uniform data collection instrument including detailed data for comorbid conditions, laboratory results, hemodialysis prescription, vascular access, and prescribed medications; uniformly ascertained deaths and other events; collected information directly from patients regarding patient-centered outcomes; and asked medical directors and nurses about their dialysis facility environment, opinions, practices, and services offered.[8] To ensure high levels of participation and high-quality data collection among selected facilities, it was necessary to provide payment for the collection of these data by the dialysis staff.

Using the DOPPS, we reassessed mortality comparisons internationally and found that even with extensive case-mix adjustment, mortality was highest in the United States, lowest in Japan, and intermediate in the 5 initial European countries.[9] Later, Pisoni et al[10] confirmed this observation, attributing some but not all of the mortality difference between the United States and Europe to differences in vascular access practices, thus emphasizing a major opportunity for improved patient care, particularly in the United States. Numerous other observations published by the DOPPS showed marked within-country and international differences in practice patterns and associated outcomes (see www.DOPPS.org for abstracts and downloadable slides from ~180 peer-reviewed publications).

ASSOCIATING TREATMENTS WITH OUTCOMES IN OBSERVATIONAL STUDIES: CONFOUNDING BY INDICATION

Although observational studies are excellent for describing patient characteristics, practices, and trends over time, these analyses usually require substantial adjustment for factors that may be correlated with outcomes. Because treatments are prescribed to patients based on specific clinical indications, observational studies may give misleading and biased results for morbidity and mortality because even adjusting for numerous recorded factors may not capture all factors that influence selection for treatment. Thus, the relationship between the exposure and the outcome may be confounded by clinical indication.

As a simple example, we know that prescribing erythropoietin (EPO) increases patients' hemoglobin (Hb) levels. However, observational data for prevalent hemodialysis patients show that those receiving EPO have on average a lower, not higher, Hb level than those not receiving EPO.[11] Furthermore, patients receiving higher EPO doses have slightly lower Hb levels than those receiving lower doses (Fig 1A).[12] This finding contrasts with dosing trials for EPO[13] that have shown incontrovertibly that these inverse associations between EPO dose and Hb level are not causal; EPO does not lower Hb levels! Instead, the reason for these findings is that patients with a higher Hb level do not have the indication to be prescribed either EPO at all or, if prescribed EPO, higher doses. Thus, we recognize that these analyses are confounded by the indication: in this case, patients' lower Hb levels.

This problem led us to the approach of using practice-based analyses with the help of our colleagues, Drs Robert Wolfe and Brenda Gillespie. For

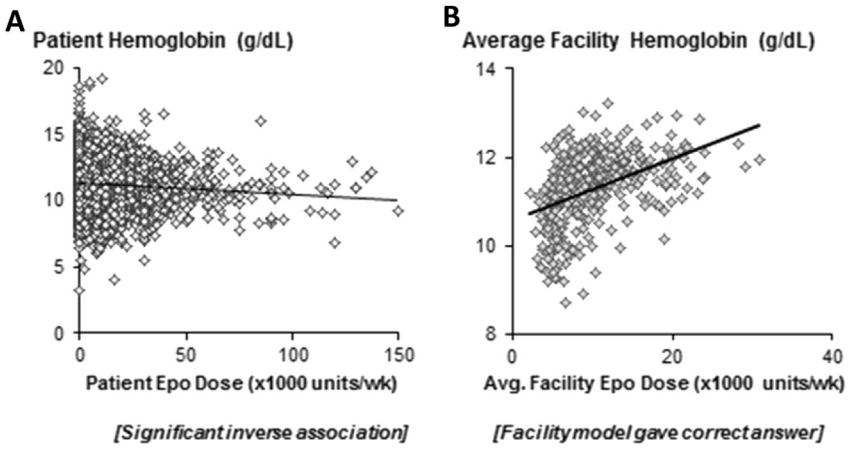

Figure 1. Hemoglobin level by weekly dose of erythropoietin (EPO) based on the DOPPS (Dialysis Outcomes and Practice Patterns Study). Scatterplot (left panel) by patient-level dose and (right panel) using facility-level mean Epo dose. Reproduced from Rayner[12] with permission of British Journal of Renal Medicine © Hayward Medical Communications.

the mentioned example, we could analyze dialysis unit practices, comparing facilities that prescribe on average higher doses of EPO to their patients with those that prescribe lower doses. With these practice-based analyses, we found that Hb level was higher when the prescribed dose of EPO was on average higher (Fig 1B). Thus, the practice-based approach, in which the dialysis facility or facility practice served as the instrument, gave the correct answer by minimizing confounding by indication.

The following examples demonstrate the problem of bias by indication through unmeasured confounders even when extensive adjustments for patient case mix are used and, in turn, illustrate advantages of practice-based analyses that may add insights into potentially causal associations. The influence of unmeasured confounders, such as the severity of a critical comorbid condition, on both treatment and outcome is shown in Fig 2 with comments on 3 study approaches. Limitations and assumptions of instrumental variable analyses are detailed later in the Discussion.

Dialysate Sodium Prescription and Outcomes

We were interested in the effect of dialysate sodium concentration on various outcomes, but wondered whether dialysate that is prescribed individually potentially may be confounded by clinical indication.

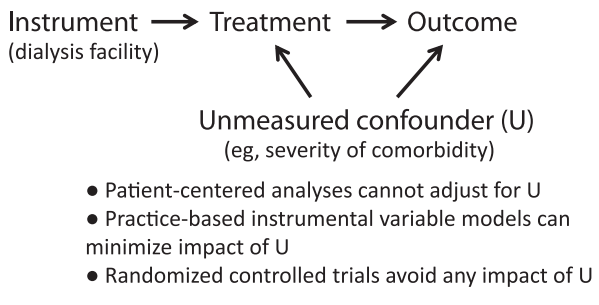

Figure 2. Approaches to dealing with unmeasured confounders.

Almost half the DOPPS facilities prescribed a variety of dialysate sodium concentrations for their patients. Among facilities that individualized dialysate sodium concentration, significantly lower dialysate sodium concentrations were prescribed for patients who were younger or had a higher predialysis systolic blood pressure (BP), whereas patients who experienced greater decreases in systolic BP from pre- to post-dialysis appeared more likely to be prescribed a higher dialysate sodium concentration. In contrast, in dialysis facilities that used a uniform dialysate sodium concentration prescription for virtually all (90%-100%) their patients, dialysate sodium concentration was by definition not tailored to individual patient characteristics. When analyzed in an overall model with predialysis systolic BP as the outcome, the patterns of association with dialysate sodium concentration prescription were significantly different between "individualized" and "uniform" facilities (interaction $P < 0.01$) and borderline different for the association between dialysate sodium concentration and pre- to postdialysis change in systolic BP (interaction $P = 0.08$).[14] This suggests that analyses of the relationship between dialysate sodium concentration and outcomes may be biased for patients treated in facilities in which dialysate sodium concentration prescription was individualized based on their predialysis systolic BP, particularly because there likely were other unmeasured indicators of patients' medical status associated with these individualized treatment decisions.

Accordingly, to avoid dialysate sodium concentration prescription being confounded by indication, we restricted the analysis of patient outcomes to dialysis facilities that prescribed dialysate sodium concentration uniformly. One may consider that patient assignment to different uniform dialysate sodium concentration practices resembled random assignment, not because of the dialysis facility's specific uniform dialysate sodium concentration prescription

(which patients are unlikely to be aware of when selecting a dialysis facility) but rather because of unrelated factors such as the distance between the facility and the patient's home. Here, we found in case-mix–adjusted analyses that lower dialysate sodium concentration was not associated with lower mortality, as had been suggested by others.[15] Mortality risk was significantly greater with lower dialysate sodium concentration than with higher dialysate sodium concentration in uniform dialysate sodium concentration facilities (hazard ratio [HR], 1.14; $P < 0.001$ per 2-mEq/L lower dialysate sodium concentration).[16] Because predialysis serum sodium level is associated inversely with mortality risk,[17] it also was important to test whether this association of dialysate sodium concentration with mortality risk was observed at a variety of serum sodium categories. As shown in Fig 3, for facilities with uniform dialysate sodium concentration prescription, mortality risk was higher with lower dialysate sodium concentration regardless of serum sodium level. This finding, generated using methods that better account for confounding by indication, is particularly striking because higher dialysate sodium concentration was associated positively with significantly greater interdialytic weight gain (and therefore higher ultrafiltration rate), likely due to increased thirst related to intradialytic sodium loading. In uniform dialysate sodium concentration facilities, this weight gain accounted on average for only 0.17% of target weight per 2-mEq/L higher dialysate sodium concentration or ~120 mL over 2 days for a 70-kg patient. Even the risk of hospitalization was not increased with higher dialysate sodium concentration despite the greater weight gain (HR, 0.97 per 2-mEq/L higher dialysate sodium concentration; $P = 0.04$).[16]

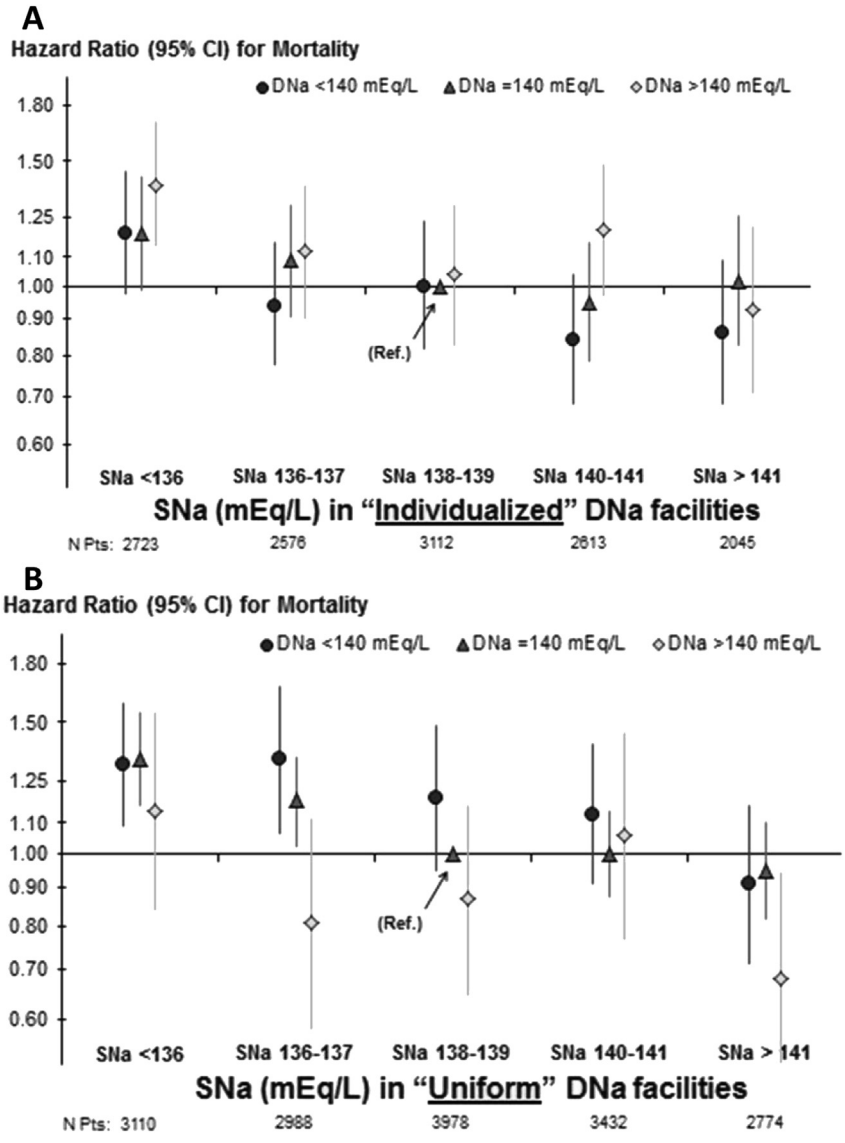

Figure 3. Adjusted mortality risk (with 95% confidence interval [CI]) by categories of dialysate sodium (DNa) concentration and predialysis serum sodium (SNa) level in (A) 535 dialysis facilities that individualized DNa prescription (by indication) and (B) 425 facilities that used a uniform DNa prescription (patients assigned without indication). Reference categories are DNa = 140 mEq/L and SNa = 138-139 mEq/L. All Cox models were adjusted for demographics, comorbid conditions, laboratory values, and 3 facility practices. Modified from Hecking et al[16] with permission of Elsevier.

Corresponding analyses for facilities that individualized dialysate sodium concentration (44% of all DOPPS facilities) yielded opposite mortality results: a lower mortality risk with lower dialysate sodium concentration (Fig 3). This finding likely is explained as bias by the indication for prescribing dialysate sodium concentration individually and appears to agree with other published work.[15]

Figure 3 for uniform dialysate sodium concentration illustrates 2 inverse associations with mortality: first, for serum sodium level at any dialysate sodium concentration (from left to right), and second, for dialysate sodium concentration within any serum sodium category. This graphic also can be read for different dialysate sodium concentration to serum sodium gradients and shows no survival benefit with a reduced gradient. Furthermore, the reported lack of association between dialysate sodium concentration and serum sodium level[17] suggests a serum sodium set point that is affected only minimally (or not at all) by dialysate sodium concentration. These findings from patients assigned to uniformly prescribed dialysate sodium concentration argue against generally lowering dialysate sodium concentration to 134-138 mEq/L or tailoring dialysate sodium concentration to the patient's serum sodium level, as recently proposed.[18] Well-designed clinical trials are needed and hopefully will confirm potential reasons for the association between higher dialysate sodium concentration and better outcomes seen in the DOPPS, such as improved intradialytic hemodynamic stability.

Predialysis Systolic BP and Outcomes

Several observational studies have evaluated associations between predialysis BP and outcomes, showing that lower systolic BP (<120 mm Hg) is associated strongly with higher mortality risk[19,20]; this pattern has been consistent for dialysis patients both with and without congestive heart failure.[19] Surprisingly, high predialysis systolic BP (160-180 mm Hg) is not associated with increased risk of death. Thus, 2 questions need to be addressed: (1) are dialysis patients overmedicated to low systolic BPs based on targets from the general population that may not be appropriate; and (2) does the observation of no elevated mortality risk for hemodialysis patients with very high predialysis systolic BPs reflect a causal relationship or is it biased?

We observed in the DOPPS that the distribution of achieved systolic BPs varies across facilities, presumably reflecting differences in treatment goals and BP targets as noted in our physician questionnaires. Figure 4 illustrates the wide variation in actual distributions of systolic BP between facilities and highlights 2 treatment patterns, one that appears to target systolic BP < 140 mm Hg and a second pattern that avoids low systolic BP based on the reported associations with elevated mortality risk.[19,20] Our study again makes the assumption that patients are assigned almost randomly to facilities with different BP management approaches (as reflected by different facility BP distributions). To evaluate this, we used 2 different methods to study the relationship between systolic BP and mortality: Cox regression at the practice level using 2-stage instrumental variable analysis and, for comparison, standard patient-centered Cox regression analyses adjusting for the same case-mix variables. As reported by Robinson et al,[21] the latter patient-centered models, which were adjusted for many comorbid conditions, confirmed earlier reports of higher mortality risk with lower systolic BP, but not with high systolic BP (160-180 mm Hg). However, the question remains as to whether other unmeasured factors that were not adjusted for may also differ by level of systolic BP and influence mortality risk. To deal with potential unmeasured confounders, the practice-based instrumental variable approach was used.

In analyses that used dialysis facility as the instrument, facilities with more patients with systolic

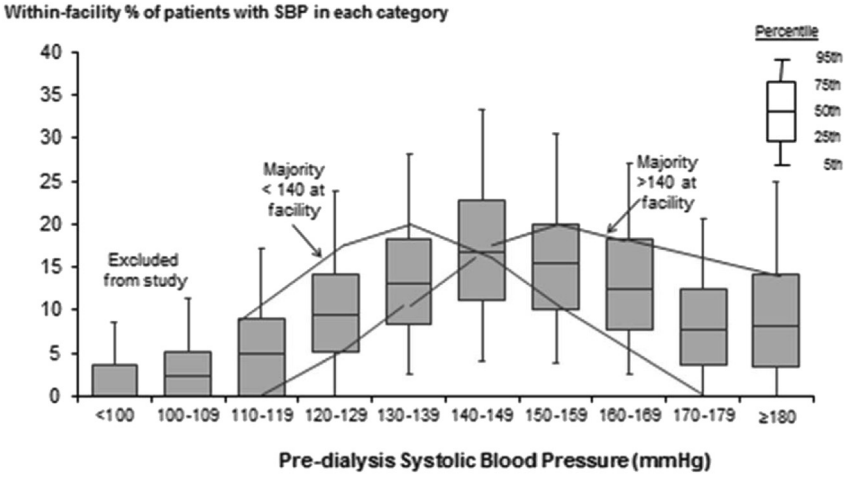

Figure 4. Distribution of predialysis systolic blood pressure (SBP) within 922 dialysis facility practices (25,907 patients) from the DOPPS (Dialysis Outcomes and Practice Patterns Study) in 12 countries. Box and whiskers show the facility percent of patients by SBP category. Patients receiving dialysis for less than 6 months are excluded. The 2 lines illustrate one facility practice pattern that seems to follow general guidelines to aim for SBP < 140 mm Hg and another practice pattern that seems to follow advice from prior dialysis studies to avoid low predialysis SBP (see text). Reproduced from Robinson et al[21] with permission of Macmillan Publishers Ltd.

BPs in the range of 130-159 mm Hg had the lowest mortality, whereas facilities with more patients in either lower or higher ranges had higher mortality risks (Fig 5). Compared with the patient-centered analyses described that showed no elevated risk of death at systolic BP > 160 mm Hg, results in instrumental variable analyses were markedly different, suggesting that unmeasured patient-level confounders biased results at systolic BP > 160 mm Hg in patient-centered models.

Because these results might be influenced by whether patients were using BP-lowering drugs, we performed separate analyses and found the mortality risk to be similar regardless of BP medication use. For patients with higher systolic BP, differences in medication use may reflect, at least in part, differences in practice, such as target BPs or attention paid to BP levels in the dialysis facility. For patients with lower systolic BPs, elevated mortality for the small group of patients not using BP medications suggests a role of heart failure, whereas elevated mortality for patients prescribed medications suggests a possible deleterious effect of treatment to low systolic BPs. We hope that a randomized trial evaluating outcomes by 2 different BP targets in dialysis patients will provide more certain guidance,[22] but results likely will take several years to become available. Until this time, our analyses suggest targeting predialysis systolic BP of 130-160 mm Hg, a level higher than suggested in the KDIGO (Kidney Disease: Improving Global Outcomes) practice guidelines.[23] Of note, predialysis systolic BP reflects peak levels during the thrice-weekly dialysis cycles, overestimating the average weekly systolic BP as obtained from 24-hour BP monitoring, typically by almost 10 mm Hg.[24]

Dialysis Treatment Time and Outcomes

Among prevalent hemodialysis patients treated with thrice-weekly in-center hemodialysis (~95% of hemodialysis patients in the initial DOPPS countries), we observed large differences among patients and among dialysis facilities regarding the length of dialysis sessions. Earlier DOPPS work that relied on standard patient-centered Cox regression models with extensive adjustment for case mix showed a significant association between longer treatment times and lower mortality risk.[25]

As analytic methodologies improved, we realized that treatment times also may be prescribed by indication. Two DOPPS findings that were at first glance surprising suggested confounding by indication: (1) longer treatment times were associated significantly with greater risk of predialysis hyperkalemia (potassium > 6 mEq/L), and (2) longer treatment times were associated significantly with greater interdialytic weight gain. Both findings are contrary to the clinical expectation that poor control of potassium levels and poor achievement of target weight would be associated with shorter dialysis sessions and suggest that longer treatment times more likely were prescribed for patients who had problems with potassium level control or reaching their prescribed target weight. These examples of treatment by indication suggest that unmeasured factors are present and bias the patient-centered associations.

To address this potential bias, we initiated a DOPPS study of thrice-weekly treatment time using dialysis unit practice as the instrument in a 2-stage instrumental variable model. The first stage predicted patient treatment time using facility indicators adjusted for case-mix variables; the second stage predicted patient mortality as a function of case-mix–adjusted facility mean treatment time (from stage 1) and other covariates. The high first-stage F statistic of 25 indicated that the facility was a strong instrument ($F > 10$ is considered strong).[26] In other words, the facility or its practice was a strong predictor of treatment time after accounting for patient characteristics,

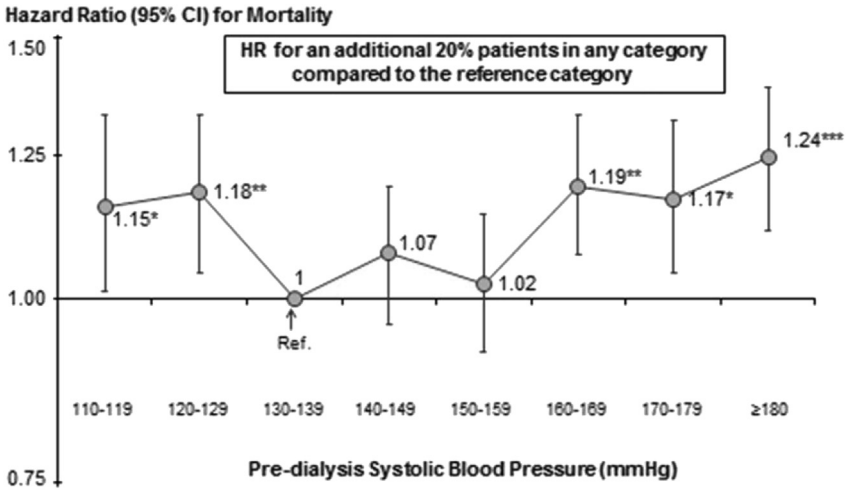

Figure 5. Adjusted mortality risk (with 95% confidence interval [CI]) by facility-level predialysis systolic blood pressure (BP) categories compared to a reference (Ref) category of systolic BP of 130-139 mm Hg. Adjustments included demographics, comorbid conditions, laboratory results, and 3 facility practices. Patients with systolic BP < 110 mm Hg were presumed to not be in a desired practice range and therefore were excluded. Abbreviation: HR, hazard ratio. Reproduced from Robinson et al[21] with permission of Macmillan Publishers Ltd.

suggesting that provider preferences for shorter or longer treatment time were an important determinant of prescribed treatment times. The final results at the practice level (dialysis facility level) confirmed that longer treatment times were associated significantly with lower mortality risk and also lower hospitalization risk (Fig 6).[27] Because the instrumental variable results and fully adjusted standard Cox model results were similar, this suggests that confounding by indication played at most a minor role. Overall, the similarity of associated mortality risk between these 2 methodologies was reassuring because it provided an additional and presumably higher level of evidence for a favorable effect of longer treatment time. The recently initiated pragmatic clinical trial on treatment time (TiME Trial) will be important to confirm these observational results.[28]

DISCUSSION

Although randomized controlled trials continue to be the gold standard for clinical evidence, such studies are rare in nephrology.[1] Some trials give only partial answers, particularly if generalizability may be questioned due to selective enrollment or results are negative because high cost limited the sample size. Furthermore, clinical trials typically cannot explore risks associated with what is presumed to be "poor" practice due to perceived lack of equipoise. For example, the HEMO (Hemodialysis) Study could not assess outcomes for low dose of hemodialysis, focusing for perceived ethical reasons on the (then) average dose of dialysis versus a high dose of dialysis.

In this context, observational studies will continue to inform clinical practice. However, limitations of observational studies can lead to misleading information due to undetected bias, particularly when dealing with treatment choices, because treatment is given selectively by indication. It was thought that extensive adjustment could overcome this limitation in observational studies; however, if important confounders are not well recorded, they clearly cannot be included in adjustments.

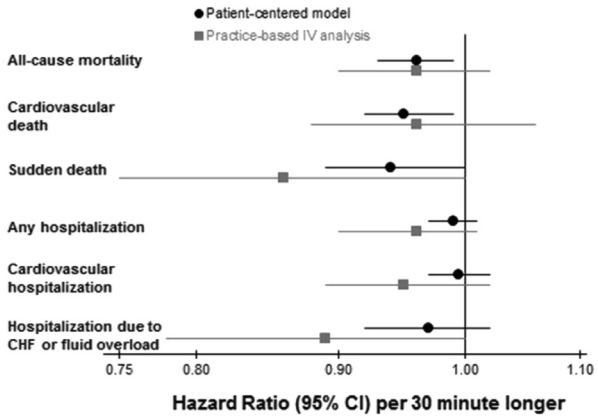

Figure 6. Adjusted associations of hemodialysis treatment time with overall and cause-specific mortality risk and hospitalization risk using patient-centered models (solid circle) and practice-based analyses by instrumental variable (IV) analysis (shaded square). Abbreviations: CHF, congestive heart failure; CI, confidence interval. Reproduced from Tentori et al[27] with permission of Oxford University Press.

The case-mix–adjusted practice-based approach, either by evaluating uniform practices (as seen in the dialysate sodium concentration example), or by formal instrumental variable analyses that use the dialysis facility (practice) as the instrument (as seen in the treatment time and BP examples), is designed to minimize or overcome the problem of unmeasured patient-level confounders.[29] The principle of practice-based instrumental variable analyses is that practice patterns differ among dialysis facilities and patients are assigned to the treatment plans used in their dialysis facilities quasi-randomly, a term suggested by Zoccali[30] and others. Although adjusting for measured indicators of case mix can identify and reduce some influences on the decision-making process for the treatment prescribed, dialysis facilities still differ (beyond these adjustments) in their preferences for treatment plans or clinical decisions. Their differential practices often arise from differential facility policies, preferences, and detailed knowledge. As we demonstrate here for associations between both dialysate sodium concentration and predialysis systolic BP with mortality risk, results can differ markedly with patient-centered versus practice-based analyses, even when considering the same patient-level confounders. In these cases, treatment-by-indication bias likely exists because it is common that treatments are given to those with the strongest clinical indication, usually those who are most sick. For clinical treatment options, we expect that unmeasured confounders are mostly at the patient level rather than the facility level. Therefore, it may not be surprising that results may differ when minimizing patient-level confounding through instrumental variable analyses. However, it is reassuring when instrumental variable analyses provide results similar to patient-center analyses as demonstrated in the dialysis treatment time example.

Although the practice-based instrumental variable approach has many advantages, in order for it to be used appropriately, 3 major assumptions must be met: (1) the instrument (dialysis facility) must be related to the treatment of interest, (2) the instrument must be unrelated to other prognostic factors, and (3) the instrument must have no direct or indirect effect on outcome (except by the pathway of the treatment of interest). Assumption 1 can be tested using partial F statistics. The larger the variation in the treatment across facilities, the stronger

the instrumental variable, the more robust the instrumental variable analysis is toward unmeasured confounders, and the more precise is the effect estimate from the instrumental variable analysis. Weak instruments can introduce bias and lead to underpowered studies. Assumptions 2 and 3 are difficult to prove, although knowledge of dialysis practice patterns can be helpful in judging their validity. The violations of assumptions 2 and 3 often are attributable to unmeasured practice-level confounders. This means that the practice of interest should not be correlated with other unadjusted facility practices that predict the same outcome. As a theoretical example, if 2 facility practices, such as vitamin D administration and fistula use, tended to always occur together, a practice-based model might credit vitamin D use with reducing mortality when the benefit was due to more fistula use. We have approached this issue by adjusting the instrumental variable analyses additionally for other practices, such as the facility's adherence to guidelines for Kt/V, phosphorus level, Hb target, and catheter use. Such adjustments for other practice indicators were used in both the BP example and the dialysate sodium example to provide additional assurance of the validity of the findings. In these examples, adding the adjustments for other practices did not substantially modify results.

FUTURE DIRECTIONS

Recent expansion of the DOPPS to new countries, led by Dr Ronald Pisoni, will allow study of greater variation of practice, such as twice-weekly hemodialysis, which is more common in China.[31] Recognizing that practice patterns and outcomes (such as peritonitis and total time on peritoneal dialysis) also differ markedly for peritoneal dialysis facilities, Arbor Research Collaborative for Health recently initiated the PDOPPS (Peritoneal DOPPS) in Australia, Canada, Japan, the United Kingdom, and the United States.[31] Similarly, to evaluate practices in nondialysis advanced chronic kidney disease, we launched the international Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps), with data collection in Brazil, France, Germany, and the United States.[32,33] Under the leadership of Dr Bruce Robinson since 2009, this expanded family of international outcomes and practice patterns studies has been developed, and we anticipate that in conjunction with the USRDS, the opportunities to apply practice-based research will continue to expand. To successfully use these observational data to improve patient care, the methods reviewed above are critical.

SUMMARY AND CONCLUSIONS

During the past 4 decades, I have witnessed remarkable advances in analytical approaches to observational data. Despite the value inherent in these advances, they should not distract from the need for randomized controlled clinical trials, which remain all too scarce. When analyzing associations between specific treatments and outcomes, observational studies often are biased through confounding by indication (treatment-by-indication bias). Although statistical adjustment for demographic data and comorbid conditions may reduce this bias, treatment decisions often are based on severity indicators or other unmeasured factors, leaving residual bias due to confounding. The DOPPS has shown marked differences in practice indicators among dialysis facilities. Three recent examples from the DOPPS provided here demonstrate the value of practice-based analyses that use the reasonable assumption that patients are exposed to different practices in a fashion that resembles random assignment (quasi-random). These practice-based analyses that use dialysis facility as the instrument can provide important new or confirmatory insights, as shown in the examples given. These examples from DOPPS hopefully will stimulate further advances toward the critical goal of identifying beneficial treatment options to improve patient care and outcomes.

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