DOPPS and K/DOQI™
Implications for Vascular Access, Anemia, Bone and Mineral Metabolism, and Nutrition

Nearly one million people worldwide are currently receiving chronic hemodialysis treatment. This number will increase dramatically over the coming decades because of aging populations and rising rates of diabetes and other diseases that may lead to end-stage renal disease (USRDS 2003 Annual Report). Since 1996, researchers involved in the Dialysis Outcomes and Practice Patterns Study (DOPPS) have looked at ways in which hemodialysis practices affect patient outcomes, such as living a longer and healthier life. In many cases, the findings of the DOPPS researchers are being used for the development of treatment guidelines for hemodialysis patients, including the National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (K/DOQI™). As more and more patients require hemodialysis, the work of the DOPPS researchers becomes even more important.

“There is a long-standing synergy between the science supporting the K/DOQI guidelines and the research findings of the DOPPS. Through the analysis of practice patterns we expect to uncover new treatment strategies that will benefit patients.” - Friedrich K. Port, M.D., M.S., president of URREA

Recently, the University Renal Research and Education Association (URREA), which coordinates the DOPPS, and the National Kidney Foundation (NKF) created a formal partnership with the goal of improving outcomes for kidney disease patients. This partnership will promote even more effective use of DOPPS data in the creation of new K/DOQI guidelines and the refinement of existing ones. In addition, a new international effort, Kidney Disease: Improving Global Outcomes (KDIGO), will make extensive use of DOPPS study results in the development and implementation of worldwide practice guidelines.

The DOPPS researchers continue to study, analyze, and publish information about how dialysis practices at over 300 dialysis centers in 12 countries affect hemodialysis outcomes. In this issue of The DOPPS Report, we summarize findings on vascular access practices, anemia, bone mineral metabolism, and nutrition, and the achievement of K/DOQI targets in these clinical areas internationally.

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The DOPPS is a worldwide hemodialysis study coordinated by the University Renal Research and Education Association (URREA). The DOPPS is supported by scientific grants from Amgen, Inc. and Kirin Brewery, Ltd. without restrictions on publications. Web site: www.dopps.org E-Mail: dopps@urrea.org
The use of an AV fistula has also been shown to reduce the risk of death among hemodialysis patients, compared to patients with a catheter [3]. In addition to a higher risk of death, patients with grafts have a three times higher risk of requiring procedures to maintain, repair, or replace the access compared with patients using a fistula [4].

In the US, 46% of patients started HD with a catheter and without a permanent vascular access created prior to starting HD [1]. This failure to place a permanent access during the pre-end stage renal disease (ESRD) period occurred despite the fact that 55% of these patients saw a nephrologist more than 30 days prior to ESRD. In Europe, approximately 25% of incident patients started HD with a temporary access and without a permanent access placed prior to ESRD. For this group of patients, 56% saw a nephrologist more than 30 days prior to ESRD.

The National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (K/DOQI) has developed guidelines that call for the use of fistulae for at least half of all new HD patients, to achieve the goals of fistula use for more than 4 of 10 existing patients and catheter use for fewer than 1 in 10 [5]. The results from the DOPPS point to numerous opportunities for improving vascular access care for hemodialysis patients.

### Vascular Access

The DOPPS has found large differences between countries in the use of the three main routes for vascular access in hemodialysis (HD) patients: the arteriovenous (AV) fistula, the AV graft, and the central venous catheter. These differences are important because the choice of vascular access can dramatically affect the risk of patient hospitalization and can also affect patient survival. DOPPS data from 1996-2001 has shown that fewer than 1 in 4 patients in the US use a fistula for vascular access, compared with 4 of 5 patients in Europe [1]. The most common access method in the US is the graft, used by nearly 6 of every 10 patients.

Findings from the DOPPS have shown that only 15% of new hemodialysis patients in the US start dialysis using a fistula, while 61% start with a catheter (Figure 1) [2]. Even when a temporary catheter is replaced with a fistula, the initial placement of a catheter shortens the time to access failure, compared to using a fistula as the initial access [1]. Furthermore, access survival for an AV fistula was nearly twice that of an AV graft as the initial access. This means the best choice for initial, as well as permanent, vascular access is the AV fistula.

![Figure 1: Significant differences in vascular accesses used for incident hemodialysis patients in Europe, Japan, and the US. Catheters are either cuffed or uncuffed. Analysis included incident patients who entered DOPPS within 5 days of their first dialysis treatment; n=3674. DOPPS data from 1996-2001 [2].](image-url)

### Anemia

Most patients with chronic kidney disease develop anemia because their kidneys no longer produce enough erythropoietin, a hormone that promotes the growth of red blood cells. Poor anemia control has been shown to be associated with development of cardiovascular disease, reduction in certain aspects of patient quality of life, and greater hospitalization and mortality risk [5]. Therefore, anemia management practices continue to be a high priority for the renal community. The DOPPS has found that the percentage of hemodialysis patients with a hemoglobin (Hgb) level below the K/DOQI guideline of 11 - 12 g/dL varies substantially across countries, ranging from 23% in Sweden to 77% in Japan (the percentage is 27% in the US) (Figure 2) [6].
Anemia is associated with higher risks of both hospitalization and death [6]. The DOPPS has shown that independent of comorbid conditions and other risk factors, for every 1 g/dL increase in Hgb level, the relative risk of death is lowered by 5% and the relative risk of hospitalization is lowered by 6% (Figure 3) [6]. Untreated anemia has also been shown to affect the heart, brain, and muscle function, as well as sexual function and overall quality of life [5].

As with vascular access, adequate care prior to starting hemodialysis is important for improving patient outcomes. The DOPPS has found that the average Hgb level at the time hemodialysis is started is less than 11 g/dL in all of the countries in the DOPPS study [6]. Although treatment with recombinant human erythropoietin can raise Hgb levels, the percentage of patients treated with erythropoietin injections before starting hemodialysis varies from 27% in the US to 65% in Sweden [6]. Treating anemic patients before the start of hemodialysis to reduce the severity of anemia may help improve patient outcomes and delay progression to ESRD [7].

**Bone and Mineral Metabolism**

Recent DOPPS research has shown that management of bone and mineral metabolism remains one of the most challenging issues in the care of hemodialysis patients. Bone mineral changes begin early in the course of kidney disease, long before hemodialysis is needed, and cause abnormal growth of the parathyroid glands, which in turn results in abnormally high blood levels of parathyroid hormone (PTH). High PTH levels, combined with reduced kidney function, lead to a buildup of serum phosphorus and movement of calcium and phosphorus from the bones into the bloodstream.

Almost every system in the body is affected by these changes. Bone disorders, including osteomalacia (lack of proper mineral deposition) and adynamic bone disease (defects in bone matrix), increase the risk of fractures and skeletal problems. Increased serum phosphorus combines with calcium and is deposited in soft tissues, leading to cardiovascular, eye, joint, and skin disorders [8].

Research from the DOPPS has shown that altered bone mineral metabolism leads to increased risk of death from a wide range of causes. The most important consequence by far is cardiovascular disease; cardiovascular mortality risk increases by 14% for every 1 mg/dL increase in serum calcium, 9% for every 1 mg/dL increase in serum phosphorus, 5% for every 5 mg²/dL² increase in calcium-phosphorus product, and 2% for every 100 pg/mL increase in PTH. Patients with a phosphorus concentration between 6.5 and 7.0 mg/dL were at a 28% higher risk of mortality (versus 4.5-5.0 mg/dL), and patients with a phosphorus concentration exceeding 7 mg/dL were at a 35% higher relative risk of mortality (versus 4.5-5.0 mg/dL) (Figure 4) [9].

Controlling mineral levels in hemodialysis patients involves maintaining a strict low-phosphorus diet, as well as treatment with phosphate binders, vitamin D analogs, and/or a calcimimetic medication to lower serum PTH. It also

### Table 1: Hemoglobin (Hgb) concentrations and achievement of K/DOQI targets for prevalent patients

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>Mean Hgb (g/dL)</th>
<th>Hgb&lt;11 g/dl (% of pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia/New Zealand (ANZ)</td>
<td>423</td>
<td>11.5</td>
<td>36</td>
</tr>
<tr>
<td>Belgium (BE)</td>
<td>442</td>
<td>11.6</td>
<td>29</td>
</tr>
<tr>
<td>Canada (CA)</td>
<td>479</td>
<td>11.6</td>
<td>29</td>
</tr>
<tr>
<td>France (FR)</td>
<td>341</td>
<td>11.1</td>
<td>45</td>
</tr>
<tr>
<td>Germany (GE)</td>
<td>459</td>
<td>11.4</td>
<td>35</td>
</tr>
<tr>
<td>Italy (IT)</td>
<td>447</td>
<td>11.3</td>
<td>38</td>
</tr>
<tr>
<td>Japan (JA)</td>
<td>1210</td>
<td>10.1</td>
<td>77</td>
</tr>
<tr>
<td>Spain (SP)</td>
<td>513</td>
<td>11.7</td>
<td>31</td>
</tr>
<tr>
<td>Sweden (SW)</td>
<td>466</td>
<td>12.0</td>
<td>23</td>
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<tr>
<td>United Kingdom (UK)</td>
<td>436</td>
<td>11.2</td>
<td>40</td>
</tr>
<tr>
<td>United States (US)</td>
<td>1690</td>
<td>11.7</td>
<td>27</td>
</tr>
</tbody>
</table>

Figure 2: Hemoglobin (Hgb) concentrations and achievement of K/DOQI targets for prevalent patients. Prevalent patients = patients on dialysis >180 days. DOPPS data from 2002-2003 [6].

Figure 3: Relative risks of death and hospitalization associated with various hemoglobin levels. DOPPS data from 1996-2001 [6].
requires that caregivers pay simultaneous attention to serum levels of PTH, calcium, phosphorus, and calcium-phosphorus product.

Bringing patients into compliance with the K/DOQI guidelines for all four mineral metabolism measures (calcium, phosphorus, calcium-phosphorus product, and PTH) can be extremely challenging. A study of DOPPS patients from 1996 to 2001 showed that although 25% to 44% of patients maintained the proper blood level of calcium, phosphorus, or calcium-phosphorus product over a 12-month period, only 11% stayed within the range specified by the PTH guideline. Only 1% of patients were able to remain within the ranges specified by all four guidelines (Figure 5) [10].

**Nutrition**

In 2000, the K/DOQI released recommendations for nutritional management in hemodialysis patients as part of the effort to improve multiple domains of care to achieve the primary goal of better patient longevity. One of the most important K/DOQI recommendations was to establish an outcome goal for serum albumin of 4.0 g/dL. Patients who fall below the albumin outcome goal should be evaluated more extensively for protein-energy malnutrition.

The K/DOQI practice guideline acknowledges that no single measure of nutritional status provides a comprehensive assessment of the adequacy of patient nutrition. Therefore, the guideline calls for patients to be regularly assessed using a range of measures, including serum albumin, body weight, subjective global assessment (a rapid four-item assessment tool), dietary interviews and diaries, and other tests. In addition, the guideline suggests that certain laboratory measures (such as creatinine, creatinine index, cholesterol, and blood urea nitrogen), if out of range, may suggest the need for a more comprehensive assessment of nutritional status.

The DOPPS has shown that adequate nutrition is a critical consideration in the management of HD patients. A large fraction of hemodialysis patients do not meet the current K/DOQI practice guideline to maintain a serum albumin level of at least 4.0 g/dL [11]. The DOPPS has estimated that a substantial gain in HD patient survival could be achieved if practice patterns could be improved to achieve K/DOQI target albumin [11].

The DOPPS has shown a strong association between poor nutritional status and increased mortality [12]. Relative to patients with serum albumin levels meeting the K/DOQI target (4.0 g/dL), the mortality risk was 22% higher in patients with albumin levels of 3.7 to 4.0 g/dL, 42% higher in patients with albumin levels of 3.3 to 3.7 g/dL, and 112% higher in patients with albumin levels less than 3.3 g/dL.

Despite the recognition that nutrition is an important factor in HD patient mortality, recent DOPPS results indicate that most patients (57% - 86%) remain below the K/DOQI target of 4.0 g/dL (Figure 6).
Deterioration of nutritional status while on hemodialysis is also an important contributor to increased mortality. In a DOPPS study of multiple nutrition measures, patients with a declining nutritional status (as indicated by decreased albumin, body mass index, and creatinine) over six months had significantly worse outcomes [12].

Summary

The DOPPS results show that significant challenges remain in optimizing vascular access, in managing anemia and nutrition, and in controlling bone-related minerals. However, by linking specific practices with specific outcomes, like hospitalization and death, DOPPS research has helped highlight ways to improve the care of hemodialysis patients.

The international focus of the DOPPS allows researchers to study practice patterns in a wide range of settings and health care systems, and across multiple ethnic and cultural boundaries. Continued research and efforts to translate DOPPS results into meaningful practice guidelines will help achieve the goal of improved outcomes and quality of life for the growing population of hemodialysis patients.

DOPPS Facilities Receive Report on How They Compare with K/DOQI Guidelines

At the end of each study year, the medical directors at all participating DOPPS facilities receive a confidential Facility Feedback Report based on the data collected during the study. The Facility Feedback Report is not a performance rating or scorecard. It is intended to serve as a comparison indicating how statistics for the DOPPS facility compare with the average of all DOPPS dialysis units in its country.

This year’s report focused on two main topics. Measurements of mortality risk was based on patients listed on the Cumulative Hemodialysis Census (CHC) and on a prevalent cross section of hemodialysis patients for whom a Medical Questionnaire (MQ) was completed. Measurements of K/DOQI guideline achievement included dialysis adequacy, anemia, bone mineral metabolism, nutrition, and vascular access.

References

The DOPPS data have matured substantially, allowing a continued strong emphasis on manuscripts and publications. Also, DOPPS research is well established within the international nephrology community, and interest in DOPPS results continues to grow with increasing visibility through worldwide presentations and symposia.

At this year’s annual congress of the European Dialysis and Transplant Association (EDTA), four DOPPS abstracts were presented as posters. In addition, a 90-minute DOPPS symposium focused on practice patterns associated with outcomes. The presentation was well received, and DOPPS investigators have been invited to present a two-hour symposium at the 2005 congress of the EDTA.

Eleven DOPPS abstracts have been accepted to the American Society of Nephrology conference this year, one of them as a “free communication” presentation. The society has also invited DOPPS investigators to present a two-hour symposium titled “Clinical Outcomes and Vascular Access, Mineral Metabolism and Anemia Practices in the DOPPS.” This symposium will highlight the synergy between DOPPS and the NKF-K/DOQI guidelines.

Table 1: DOPPS Research Presentations at Major Renal Meetings in 2004

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Date</th>
<th>Meeting, Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Results from the International Dialysis Outcomes and Practice Patterns Study (DOPPS)</td>
<td>February</td>
<td>Nephro-Asia Congress, Singapore</td>
</tr>
<tr>
<td>DOPPS Results on Cardiac Outcomes</td>
<td>February</td>
<td>Annual Dialysis Conference, San Antonio, TX, USA</td>
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<tr>
<td>DOPPS and the Role of Antioxidants</td>
<td>April</td>
<td>National Kidney Foundation Clinical Meetings, Chicago, IL, USA</td>
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<tr>
<td>Symposium: Practice Patterns and Outcomes</td>
<td>May</td>
<td>EDTA, Lisbon, Portugal</td>
</tr>
<tr>
<td>Lessons Learned from the DOPPS</td>
<td>June</td>
<td>Annual Renal Society of Australasia Conference, Adelaide, South Australia</td>
</tr>
<tr>
<td>Update on the DOPPS</td>
<td>June</td>
<td>Japan Society of Dialysis and Transplantation, Tokyo, Japan</td>
</tr>
<tr>
<td>Uremic Patients with Cardiac Drugs: Results from the DOPPS</td>
<td>August</td>
<td>International Federation of Kidney Foundations, Adelaide, Australia</td>
</tr>
<tr>
<td>Modifiable Risk Factors: Results from the DOPPS</td>
<td>September</td>
<td>National Congress of Nephrology and Transplantation, Antalya, Turkey</td>
</tr>
<tr>
<td>Vascular Access: Results from the DOPPS</td>
<td>September</td>
<td>Italian Society of Nephrology, Venice, Italy</td>
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<tr>
<td>DOPPS Update</td>
<td>October</td>
<td>Spanish Society of Nephrology, Tenerife, Spain</td>
</tr>
<tr>
<td>Symposium: Modifiable Practice Patterns</td>
<td>October</td>
<td>American Society of Nephrology, St. Louis, MO, USA</td>
</tr>
<tr>
<td>DOPPS Results</td>
<td>November</td>
<td>Swedish Society of Nephrology, Göteborg, Sweden</td>
</tr>
<tr>
<td>Vascular Access Outcomes</td>
<td>December</td>
<td>French Society of Nephrology</td>
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</tbody>
</table>
An early result of the collaboration between the DOPPS and NKF-K/DOQI is a Supplement to the November 2004 issue of the *American Journal of Kidney Diseases* entitled “Evidence for Improving Patient Care and Outcomes: The Dialysis Outcomes and Practice Patterns Study (DOPPS) and Kidney Disease Outcomes Quality Initiative (K/DOQI).” The Supplement includes 10 peer-reviewed articles that build on the natural overlap of DOPPS findings and the evidence-based guidelines of K/DOQI.

Several introductory articles describe the parallel and mutually supportive development of the DOPPS and the K/DOQI Guidelines, the usefulness of observational trials in confirming the evidence for both established and changing guidelines, and the methodology of the DOPPS — its data collection, its methods of analysis, and its extensive case-mix adjustments on the basis of comorbidities. Five subsequent articles review previous DOPPS findings in the context of K/DOQI Guidelines and other international sets of clinical practice guidelines. The topics covered in these articles are vascular access, anemia management, mineral metabolism, nutrition, and dialysis dose. Lastly, two articles review the numerous DOPPS findings in two areas not specifically addressed by K/DOQI Guidelines — health-related quality of life and medication use among patients receiving hemodialysis.

It is the hope of both organizations that collecting DOPPS findings in one place and reviewing them in light of K/DOQI guidelines will bring awareness of important practice patterns to a wider audience.

**Major Publications**

To date, DOPPS data have been published in 30 peer-reviewed manuscripts and eight invited publications, with an additional 16 manuscripts currently in press. The National Kidney Foundation (NKF) will feature DOPPS data in its forthcoming publication, *Chronic Kidney Disease Best Practice*. The organizations will seek to co-present results from their partnership at nephrology clinical meetings, including NKF Clinical Meetings, ASN Renal Week, ANNA, and the International Dialysis Conference. A listing of all published manuscripts and abstracts, as well as links to Pub Med and downloadable PowerPoint presentations of published DOPPS research, can be found on the DOPPS website at www.dopps.org. Below are the citations of the DOPPS manuscripts published so far in 2004.

The data collection for DOPPS II is coming to a close with a majority of sites having completed two years of data collection. The study will continue in 2005 as DOPPS III. The goals for this next phase of the study are to continue to monitor internationally representative samples of hemodialysis patients and to evaluate participating dialysis units’ “Processes of Care,” that is, strategies used by facilities to reach target guidelines and other positive outcomes. DOPPS III will introduce electronic data collection to minimize the data collection burden of the site staff and to improve data consistency and quality. The study will continue the same protocol for patient selection and consent. The same patient-level questionnaires will be used with some refinements and improvements.

The Unit Practices Survey and Medical Director Survey will be refined to better study “Processes of Care.” The DOPPS hopes to identify processes of care that impact dialysis practices, how they vary, and the factors that help facilities reach optimal practices or the factors that keep facilities from reaching them. DOPPS III will document the impact on outcomes of changes in dialysis practices and policies and investigate the “how-to” of improving performance.

The American Society of Nephrology (ASN) will present the 2004 Belding H. Scribner Award for outstanding contributions to care of patients with renal disorders to DOPPS investigators Drs. Philip J. Held, Friedrich K. Port, and Robert A. Wolfe. The ASN will present this award at the 2004 Renal Week Conference in St. Louis, Missouri, USA.

The Belding H. Scribner Award is presented annually to one or more individuals who have made outstanding contributions that have a direct impact on the care of patients with kidney disorders or have substantially changed the clinical practice of nephrology. Established in 1995, this award honors the physician who developed the arteriovenous shunt that first made long-term hemodialysis for chronic renal failure possible.

“I feel that this award recognizes the importance of the new field of evidence-based medicine and outcomes research,” said Dr. Port. “From my perspective, it is very appropriate that the three of us were honored jointly. Our clinically relevant work and new direction to successful outcomes research in kidney disease, dialysis and transplantation could not have been possible without working closely as a team for almost 20 years.”

Drs. Held, Port, and Wolfe are prominent researchers with expertise in health economics, clinical nephrology epidemiology, and biostatistics, respectively. They continue to be pioneers and leaders in health outcomes and clinical research for kidney disease and transplantation. Besides leading the DOPPS study, this multidisciplinary team has coordinated and launched significant projects, including the United States Renal Data System (USRDS) and the Scientific Registry of Transplant Recipients (SRTR). Over a span of many years, they have published extensively on a wide range of topics related to nephrology, including cost-effectiveness, dialysis and transplant practices, and study design. Each of their collaborative projects has had the goal of improving patient lives through the clinical integration of medical practice and outcomes research.

“What keeps us so committed,” adds Dr. Port, “is that there are patients’ lives behind these efforts.”

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