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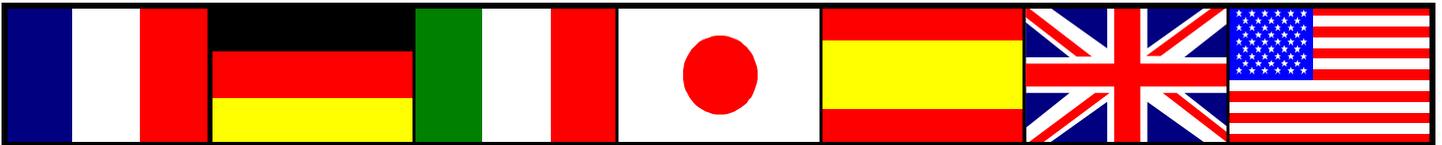
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The DOPPS Report

Newsletter of the Dialysis Outcomes and Practice Patterns Study

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DOPPS Update

The Dialysis Outcomes and Practice Patterns Study is moving forward in all areas of data collection and research analysis. This international study of hemodialysis treatment and practice patterns continues to be operational in the seven countries of France, Germany, Italy, Japan, Spain, the United Kingdom and the United States. With the presentation of 12 abstracts at the ASN in November 1999, DOPPS is gaining a noteworthy reputation in the international renal community. Important research analyses are underway with several manuscripts nearing publication.

The DOPPS database is an unparalleled source of information for investigating hemodialysis treatment and patient outcomes. In a representative study such as DOPPS, the statistical power of the

database is based on several aspects of the design, not just the number of facilities and the number of patients enrolled. The number of “patient years” of observation and the number of events such as deaths and hospitalizations also contribute to statistical power. The total number of “patient years” is the sum of all periods of study observation for all enrolled patients. For example, if Patient A is observed for 12 months, Patient B for 24 months and Patient C for 36 months then the total number of “patient years” is six (72 months). The period of observation is defined as the date the patient was entered on the Cumulative Hemodialysis Census (CHC) to the date of departure from the facility (due to transfer to another facility or death). In DOPPS, patients are divided into two groups. The first is a listing of all hemodialysis patients. This includes all patients listed on the facility’s CHC. The second

Euro-DOPPS Country Investigators: *France:* • Bernard Canaud, MD • Christian Combe, MD; *Germany:* • Jürgen Bommer, MD

• Erwin Hecking, MD; *Italy:* • Vittorio Andreucci, MD • Francesco Locatelli, MD; *Spain:* • Luis Piera, MD

• Fernando Valderrábano, MD; *United Kingdom:* • Roger Greenwood, MSc, MD, FRCP • Hugh C. Rayner, MD, FRCP;

Members at Large: • Nathan W. Levin, MD • Severin Ringoir, MD, PhD

Japan-DOPPS Investigators: • Kiyoshi Kurokawa, MD, MACP • Fumiaki Marumo, MD, FACP • Akira Saito, MD

• Tadao Akizawa, MD, PhD • Takashi Akiba, MD, PhD • Shunichi Fukuhara, MD, MSc, DMSc

U.S. DOPPS Investigators: • Philip J. Held, PhD • Kenneth Chen, MS • David A. Goodkin, MD • Marcia L. Keen, PhD

• Donna L. Mapes, DNSc, MS • Bradley J. Maroni, MD • Friedrich K. Port, MD, MS† • Robert A. Wolfe, PhD† • Eric W. Young, MD, MS†

DOPPS is a worldwide hemodialysis study coordinated by the University Renal Research and Education Association (URREA).
DOPPS is supported by a grant from Amgen and Kirin-Amgen. URREA Web Site: www.urrea@urrea.org

group of patients is the sampled patients (this group is a subset of the CHC). This refers to those patients randomly selected for participation in DOPPS.

As indicated in **Table 1**, the database contains patient-specific data for 51,910 CHC patient years and 18,673 sampled patient years. These data provide sufficient statistical power for analyses in a wide range of treatment areas.

Table 1: DOPPS Status September 1, 2000: Patient Years

DOPPS Region	Months of Operation	Patient Years	
		Census	Sample*
Europe (started in 1998)	28	10,615	4,885
Japan (started in 1999)	19	7,511	2,525
United States (started in 1996)	53	33,784	11,263
Total		51,910	18,673

*Medical Questionnaires returned

Another important measure of the statistical power of the DOPPS database is the number of events such as deaths, hospitalizations and vascular access procedures. Since a major objective of DOPPS is to investigate the associations between practice patterns and mortality, information about patients who have died is vitally important to the study. For this reason, the importance of listing all chronic hemodialysis patients on the CHC, obtaining consent (in Europe and Japan) from all selected patients, and providing the reason for departure for every patient on the CHC has been consistently emphasized. Adherence to these procedures ensures

Table 2: Numbers of deaths recorded by DOPPS as of September 1, 2000 for Europe, Japan, and US.

	Census	Sample
Total Deaths in DOPPS	10,054	3,943

the collection of information about patients who have died. Studies of all types can only work if there are comparable data for patients with and without events. **Table 2** indicates the total number of deaths recorded for CHC patients and sampled patients in Europe, Japan, and the US.

The Future of DOPPS

The Worldwide DOPPS project has been gaining an international reputation and is widely recognized as an authoritative source of longitudinal hemodialysis information. Many exciting research studies using DOPPS data are nearing completion and we expect that these will culminate in a number of important publications this year.

DOPPS has been underway for four years in the United States and for almost two years in Europe. In Japan, data collection is planned for a two-year period ending in the Spring of 2001. Now is the time for the DOPPS investigators to re-evaluate the goals of this project and plan for the future.

Many Study Coordinators have been asking about the future of DOPPS and whether data collection is planned for the next several years. Amgen and Kirin-Amgen have been the generous sponsor of DOPPS and may continue with additional support beyond the current period. While we wait for more information from Amgen and Kirin-Amgen about possible future funding, we will be considering refinements of the DOPPS protocol with special attention to ways of reducing the burden of data collection on Study Coordinators. This will include close examination of all aspects of DOPPS, from study objectives and sample size to questionnaire content, frequency, and data quality.

It is well-recognized that collecting data for DOPPS has been a very time-consuming and difficult task for the many dedicated Study Coordinators in Japan, Europe and the US. For the next several months we will be giving special attention to the

relative utility of the data collected. To date, all the data collected have been very important to the analyses of practice patterns and patient outcomes. All the same, we recognize the need to simplify and shorten DOPPS data collection. We will carefully scrutinize all the questionnaires and data items in an effort to substantially reduce the burden of data collection.

We understand that the Study Coordinators are strongly committed to the DOPPS objective of improving patient outcomes. Nevertheless, completing the DOPPS questionnaires can be demanding of time and effort. Therefore, we will also be exploring alternative strategies to reduce the burden of data collection.

DOPPS has earned an international reputation, and its proposed continuation has wide support from the worldwide renal community. There are many important issues to be considered for the future. Should DOPPS be expanded to other continents or countries? How can we make the DOPPS sample more representative? How can we reduce the burden of data collection while maintaining a powerful database for research? Is there a way to collect data electronically? We will be approaching these questions with great enthusiasm and excitement, since a continuation of DOPPS would be a great opportunity to continue helping renal patients throughout the world.

We will be communicating further with the DOPPS Study Coordinators over the next few months as we learn more about future funding and plans for a DOPPS continuation. Please feel free to share your thoughts and ideas about the future of DOPPS with us. We'd love to hear from anyone involved in DOPPS.

If you have thoughts and ideas on the future of DOPPS, please contact Liz Holzman:

**E-mail: eholzman@urrea.org
Fax: 001-734-665-2103
Phone: 001-800-367-7760**

DOPPS Presentations

DOPPS is gaining visibility and recognition from its presence at several major renal meetings:

- On July 11, 2000 a DOPPS Symposium was held at the European Dialysis and Transplant Nurses Association (EDTNA) Meeting in Lisbon, Portugal. This symposium, entitled "The Dialysis Outcomes and Practice Patterns Study (DOPPS): A world-wide hemodialysis study of treatment and patient outcomes that includes 5 European countries", was well-attended and very well received. Exciting preliminary research results were presented that focused on treatment practice involving the dialysis nurse.
- On September 6, 2000, at the 18th Annual Meeting of the International Society of Blood Purification, Dr. Eric Young, DOPPS Co-Investigator, and Dr. Francesco Locatelli, Euro-DOPPS Country Investigator, presented DOPPS results at the "Renal Failure in the 3rd Millennium: Outcome Resources Strategies Symposium". Dr. Locatelli presented quality of life outcomes analyses. Dr. Young presented preliminary results on resource allocation and outcomes in hemodialysis.
- On September 18, 2000 from 12:15 pm-2:45 pm there will be a DOPPS Symposium held at the European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA) meeting in Nice, France. This symposium is entitled "The DOPPS Initiative: A global study of hemodialysis treatment and patient outcomes". Research results from Europe, Japan, and the United States will be presented, including analyses of practice patterns, patient characteristics and patient outcomes.

At the American Society of Nephrology (ASN) meeting in October 2000, DOPPS research will be presented at several different meetings. Dr. Philip Held, Principal Investigator for the DOPPS will be presenting at a symposium on dialysis dose. Dr. Eric Young, DOPPS Co-Investigator will be presenting at a symposium on vascular access. In addition, 12 DOPPS abstracts have been accepted for either an oral communication or a poster presentation. (Last year 12 DOPPS abstracts were presented at ASN.)

The ASN meeting will clearly be an exciting opportunity to present many important research findings from the DOPPS project. We recognize that none of this would be possible without the effort and dedication of more than 300 Study Coordinators worldwide. **Table 3** provides a schedule for ASN symposia and abstract poster and oral presentations featuring results from the DOPPS.

Table 3: DOPPS Abstracts and Symposia to be presented at the American Society of Nephrology, October 2000.

Abstracts at ASN 2000	Author	Free Communication or Poster Session	Date, Time, Program Number, Location
Delivered Dialysis Dose Predicts Mortality for Hemodialysis Patients in US and Europe	McCullough	Free Communication	Fri, 10/13/00, 4:15 PM F1122 Room: 718B, Metro Convention Centre
Hepatitis C in Hemodialysis Patients from Three Continents: The DOPPS	Bragg	Free Communication	Sat, 10/14/00, 4:15 PM SA1148 Room: 803A, Metro Convention Centre
Body Mass Index Mortality Relationship for Hemodialysis Patient Populations in Europe and the US by Comorbidity, Age and Smoking Status	Leavey	Free Communication	Sun, 10/15/00, 4:30 PM SU1075 Room: 715B, Metro Convention Centre
Nutritional Status across Three Continents: The DOPPS	Akizawa	Free Communication	Sun, 10/15/00, 4:00 PM SU1073 Room: 715B, Metro Convention Centre
Hepatitis B in Hemodialysis Patients from Three Continents: The DOPPS	Woods	Poster Session	Fri, 10/13/00, 10:30 AM - 12:30 PM Halls D & E, Metro Convention Centre
Renal Function at Initiation of Hemodialysis in US and Europe	Woods	Poster Session	Fri, 10/13/00, 10:30 AM - 12:30 PM Halls D & E, Metro Convention Centre
Hospital Readmissions and Length of Stay: The DOPPS	Young	Poster Session	Sat, 10/14/00, 10:00 AM - 12:30 PM Halls D & E, Metro Convention Centre
Blood Flow and Vascular Access Failure	Dykstra	Poster Session	Sun, 10/15/00, 10:00 AM - 12:30 PM Halls D & E, Metro Convention Centre
Components of Hemodialysis Dose: Results from 7 Countries in the DOPPS	Goodkin	Poster Session	Sun, 10/15/00, 10:00 AM - 12:30 PM Halls D & E, Metro Convention Centre
International Variation in the Disability Status of Hemodialysis Patients: Results from the DOPPS	Mapes	Poster Session	Sun, 10/15/00, 10:00 AM - 12:30 PM Halls D & E, Metro Convention Centre
International Variation in the Employment Status of Hemodialysis Patients: Results from the DOPPS	Dickinson	Poster Session	Sun, 10/15/00, 10:00 AM - 12:30 PM Halls D & E, Metro Convention Centre
Vascular Access Failure and Timing of First Cannulation	Young	Poster Session	Sun, 10/15/00, 10:00 AM - 12:30 PM Halls D & E, Metro Convention Centre
Symposia At ASN	Presenter	Title	Date, Time, Location
International Federation of Renal Registries	Friedrich Port	Feedback to Dialysis Units to Improve Care	Thurs, 10/12/00, 12:15 PM-12:45 PM Metro Convention Centre
International Federation of Renal Registries	Philip Held	New Information from the Dialysis Outcomes and Practice Patterns Study	Thurs, 10/12/00, 2:15 PM-2:45 PM Metro Convention Centre
New Insights Into Hemodialysis Adequacy	Philip Held	Worldwide Comparison of Outcomes: The DOPPS Study	Fri, 10/13/00, 1:30 PM-3:30 PM Metro Convention Centre
Vascular Access: Current Practice and Practical Aspects of Management	Eric Young	Descriptive Epidemiology of Vascular Access Techniques: Current Practices and Trends	Sat, 10/14/00, 4:00 PM-6:00 PM Metro Convention Centre

Water Quality Study

In March 2000, the DOPPS Water Quality Study was initiated. The DOPPS Water Quality Study is the largest study of its kind to simultaneously test hemodialysis treatment water in more than 300 facilities on 3 continents using one central testing laboratory. Two major goals of the Water Quality Study are: (1) assess the quality of water used for hemodialysis treatments in the 7 countries participating in DOPPS, and (2) analyze relationships between patient outcomes and the levels of various water constituents. An important part of the Water Quality Study design is that many of the analyses will be performed by a single laboratory so that test results can be easily compared across countries and continents. The laboratory chosen for this task was Spectra Laboratories in the US, which has extensive experience and sensitive detection systems for the analysis of dialysis water samples.

Table 4: Total number of Water Testing Kits Sent and Returned to Spectra Laboratories, March through July 2000.

DOPPS Region	Number of Testing Kits Sent	Number of Testing Kits Returned to Spectra
Europe	101	92
Japan	64	64
United States	136	115
Total	301	271

Two rounds of water sample collection have been planned for the Water Quality Study. In the first round, from March through July 2000, DOPPS dialysis units shipped a purified water sample and a tap water sample to Spectra Laboratories. Participation by DOPPS units in this effort was excellent with more than 90% of dialysis units providing water

samples for analysis (**Table 4**). The purified water samples have been analyzed by Spectra Laboratories to determine the levels of 17 different substances including silver, aluminum, arsenic, barium, calcium, cadmium, chromium, copper, fluoride, mercury, potassium, magnesium, sodium, nitrate, lead, selenium, and zinc. Preliminary results of this initial testing suggest excellent water quality on all 3 continents. The second round of water collection is currently being considered for September-November, 2000. Throughout the Water Quality Study, strict confidentiality of test results will be maintained. However, URREA will be happy to provide any dialysis unit with a copy of their own test results if requested by the facility's medical director.

Nutrition

There is currently great interest in the role of nutrition and its impact on patient outcomes for the ESRD population. However, assessing nutritional status is complicated and difficult since there is no single nutritional indicator that can provide a complete and accurate assessment. Often, the best approach is to examine a variety of indicators including anthropometric measures (e.g., height, weight) and clinical laboratory values.

One of the most commonly used anthropometric measures is body mass index (BMI), also called the Quetelet index. Calculating BMI is a quick and inexpensive method of measuring overweight and obesity. It can be calculated using the following formulas:

$$\text{BMI} = \text{weight (kg)} / \text{height (m)}^2$$

or

$$\text{BMI} = [\text{weight (lbs)} / \text{height (in)}^2] \times 704.5$$

Figures 1, 2, and 3 illustrate the differences in the average height, weight and BMI for all three geographic locations of DOPPS. Not surprisingly, Japanese HD patient have the lowest height, weight and BMI compared to Europe and the US.

BMI does not directly measure percent of body fat, but it provides a more accurate measure of overweight and obesity than weight alone. The definitions of overweight and obesity have varied over time, from study to study, and from one country to

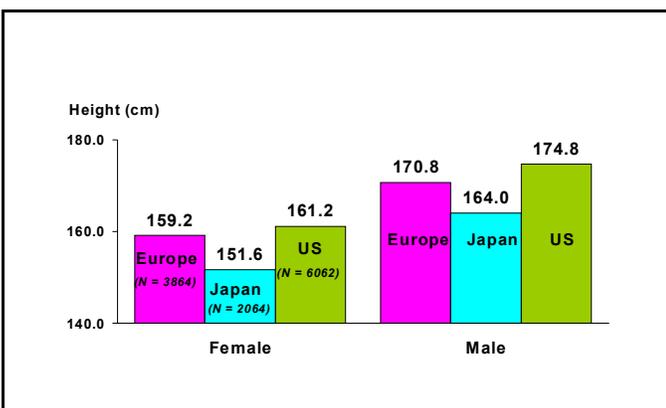


Figure 1: Mean Height for Europe, Japan and the US HD Population by Sex, DOPPS 1996-2000

another. Older studies in the US used the 1959 or 1983 Metropolitan Life Insurance tables of desirable weight for height as the reference for overweight. More recently, many US government agencies have used data from a series of cross-sectional surveys called the National Health and Nutrition Examination Surveys (NHANES) to determine a statistically derived definition of overweight. Based on these

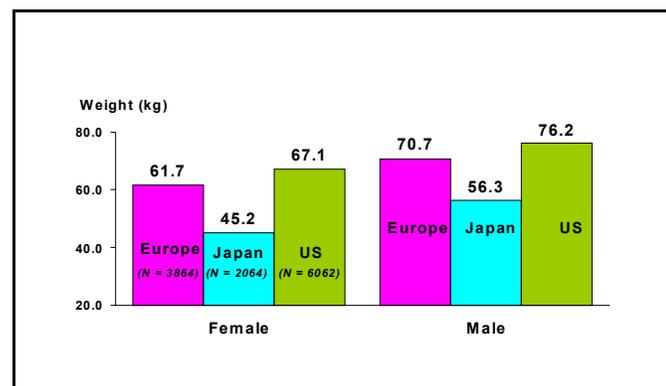


Figure 2: Mean Weight for Europe, Japan and the US HD Population by Sex, DOPPS 1996-2000

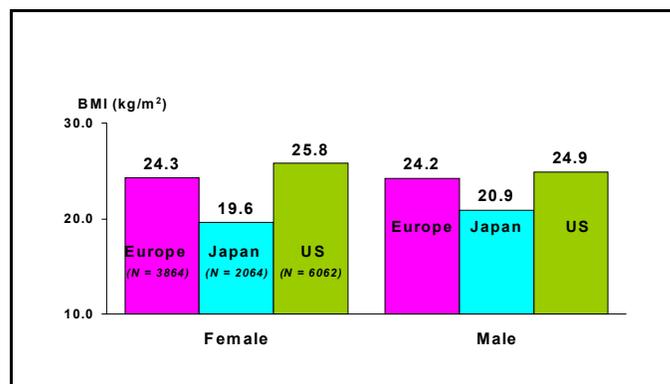


Figure 3: Mean BMI for Europe, Japan and the US HD Population by Sex, DOPPS 1996-2000

data, the National Center for Health Statistics defined overweight in the US as a BMI ≥ 27.3 for women and ≥ 27.8 for men. However, in June 1998, the US federal government issued new guidelines for BMI based on the classifications established by the World Health Organization (WHO) in 1995 (Table 5).

Table 5: Classification of Overweight and Obesity by BMI, World Health Organization (WHO)

Classification	Obesity Class	BMI (kg/m ²)
Underweight		<18.5
Normal		18.5-24.9
Overweight		25.0-29.9
Obesity	I	30.0-34.9
	II	35.0-39.9
	III	≥ 40

These guidelines are useful for clinicians and epidemiologists in tracking the problem of overweight and obesity. This is a growing public health concern since there are many risk factors associated with obesity including type II diabetes, hypertension, lipid disorders, coronary heart disease, stroke, sleep apnea, and certain cancers. Furthermore, the total costs attributable to obesity-related diseases continues to rise every year, approaching \$100 billion annually in the US.

In large epidemiologic studies, BMI has been shown to be a significant predictor of increased

morbidity and mortality for the general population. Studies have shown that both a very low BMI and a high BMI are associated with increased risk of death for the general population. However, in the chronic ESRD population a high BMI appears to be associated with a lower risk of death. It has been speculated that this protective effect may be due to the greater energy reserves of HD patients with a high BMI, which means that these patients will be less likely to suffer from malnutrition.

Figure 4 shows the distribution of each weight classification in DOPPS according to the WHO guidelines. For the proportion of overweight patients (BMI>25), the Japanese have the lowest percentage (6.0%) compared to Europe (38.5%) and the US (44.1%). While the US has the highest proportion of overweight and obese patients, it is not necessarily the case that the US also has the lowest mortality rate since there are obviously many other factors that affect mortality.

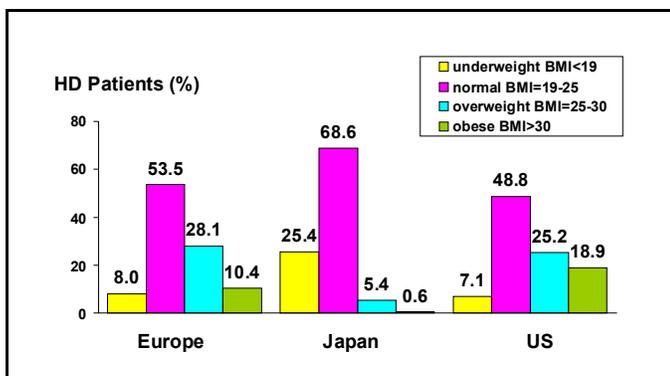


Figure 4: Distribution of BMI in Europe, Japan and US HD Population, DOPPS 1996-2000

Furthermore, despite the advantages of using BMI as a nutritional indicator and a predictor of patient morbidity and mortality, there are several limitations that should be recognized. BMI does not distinguish body fat from lean body mass, which may overestimate body fat in persons who are very muscular. In addition, BMI may not be accurate in the presence of edema or extreme muscle wasting.

Another simple nutritional indicator is serum al-

bumin. This is also an inexpensive and readily available method for assessing a patient's nutritional status. **Figure 5** shows the average albumin levels for each region in DOPPS.

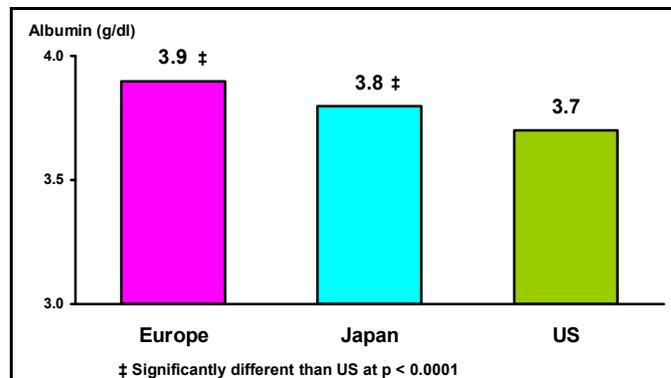


Figure 5: Mean Albumin* by DOPPS Geographic Location
*At enrollment; values adjusted to Wednesday-Thursday Value

Serum albumin reflects a patient's protein storage, therefore, a low serum albumin may reflect protein-energy deficiencies. Furthermore, numerous studies have shown that serum albumin is a significant predictor of mortality in the HD patient population. However, just as with BMI, serum albumin is not a perfect indicator of a patient's nutritional status. There are many other factors that may affect albumin such as stress, infection, inflammation, and edema.

It is extremely important to assess the nutritional status of HD patients as it is strongly associated with outcomes. However, a variety of nutritional indicators should be analyzed to obtain a more accurate assessment of nutritional status including anthropometric measures and clinical lab values.

Technical Notes:

- All DOPPS data are based on Interval Summaries, Cumulative Hemodialysis Census, and Medical Questionnaires collected from 1996-2000.
- Weighting is employed in graphics representing the total DOPPS sample (all seven countries). This is done to ensure the correct representation for the ESRD populations in the corresponding countries.
- Albumin analyses are not adjusted for type of assay.
- †Indicates investigators subcontracted with the University of Michigan

References:

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- Leavy SF, Strawderman RL, Jones CA, Port FK, Held PJ. Simple nutritional indicators as independent predictors of mortality in hemodialysis patients. AJKD 31:997-1006, 1998.

Questions & Answers

Frequently Asked Questions from Participating DOPPS Facilities

Q: A patient at my facility who was sampled to participate in DOPPS recently died. I have an Interval Summary for this patient. Do I need to complete this form?

A: Yes! Please complete an IS for all patients who dialyzed during that interval, even if the patient died or departed. Every Interval Summary collects data about the treatment the patient received at your facility during a specific four-month period. Please complete this particular IS if the patient received hemodialysis treatment at your facility at any time during the reporting interval, using the last available lab data before the patient died. In other words, if a patient dialyzed at your facility at the beginning of the reporting interval but not the end, please complete the IS. Updated information about dead or departed patients is extremely valuable to us.

Q: I am a Study Coordinator in a city that is a popular vacation destination. Therefore, many of the patients who visit my facility only dialyze a few times and then return to their units of origin. I know that these transient patients are not selected to participate in DOPPS. What exactly is a transient patient, and should this type of patient be listed on the census?

A: All transient patients should be listed on the CHC. A transient patient is one who visits your facility with the intention of returning to his or her primary dialysis facility. For a patient to be considered transient according to DOPPS protocol, he or she must leave your facility within six weeks of his or her first treatment. These patients should be listed on the CHC, using the departure code 7 for Japan-DOPPS and US-DOPPS, or code 9 for Euro-DOPPS. When patients are listed in this manner, they will not be selected for inclusion in DOPPS, as long as they depart within six weeks.

Q: I gave a Patient Questionnaire to one of my patients. He completed a portion of the PQ, but then stopped because he thought some of the sections were too personal. What should I do with this questionnaire?

A: Although we would prefer that the patient answer all the questions, it is perfectly acceptable for him/her to leave blank any questions found to be too personal or intrusive. Please have the patient complete the rest of the questionnaire, then return it to the DOPPS Coordinating Center or your CRA.

Q: A patient in my dialysis facility left for a three-month vacation. While she was gone, I sent in an updated CHC, which stated that she had transferred to another facility, since she was not receiving treatment at my facility at that time. Now she has returned. How should I list her on the census?

A: A patient who returns to the facility after an absence of more than six weeks should be entered on the census as a new patient. The date of first dialysis will be the date she returned to the facility. This patient will not automatically receive DOPPS forms; she must be randomly sampled to participate in DOPPS again. If she is selected, she will be assigned a new patient identification number.

Q: There are approximately 100 patients who dialyze at my facility. However, only 30 are selected to participate in DOPPS. Why do I need to provide departure and death information on the CHC for those patients who were never sampled to participate in DOPPS?

A: Although DOPPS questionnaires are completed for only sampled patients, we perform a number of analyses using data about all patients listed on the census. For example, we use the dates of death listed on the CHC to analyze mortality. We would not be able to generate an analysis like this without valuable departure and death dates.

Questions? Contact:

Euro-DOPPS (Quintiles Clinical Research Associates):

France: David de Leiris

Germany: Christiane Schirmer, Leonhard Purmann,
Ingrid Gerber

Italy: Simona Re, Mariagrazia Colombetti

Spain: Amaya Sanz, Susana Esteban

United Kingdom: Stephen Jaspers, Nicola Flynn

Japan-DOPPS (Quintiles Asia): Akira Nishimura

U.S. DOPPS: Trinh Pifer, Sue Countryman,
Mike Davidson, Theresa Helm

DOPPS Coordinating Center
001-800-367-7760