



Stage 4-5 CKD Registries: a challenge to take From Carmine Zoccali, ERA-EDTA Registry Chairman

Chronic kidney disease (CKD) is now recognized as a worldwide public health problem. The KDOQI CKD staging system is a formidable instrument for deploying interventions calibrated to the various CKD stages and also a useful intellectual framework for stimulating well focused research on kidney diseases. Stage 4 (severe CKD) is a critical phase in this staging system because it is precisely at this phase that the renal team should prepare the patient and his family for kidney replacement therapy. Observational studies in various European countries indicate an increasing stage 4-CKD prevalence coupled with poor outcomes and concerning costs. Unfortunately, notwithstanding tantalising efforts by nephrologists for addressing attention of other doctors and health authorities to the risk posed by moderate and severe CKD, late referral still remains a problem in most countries. This is unfortunate because the adverse outcomes of kidney failure, cardiovascular disease and the short life expectancy of CKD patients can be modified by available treatments and by streamlining their access to renal units. Many countries have registries for patients treated by dialysis and transplantation. However, these programs neglect patients with severe CKD who die before the onset of kidney failure or who don't receive renal replacement treatment when they reach the terminal phase of disease. A surveillance program for CKD stages 4 and 5 would enable monitoring the magnitude and the care of this high-risk, high-cost segment of the population, and possibly to reduce both the risk of progression to kidney failure and the cost of dialysis and transplantation. The Kidney Disease Improving Global Outcomes (KDIGO) initiative now recommends the establishment of surveillance programs for CKD stages 4-5.



Carmine Zoccali

ERA-EDTA President
Jorge B. Cannata-Andía
Oviedo, Spain

Registry Committee

Carmine Zoccali (Chairman)
Reggio di Calabria, Italy

David Ansell
Bristol, United Kingdom

Christian Combe
Bordeaux, France

Reinhard Kramar
Wels, Austria

Torbjørn Leivestad
Oslo, Norway

Fernando García López
Madrid, Spain

Alison MacLeod
Aberdeen, Scotland

Jane Tizard
Bristol, United Kingdom

Enrico Verrina
Genoa, Italy

Christoph Wanner
Würzburg, Germany

Staff

Kitty Jager
Managing Director

Ronald Cornet
Senior IT Specialist

Friedo Dekker
Senior Epidemiologist

Vianda Stel
Epidemiologist

Marlies Noordzij
Epidemiologist

Karlijn van Stralen
Epidemiologist

Anneke Kramer
Medical Information scientist

Annick van den Broek
Datamanager

Gita Guggenheim
Secretary

[continued on page 2](#)

ABC of Epidemiology – Kidney International From Kitty Jager, ERA-EDTA Registry Managing Director and Carmine Zoccali, ERA-EDTA Registry Chairman

The ERA-EDTA 'Introductory courses on Epidemiology' have found their way to the nephrology literature. The course lectures and hands-on sessions are being transferred into a series 'ABC of Epidemiology' for Kidney International. By now 7 papers have been published by the authors group including ERA-EDTA Registry Office staff (AMC, The Netherlands), Registry Committee Members, epidemiologists and biostatisticians from CNR Reggio Calabria (Italy) and LUMC (The Netherlands). The articles are specifically targeted at an audience of nephrologists and nephrology researchers and discuss epidemiological concepts at an introductory to intermediate level. In our experience such concepts are better understood if they are presented in the context of the nephrology literature. The fact that a thorough knowledge of renal pathophysiology is needed to apply epidemiological methods in the correct way makes learning even more attractive.

Every article presents at least three to four examples from studies to illustrate well performed analyses together with common pitfalls. Much attention is paid to a simple writing style without avoiding the discussion of important more complicated subjects. The series is meant to provide a solid epidemiological basis to those nephrologists who are performing clinical epidemiological research or who wish to increase their ability to critically appraise the literature. In addition to the papers already published, quite a few others are in preparation covering subjects like survival analysis, including Kaplan Meier, Cox regression and time dependent effects as well as other topics like agreement between methods and interaction. This ABC will provide a comprehensive overview of the most commonly used epidemiological techniques in nephrology research.

More information on www.nature.com/ki/abcarchive/index.html

Study design: RCT or observational study? From Marlies Noordzij, ERA-EDTA Registry epidemiologist



Marlies Noordzij

In clinical epidemiology several study designs are applied to investigate relationships between an exposure (medical treatment, environmental factor, etc.) and an outcome (development of a disease, death, etc.). Randomized Controlled Trials (RCTs) on the one hand, and observational studies such as cohort and case-control studies on the other hand, are important study designs that are used in the field of nephrology research.

To study the effect of therapy or other interventions, the RCT is an almost unbeatable standard in research: the problems that may occur in the other study designs do not exist or to a lesser extent using an RCT. The main advantage of an RCT is that the randomization procedure helps to prevent selection bias by the investigator. Although randomization of large groups of patients will often result in a similar distribution of measured and unmeasured variables in the experimental and control group, it is unlikely that the intended balance will be achieved for all patient characteristics. This is easy to understand given the large

variability in genotypes. Though the balance will not be complete, the randomization process does guarantee that any differences between the two groups are due to chance and not to the investigator's choice.

However, RCTs are often inappropriate to answer research questions relating to etiology, diagnosis, prognosis, and adverse effects and in these cases an observational study design is a better choice than an RCT. Observational studies are in general more useful for non-therapeutic studies than RCTs and even in therapeutic studies there are a number of cases in which RCTs are impossible, inappropriate, inadequate, or unnecessary. Because of the extremely large number of existing and new health care interventions, it will not be possible to test all of them in an RCT. This is not only due to the scale of the task, but also to financial constraints, since RCTs are much more expensive than observational studies. In addition, ethical objections may prevent interventions to be tested within an RCT setting. Furthermore, there are examples of cases

where RCTs are possible but inappropriate, such as the detection of adverse events that are rare or take years to develop. Finally, there are some exceptional, historical, examples (e.g. insulin in type 1 Diabetes mellitus) where the effects of health interventions were dramatic and observational studies were sufficiently adequate to demonstrate the effectiveness of the intervention.

These facts emphasize that also observational studies are essential in research and we can conclude that both observational studies and RCTs fulfill a complementary and valuable role in nephrology.

For further reading:

1. Stel VS, Jager KJ, Zoccali C, Wanner C, Dekker FW. The randomized clinical trial: An unbeatable standard in clinical research? *Kidney Int* 2007; 72: 539-542
2. Jager KJ, Stel VS, Wanner C, Zoccali C, Dekker FW. The valuable contribution of observational studies to nephrology. *Kidney Int* 2007; 72: 671-675

Registry activities during the XLV ERA-EDTA Congress in Stockholm, Sweden (May 10-13, 2008)

11 May - 8.00 to 9.30 a.m. - ERA-EDTA Registry Symposium.

12 May - 8.00 to 9.30 a.m. - Compact Primer: Observational studies in Nephrology - under STROBE scrutiny.

More information available at www.eraedta2008.org

Stage 4-5 CKD Registries: a challenge to take From Carmine Zoccali, ERA-EDTA Registry Chairman

continued from page 1

Some European countries have already expressed the intention of starting programs of the kind and, in general, these are expected to be based on existing renal registries or associated with diabetes, hypertension, cardiovascular diseases and oncology registries.

While the creation of these registries represents a great opportunity for ameliorating secondary and tertiary prevention in nephrology, we should be aware that they constitute an enormous challenge for the organizational and logistic problems they pose. In this regard standardized data collection is a challenge that should be taken just now, in the creation phase of stage 4-5 CKD registries. It is fundamental

for the various registries to start with a common language. Such a language is needed for comparing indicators of disease severity and other parameters among different regions and nations and for performing sound analyses useful for resource planning, for benchmarking and for epidemiologic research in general. Forty-two years ago, when the ERA-EDTA Registry was created, notwithstanding the efforts of our founder fathers, each country set up his own set of indicators and definitions. Only recently, with NephroQuest, an agreement was established among European renal registries on an enlarged set of well defined clinical indicators. Making treasure of this experience, an early collaboration between

stage 4-5 CKD registries may be very useful to build a common language for future collaboration and data sharing. The ERA-EDTA Registry feels as an ethical obligation starting this process. For this reason, also as a continuation of contacts started in Barcelona in 2007, this year in Stockholm we will explore the possibility of a stage 4-5 ERA-EDTA European Renal Registry. We invite all colleagues interested in CKD epidemiology and in renal registries to join us on May 10th at 12 am at the Stockholm International Fairs (Hall A8) for the Second Pre-Congress Meeting on "The Epidemiology of CKD in Europe: National Societies surveys and initiatives".