Improving Outcomes in Patients Receiving Dialysis: The Peer Kidney Care Initiative

James B. Wetmore,*† David T. Gilbertson,* Jiannong Liu,* and Allan J. Collins*‡

Abstract
The past decade has witnessed a marked reduction in mortality rates among patients receiving maintenance dialysis. However, the reasons for this welcome development are uncertain, and greater understanding is needed to translate advances in care into additional survival gains. To fill important knowledge gaps and to enable dialysis provider organizations to learn from one another, with the aim of advancing patient care, the Peer Kidney Care Initiative (Peer) was created in 2014 by the chief medical officers of 14 United States dialysis provider organizations and the Chronic Disease Research Group. Areas of particular clinical importance were targeted to help shape the public health agenda in CKD and ESRD. Peer focuses on the effect of geographic variation on outcomes, the implications of seasonality for morbidity and mortality, the clinical significance of understudied disorders affecting dialysis patients, and the debate about how best to monitor and evaluate progress in care. In the realm of geovariation, Peer has provided key observations on regional variation in the rates of ESRD incidence, hospitalization, and pre-ESRD care. Regarding seasonality, Peer has reported on variation in both infection-related and non-infection-related hospitalizations, suggesting that ambient environmental conditions may affect a range of health outcomes in dialysis patients. Specific medical conditions that Peer highlights include Clostridium difficile infection, which has become strikingly more common in patients in the year after dialysis initiation, and chronic obstructive pulmonary disease, the treatments for which have the potential to contribute to sudden cardiac death. Finally, Peer challenges the nephrology community to consider alternatives to standardized mortality ratios in assessing progress in care, positing that close scrutiny of trends over time may be the most effective way to drive improvements in patient care.


Introduction

The Surgeon General’s first Healthy People (HP) report in 1979 (1) was a landmark event formalizing the concept that improvement of the health of the United States population should be a societal priority. The HP endeavor establishes key decennial public health goals for the nation (2) and has been joined by similar efforts in other developed countries (3). In more affluent countries, public health efforts are focused on major noncommunicable diseases (NCDs), such as cardiovascular disease (CVD) and diabetes. Such efforts appear to be yielding results because the developed world has recently witnessed dramatic, and in some ways underappreciated, decreases in deaths attributed to NCDs. For example, between about 2000 and 2012, overall rates of death due to CVD declined approximately 35 percent in the United Kingdom, France, Canada, and Australia (4); in the United States, rates of death due to CVD have decreased nearly 30 percent. Indeed, declines in CVD deaths have been so prodigious that cancer is now the leading age-adjusted cause of death in many developed countries.

Because CVD and diabetes are also major causes of ESRD, it is fitting that efforts to reduce deaths among patients receiving maintenance dialysis have also become a public health priority. Although kidney disease–specific goals were first elucidated in HP 2010, the HP 2020 goals explicitly list a series of CKD-related public health targets (5), crystallizing this effort. The World Health Organization has also targeted kidney disease for scrutiny; item 19 of the United Nations Political Declaration on NCDs (6) says that “renal, oral and eye diseases pose a major health burden for many countries and that these diseases share common risk factors and can benefit from common responses to non-communicable diseases.” Fortunately, during the past decade, the death rate in patients undergoing maintenance dialysis has fallen substantially from 230 per 1000 patient-years in 2001 to 169 in 2013, resulting in a roughly 30 percent increase in mean survival (7). Nevertheless, challenges remain for the kidney disease community. First, because the reasons for this phenomenon are poorly understood, closing this critical knowledge gap is likely to inform future efforts to increase longevity. Second, determining whether these improvements have been shared uniformly or are concentrated in certain areas is important because societal efforts should aim to assure that all dialysis patients benefit from public health advances. Finally, debating the most appropriate and informative ways to track progress in reducing morbidity and mortality is incumbent on the kidney disease community.

To help inform the discussion of these and other issues, the Peer Kidney Care Initiative (Peer) was formed.
Complementing public health efforts, such as the US Renal Data System (USRDS) (8) and the Dialysis Outcomes and Practice Patterns Study (9), Peer was created in 2014 by the chief medical officers (CMOs) of 14 United States dialysis provider organizations to render novel insights, fill important knowledge gaps, and allow provider organizations to learn from one another in order to advance patient care. Certain areas of particular clinical importance were targeted in an attempt to help shape the public health agenda in CKD and ESRD. In this report, we first describe the genesis of the Peer initiative, then demonstrate novel findings from Peer, focusing on the importance of geographic variation on outcomes, the implications of seasonality on hospitalization, and the clinical importance of traditionally under-appreciated disorders affecting the dialysis population. Finally, we discuss the strengths and weaknesses of different paradigms that can be used to monitor progress in the care of dialysis patients.

Peer: A New Public Health Initiative for Dialysis Patients

Peer was formed in 2014 when investigators from the Chronic Disease Research Group (CDRG; Minneapolis, Minnesota) approached the CMOs of the organizations providing maintenance dialysis in freestanding units across the United States about avenues of collaboration. In contrast to other public health initiatives focused on the dialysis population, Peer was created as a collaborative venture to study cause-specific issues that could affect patient outcomes and that dialysis providers may be able to address. Peer was specifically interested in studying geographic variation in care, the effect of seasonality on outcomes, and how certain underappreciated disease processes and comorbid conditions affect dialysis patient outcomes. CDRG proposed the collaboration, to which the CMOs of 14 dialysis providers agreed; each provider funds the endeavor in approximate proportion to the size of the population it serves. The 14 geographically diverse providers represent approximately 90% of prevalent dialysis patients in the United States.

CDRG, which held the contract for the USRDS from 1999 to 2014 and currently holds the contract for the Scientific Registry of Transplant Recipients (2010–present), was designated as the analytic center and the investigative arm of Peer. A master services agreement governs the relationship between each provider and the Minneapolis Medical Research Foundation, which has regulatory and legal oversight over CDRG. The collaborative interface between CDRG investigators and the CMOs occurs via a Peer Executive Committee, which meets regularly and includes four of the CMOs. This arrangement provides oversight of the endeavor and establishes the content of deliverables specified by the contract. The contract calls for an annual report and several peer-reviewed manuscripts annually, as well as for analysis of provider-specific data. CDRG investigators proposed the overarching focus areas before Peer was formed, and the CMOs agreed; subsequently, as defined by the contract and master services agreement that govern Peer, both CDRG investigators and the CMOs can propose specific ideas for study. CDRG considers input from the providers and works with the CMOs on the data report, research projects, and policy initiatives but has final control over all content and retains ultimate authority to design studies and to publish.

Although data were initially procured via the USRDS, Peer now has a data use agreement (DUA) in place with the Centers for Medicare & Medicaid Services (CMS) to use CMS data. Data are updated annually and are for use only by the Peer investigators and the providers under the terms specified by the DUA; CDRG and the Peer group are precluded from secondary release of the data under the terms of the DUA. Thus, the data sources are, at present, a reformating of existing datasets, with the anticipation that provider-specific data may be added at a future date.

Geographic Variation in Kidney Disease Care and Outcomes

Exploring geographic variation in kidney disease care is a major focus of Peer. Variation in care is an issue across all fields of medicine and, broadly speaking, can be partitioned into variation in the distribution of underlying disease processes, variation in care delivery, variation in cost, and variation in outcomes (10). All such variation may be related to historical, social, cultural, economic, and demographic factors and to “natural” factors, such as climate or geologic features. Ultimately, the goal of studying geographic variation is to determine how to achieve the best medical outcomes and then to ascertain which of the preceding factors, if any, may be modifiable toward that end. Study of geographic variation can then help focus the attention of public entities, such as state health departments, ESRD networks, regulatory bodies, and payers (e.g., CMS) to change practice in the hopes of reducing variation in care.

In a geography-based approach, the size of the geographic unit of analysis must be carefully considered. Small units, such as areas defined by zip (postal) codes or counties, might be subject to fluctuations based on small numbers of events, compromising the value of inferences. Although the optimal size of the geographic unit selected for analysis depends on the specific question being asked, US state might be the smallest area that could be routinely used with confidence. An additional benefit is that state boundaries correspond to the boundaries of many regulatory bodies, such as state departments of health. Census regions are also an obvious choice; these traditional groupings were initially selected because they share historical, economic, cultural, and transportation features.

With these considerations in mind, Peer has presented detailed information on geographic variation in kidney disease care, typically at the level of the US Census regions (11). Although longevity while undergoing dialysis has improved substantially over the past decade, major differences in ESRD incidence, hospitalization, and care remain. For example, although the ESRD incidence rate has stabilized in the United States as a whole (8), rates vary considerably by US Census region (12) and remain troublingly high in many areas. Figure 1 shows the standard United States health service areas, with the data smoothed using a Bayesian spatial hierarchical model, as has been done previously (13). The highest absolute regional incidence rates are nearly double the lowest, and although the data are unadjusted, it is unlikely that case mix could account for all of the variation present. Regarding hospitalization rates
in incident dialysis patients, some regions experienced steady improvement between about 2003 and 2009, whereas others, most notably the East North Central region, saw little improvement during this period; fortunately, hospitalization rates subsequently improved from 2010 to 2012, although geographic differences remain, as shown in Figure 2 (12). Even closer examination, as provided by the Peer data, shows that substantial geographic variation is present for several key reasons for hospitalization, such as CVD, infectious disorders, chronic obstructive pulmonary disease (COPD), and gastrointestinal (GI) bleeding.

A particularly striking finding in pre-ESRD care is the variation in the percentages of patients who are under nephrologist care before starting dialysis. As of 2011, nearly 80% of patients in New England had seen a nephrologist before initiating dialysis, compared with only 62% in the West South Central region (12). Even if case-mix adjustment were to attenuate some of these differences, increased emphasis should be placed on facilitating nephrologist care before dialysis initiation in all regions, especially in regions that may be underperforming.

Study of geovariation is essential to patients, health care providers, payers, and other stakeholders to identify which practices lead to the best outcomes (14). Ample opportunity exists for Peer and other research endeavors to identify underperforming regions and to leverage the findings of well performing regions to improve the care of all patients receiving maintenance dialysis.

**Seasonality**

With few exceptions (15), potential effects of ambient environmental conditions have been underexplored in the dialysis literature. The importance of seasonality is, however, given substantial treatment in Peer, as shown in Figure 3. Hospitalizations were ascertained from Medicare Part A claims for inpatient care and were categorized by the principal discharge diagnosis, as was done for the 2014 Peer Report (12). The report demonstrates substantial seasonal variation in hospital admissions in prevalent dialysis patients (patients currently undergoing dialysis at a freestanding facility who had been doing so for at least 3 continuous months previously). Some of these findings are intuitive: Hospitalizations for certain infections, such as pneumonia and influenza, primarily peak in colder months, a phenomenon generally consistent with occurrences in the general population (16,17).

However, Figure 3 demonstrates that admissions for cardiovascular causes also increase during the winter. This suggests that other, less obvious factors may influence the relationship between seasonality and outcomes. One area of intense recent interest in the public health community is influenza-like illnesses (ILIs). Noninfluenza viruses that can infect the upper and lower respiratory tracts, such as rhinovirus, adenovirus, respiratory syncytial virus, parainfluenza virus, and human metapneumovirus, may contribute to morbidity and lead to hospitalizations for infection. Data suggest that substantially <50%, perhaps as low as 25%–30%, of ILIs may be due to true influenza
ILIIs may, in part, explain a less intuitive link between seasonality and hospitalization, and perhaps even with the patterns of death in incident patients. For example, although exacerbations of COPD occur more frequently in winter (20) (as expected), other conditions that might appear to have more tenuous associations with season also manifest more dramatically in winter months. Admissions for overall cardiovascular diseases, acute coronary syndrome, and heart failure/cardiomyopathy also appear to spike in colder months. This suggests a possible link in dialysis patients

Figure 2. | First-year hospital admission rates among incident dialysis patients, overall and by US Census division.

Figure 3. | Seasonal variation in hospital admissions in prevalent United States dialysis patients for a variety of infectious and noninfectious causes. Vertical lines represent the transition between calendar years, thereby demarcating the winter season. C. difficile, Clostridium difficile; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; PY, patient-year.
between cardiovascular events—and perhaps other ostensibly noninfectious events—and seasonally related environmental conditions. One hypothesis proposed by the Peer investigators is that subclinical and incompletely diagnosed infections such as ILI, and the systemic inflammation they promote, might “provoke” or “unmask” cardiovascular events in poorly defined ways, but this is far from certain and requires future study.

How might this information be used to improve patient care? Perhaps increased efforts to clean surfaces and touchpoints within the dialysis unit during the winter months are warranted; this hypothesis should be tested. Second, clinicians might consider altering their index of suspicion for certain events, including cardiovascular events, during less temperate months. Although they may be difficult, efforts to improve the detection of impending cardiovascular events during periods of increased inflammatory potential, such as colder months, should be discussed by the kidney disease community.

**Novel Disease Findings**

Peer also seeks to explore the clinical and public health implications of morbidities that have traditionally been underemphasized. Close examination of congestive heart failure (CHF) and volume overload, intestinal infection with *Clostridium difficile*, chronic lung disease, and GI bleeding provides new insights.

CHF is one of the most common reasons for admission in both the general (21,22) and the dialysis (12) populations; because of high readmission rates, CHF is a major target of CMS quality improvement efforts (23). As a clinical entity, CHF in dialysis patients is a wholly different phenomenon than in the general population. Many admissions for “heart failure” in dialysis patients might more properly be termed “circulatory overload,” reflecting inadequate ultrafiltration rather than true compromised left ventricular systolic function. Inability to achieve a patient’s true weight, resulting in an ultrafiltration-requiring admission, might therefore more properly be coded as “fluid overload,” a diagnosis with its own International Classification of Diseases, Ninth Revision, Clinical Modification code. However, close inspection of the data demonstrates the dangers present in attempts to draw informed conclusions.

Peer showed that admissions for heart failure decreased nearly 40% in prevalent patients between 2004 and 2013, from roughly 16.3 (95% confidence interval [95% CI], 16.1 to 16.5) admissions per 100 patient-years to 9.8 (95% CI, 9.6 to 9.9), a welcome development (12). However, admissions for fluid overload during this time increased nearly 2.5-fold, from roughly 2.1 (95% CI, 2.0 to 2.2) admissions per 100 patient-years to 5.2 (95% CI, 5.1 to 5.3), suggesting that the decline in CHF admission rates is not as great as it might first appear. Whether this change in coding pattern represents a genuine effort to apply greater specificity to diagnoses or reflects attempts by facilities to avoid penalties for 30-day readmissions is uncertain.

Infection with *C. difficile*, a major focus for hospitalized patients in the general population (24–26), was also specifically examined in the Peer report (12). Admissions for *C. difficile* infections among dialysis patients within the first 12 months of initiation increased nearly 44% between 2004 and 2012, from approximately 1.6 (95% CI, 1.5 to 1.7) to 2.3 (95% CI, 2.1 to 2.4) admissions per 100 patient-years. This is important because *C. difficile* infection can contribute to malnourishment at a time (initiation) when patients are especially vulnerable to illness and death. Likewise, *C. difficile* admissions in prevalent patients have also increased. This pattern shows evidence of seasonality, perhaps as a “trailing phenomenon” relative to other infections that require treatment with broad-spectrum antibiotics. Given increased scrutiny afforded readmissions by payers, *C. difficile* should be a target for quality improvement efforts, given the high recurrence and readmission rates (27,28).

COPD was also examined in detail in Peer (12). Whereas rates of admission for both incident and prevalent patients have been fairly stable since approximately 2008, there is a substantial (greater than two-fold) unadjusted geographic variation across regions, the reasons for which should be investigated. Not unexpectedly, this disorder also showed substantial seasonality, whether coded as the primary or leading secondary diagnosis, with admissions rising sharply during the coldest months. COPD is an important area for study because it may be associated with preventable deaths. In addition to the seasonality implications described above, treatments for COPD can be hypothesized as potentially exposing patients to risk: β-adrenergic agonists can cause cardiac excitability, and commonly used antibiotics, such as trimethoprim-sulfamethoxazole, quinolones, and macrolides are associated with QT prolongation and sudden cardiac death. Therefore, decreasing occurrences of COPD exacerbations in dialysis patients might reduce the death rate in several ways; this should be further studied.

GI bleeding is an increasingly common cause of hospital admissions in dialysis patients (29–31). On the basis of billing claims data, admissions attributed to GI bleeding have gradually increased since at least 2004 and began a more pronounced rise after 2010. Indeed, the rate among prevalent patients increased by approximately 21% between 2004 and 2013, from about 1.9 (95% CI, 1.9 to 2.0) to 2.3 (95% CI, 2.3 to 2.4) admissions per 100 patient-years. Notably, 2011 corresponds to the introduction of the revised Prospective Payment System (PPS), a bundled payment system designed to control costs that included services previously reimbursed separately, such as erythropoiesis-stimulating agents, intravenous iron, activated vitamin D analogues, and certain laboratory tests. How admissions for GI bleeding and the PPS introduction might be linked is uncertain, but it is possible that the lower mean hemoglobin levels in evidence since the introduction of the PPS (32–36) may have “revealed” subclinical GI bleeding, the main signal for which may be decreased hemoglobin levels. Another possibility is that lower hemoglobin levels prompt a clinical workup for presumed GI bleeding, which may be diagnosed “empirically” in the absence of endoscopically proven findings. Whether GI bleeding is truly increasing and if so whether this is associated with lower mean hemoglobin levels is uncertain but should be studied further. A final possibility that could be explored is whether and how use of agents such as aspirin, antiplatelet agents, warfarin, and the novel thrombin inhibitors may be related to the increased frequency of GI bleeding, given that the underlying pathophysiologic processes that cause GI bleeding (such as gastric ulcers,
Monitoring Progress: What Is the Most Appropriate Framework?

Substantial progress has been made regarding the outcomes of dialysis patients, with a decrease in the incidence rate (after adjustment for age, sex, race, and cause of ESRD) observed circa 2003. The HP 2020 goal CKD-8 (5), which calls for “reduc[ing] the number of new cases of ESRD per million population,” has been met, with new cases falling from 385 per million population in 2003 to 344 in 2012, a decline of >6%. Even more striking are the findings in certain disadvantaged groups. For example, for blacks, the decline has been 15%; for Native Americans, 24%; for Hispanics, 17%; and for women, 12% (8). The declines in incidence rates in these at-risk groups, which are greater than the overall decline, are the opposite of what might be expected.

Likewise, improvements have occurred in the outcomes of prevalent dialysis patients. The annualized mortality rate has declined by about 30% relative to 1999. The death rate, which was 237 per 1000 patient-years, substantially fell from 387 per 1000 patient-years in 2003 to 312 per 1000 patient-years in 2012, exceeding the target of 328.7 (HP goal CKD-14.2) (5), while the death rate from CVD fell from 387 per 1000 patient-years in 2003 to 312 per 1000 patient-years over the corresponding interval (8), again exceeding the HP goal (CKD-14.3) (5) of 80.9.

Given these fairly dramatic improvements across the dialysis landscape, it is incumbent on the kidney care community to frankly debate how progress is best measured. One metric commonly used in attempts to measure quality of care is the standardized morality ratio (SMR), which relies on direct or indirect standardization to adjust for case-mix differences (37,38). SMRs are commonly used to assess whether there are differences in outcomes between, for example, hospitals that perform coronary artery bypass surgery (39) or in all-cause mortality between hospitals (40). Indeed, SMRs have been used by the USRDS to compare standardized mortality and hospitalization ratios among the large dialysis providers (41). An SMR-based approach can be useful in determining whether large variations in care exist (42) across regions, such as those defined by the US Census Bureau. SMR-based comparisons can highlight potential disparities within a country to highlight underperforming regions. For example, Peer reported that the East North Central region of the United States (encompassing Illinois, Indiana, Michigan, Ohio, and Wisconsin) has seen little progress in mortality compared with other regions over the past decade, a situation that only now appears to be improving. Contrasts between regions with high and low SMRs present an opportunity to discern whether differences in practice patterns across regions can be leveraged to improve care for all. In this way, SMRs can assist efforts to improve consistency of care by narrowing variation in outcomes.

However, overreliance on SMRs can be uninformative and perhaps even misleading. For example, recent criticisms have been expressed regarding the appropriateness of using SMRs for measuring care quality. Hogan et al. argue that when the units being assessed are relatively small, such as hospitals, there is poor correlation between hospital SMRs and avoidable deaths, as judged by experts conducting chart review (40), and in so doing challenge established paradigms about the utility of SMRs. They argue that SMRs are best used under conditions in which case-fatality rates are high and causes of death can be relatively easily determined. This suggests that use of SMRs may be suboptimal when small units of measure, such as individual outpatient dialysis facilities, are being compared. Additionally, and perhaps more profoundly for public health, overall societal progress cannot be adequately measured by SMRs because it is by nature cross-sectional and by definition centered (e.g., at 1.0 or 100) (43). SMRs are not especially informative when care is likely to be improving across a population as a whole, as in the case of United States dialysis patients since the turn of the millennium.

An alternative approach, used by the World Health Organization (4), measures progress over time within a geographic region, with each region serving as its own control over time. Although not unique in reporting trends over time (13), Peer heavily emphasizes the importance of time trends, as can be seen throughout the 2014 report (14). Use of time trends does not invoke adjustments, essential when calculating SMRs, use of which is often incomplete or unsatisfying. While straightforward adjustments for factors such as age, sex, race, and cause of ESRD are common, these provide little insight to guide opportunities for improvement because such factors are unmodifiable.

Another benefit of trending improvements over time is that geographic factors that likely affect care, such as socioeconomic factors, environmental factors (e.g., pollution), local factors (e.g., barriers to care), and idiosyncrasies of care delivery systems, are poorly captured in SMRs. In contrast, these are inherently accounted for, at least over the short term, when a facility is compared with itself over time because these factors are unlikely to change rapidly within a geographic unit. In this way, “unfair” comparisons, such as between an affluent population base in the northeastern United States and a more socioeconomically depressed area in the Deep South of the United States, and unrealistic expectations that might accompany them, are avoided.

Conclusions

Peer was formed by 14 United States dialysis providers (who collectively provide care for roughly 90% of all patients undergoing dialysis in the United States) and CDRG in an attempt to present key issues facing the dialysis community and to foster quality-improvement efforts from which all dialysis patients can benefit. To this end, Peer has reported on geographic variation in care between regions, presented novel data on the potential role of seasonality on outcomes, and highlighted the clinical implications of traditionally underappreciated conditions affecting patients receiving maintenance dialysis. Future studies will investigate these and many other areas. Additionally, given the limitations of SMRs in judging
long-term trends in the progress of care, the Peer effort highlights the importance of tracking and understanding trends over time, a process that may provide insights to foster improvements in the care of patients receiving dialysis.

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Disclosures

None.

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