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Factors affecting outcomes in patients reaching end-stage kidney disease worldwide: differences in access to renal replacement therapy, modality use, and haemodialysis practices

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Abstract

More than 2 million people worldwide are being treated for end-stage kidney disease (ESKD).

This Series paper provides an overview of incidence, modality use (in-centre haemodialysis, home dialysis, or transplantation), and mortality for patients with ESKD based on national registry data.

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Contributors

BMR, TA, KJJ, PGK, RS, and RLP had the original research idea and for study design. BMR, TA, KJJ, RS, and RLP did data acquisition. BMR, TA, KJJ, PGK, RS, and RLP did data analysis, data interpretation, and contributed to the writing of the manuscript. BMR, KJJ, PGK, RS, and RLP did statistical analysis.

Declaration of interests

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We also present data from an international cohort study to highlight differences in haemodialysis practices that affect survival and the experience of patients who rely on this therapy, which is both life-sustaining and profoundly disruptive to their quality of life. Data illustrate disparities in access to renal replacement therapy of any kind and in the use of transplantation or home dialysis, both of which are widely considered preferable to in-centre haemodialysis for many patients with ESKD in settings where infrastructure permits. For most patients with ESKD worldwide who are treated with in-centre haemodialysis, overall survival is poor, but longer in some Asian countries than elsewhere in the world, and longer in Europe than in the USA, although this gap has reduced. Commendable haemodialysis practice includes exceptionally high use of surgical vascular access in Japan and in some European countries, and the use of longer or more frequent dialysis sessions in some countries, allowing for more effective volume management. Mortality is especially high soon after ESKD onset, and improved preparation for ESKD is needed including alignment of decision making with the wishes of patients and families.

Introduction

An estimated 2-6 million people worldwide were treated for end-stage kidney disease (ESKD) in 2010, and one to three times that number might have died because they reached ESKD but renal replacement therapy (RRT) was declined or could not be accessed.¹ Our Series paper first provides an overview of incidence, modality use (in-centre dialysis, home dialysis, or transplantation), and mortality for patients with ESKD based on data from many national registries. In addition to population differences in the incidence of kidney failure, these data illustrate disparities in access to RRT of any kind, and disparities in the use of transplantation or home dialysis, widely considered preferable to in-centre haemodialysis for many patients with ESKD where infrastructure permits. Worldwide, most patients with ESKD are treated with in-centre haemodialysis, and, though survival outcomes are poor overall, survival in some Asian countries substantially exceeds survival elsewhere. In this Series paper we then present international cohort study data that demonstrate differences in key in-centre haemodialysis practices, highlighting opportunities to improve survival and the experience of the millions of patients who rely on this therapy, which is both life-sustaining and profoundly disruptive to their lives.

Comparisons of national ESKD registries

Data sources

We collected data from the US Renal Data System (USRDS) Annual Data Report,² which compiles and publishes incidence and prevalence data annually from more than 50 national registries. National ESKD registry data are not available for countries that include at least half of the world's population, such as in many low-income and middle-income countries in Africa and in the world's two most populous nations China and India. In China, regional registries are in place and efforts towards a national registry are underway.

ESKD incidence

Registry data are provided for patients with ESKD treated by RRT (defined here as chronic dialysis or kidney transplantation). Table 1 summarises some factors that might affect

incidence of treated ESKD. Gross domestic product (GDP) per person and percentage of GDP spent on health care are positively associated with incidence of treated ESKD,³ reflecting the reality that many countries have unrecognised diagnoses of ESKD or reduced access to RRT. As a result, reported ESKD incidence almost certainly underestimates the incidence of kidney failure in these countries. Even in countries where RRT is widely available, ESKD incidence probably underestimates irreversible kidney failure to some extent because some patients choose to decline dialysis or transplantation. The term “conservative kidney management” has been applied to the choice to forego or postpone RRT while continuing active medical care by nephrologists and other providers. Conservative kidney management has been promoted for some time in Australia, the UK, and other countries, and has become an increasingly visible option worldwide.^{4–7}

Both absolute rates of treated ESKD and trends in these rates are informative. Of higher-income countries, ESKD incidence is lowest in Nordic countries, other European countries, Australia, and New Zealand (figure 1). These countries have nearly universal access to RRT, so these rates are presumably due to relatively low incidence or progression of chronic kidney disease. Selection of conservative kidney management in lieu of RRT is probably not a major determinant of low ESKD incidence, although the extent of its use is not well known. By contrast, ESKD incidence is much higher in the USA and high-income eastern or southeastern Asian countries, presumably reflecting high burden of chronic kidney disease and antecedent risk factors such as diabetes, hypertension, obesity, and glomerular diseases (eg, IgA nephropathy in Asian populations).

Also in higher-income countries, ESKD incidence rates have plateaued during the past decade, not only in Nordic and other European countries but also in the USA, which has a much higher ESKD incidence.² Stabilisation of ESKD incidence might suggest increased success in prevention of chronic kidney disease or slowing its progression to avoid kidney failure. In support of either possibility, incidence of ESKD due to diabetes has plateaued or declined in nearly all of these countries in 2008–13.² Both reasons would be important public health achievements. Other factors that might have contributed to reductions in the observed incidence rates of ESKD are increases in the delay to start RRT or in patients who choose to avoid RRT entirely in favour of conservative kidney management. By contrast, incidence of ESKD continues to rise in higher-income eastern and southeast Asian countries.

In lower-income countries, reported incidence of ESKD varies greatly (figure 1) and substantial increases in recent years have been reported. From 2000 to 2013, increases of 13 times in Thailand, seven times in Bangladesh, and almost four times in Russia were reported, whereas rises of two to three times were seen in the Philippines, Malaysia, the Jalisco region of Mexico, as well as South Korea. As a whole, expansion of governmental support for dialysis programmes was the largest contributor to the rise in ESKD incidence counts, with smaller contributions from increased population size, rise in ageing populations, and growing prevalence of hypertension and diabetes.⁸ Although expanded access to RRT in many countries is commendable, reduced or no access to RRT is all too common in other countries. The substantially lower incidence reported for ESKD in Indonesia, the Philippines, and Bangladesh than in higher-income countries in east and southeast Asia presumably reflects, at least in part, reduced access to RRT. Worldwide, and as previously

noted, the number of people who reach ESKD without access to RRT is estimated at up to three times higher than the number who receive RRT.¹

In many countries, the incidence of ESKD due to diabetes has risen much faster than the overall rise in ESKD incidence, presumably reflecting the rising population burden of diabetes and improving survival for people with diabetes. Diabetes was the primary cause of ESKD in 32% of incident patients in the median country in 2013 from 46 national registries,² varying from 15–25% in many European countries to about 60% in Malaysia, Singapore, and the Jalisco region of Mexico. The global rise in diabetes and its end-organ complications has also affected the burden of comorbidities and overall frailty of patients with ESKD. The complexity of disease management and risks for adverse outcomes (ie, mortality, admission to hospital, cardiovascular events, stroke, vascular access complications, infections, amputations, and others) are higher in patients with ESKD and diabetes than in those without diabetes.^{2,9–11}

ESKD prevalence

Reported ESKD prevalence varies by almost 50 times between countries (figure 1)² and is strongly correlated with ESKD incidence (regression coefficient [R^2]=0.66 across all countries). Unlike trends in ESKD incidence which vary from strongly positive to negative, the prevalence of ESKD per million population has increased in all 32 registries contributing data,² with a median increase of 50% (range 29–839) during 2000–13. Several observations are pertinent to this Series paper. First, increases in ESKD prevalence in countries with little change in the incidence are strongly indicative of declines in ESKD mortality, now generally confirmed by data from registries that publish mortality trends. Second, in countries such as Indonesia, the Philippines, and Bangladesh, ESKD prevalence is disproportionately very low in relation to the incidence. In these countries, government or third party payment for dialysis is limited to a finite period of time. Third, overall upward trends in ESKD prevalence, and similar projections for the near future, support the need for expanded access to in-centre dialysis, home dialysis, and kidney transplantation services to meet the growing worldwide burden of ESKD.^{2,8}

ESKD treatment modalities

Kidney transplantation is the treatment of choice for eligible patients with ESKD, which results in a substantially improved quality of life and median survival similar to survival for patients without ESKD. Stark differences exist in access to and use of kidney transplantation. In 2013, transplantation use for patients with ESKD ranged from 57–72% in Nordic countries, Estonia, and the Netherlands, to less than 10% in some Asian and eastern European countries (figure 2). A striking observation is that the countries with the highest proportion of kidney transplants in patients with ESKD—mostly Nordic and several other European countries—also have some of the lowest incidence rates of ESKD. One implication, of public health importance, is that efforts to slow progression of chronic kidney disease might have additional downstream benefits, namely that kidney transplantation can be offered to a higher proportion of patients with ESKD because of a relatively low number of incident cases. Some European countries have a much larger proportion of incident ESKD cases who receive a pre-emptive kidney transplant (18–40% in Denmark, Iceland, Norway,

Sweden, the Netherlands, and the UK) than other countries (1–2% in the USA;¹² Kramer A and Pippias M, European Renal Association/European Dialysis and Transplant Association (ERA-EDTA) Registry, personal communication). As such, these countries provide a substantial fraction of their incident patients with ESKD the opportunity to avoid dialysis as their first treatment for this disease, and potentially altogether. The optimum timing of pre-emptive transplantation remains controversial, because it balances dialysis avoidance with early exposure to chronic immunosuppressive therapy.

Of dialysis modalities, home dialysis options (peritoneal dialysis or home haemodialysis) are considered to have clinical outcomes that are better or at least comparable to in-centre haemodialysis, and are substantially less disruptive to patients' lives.¹³ Countries that provide home dialysis to at least 20% of patients with ESKD include Hong Kong (45%), and New Zealand, Colombia, Thailand, and the Jalisco region of Mexico (23–31%; figure 2). These countries' performances suggest that a large pool of patients receiving in-centre haemodialysis in other countries could use home dialysis if it were made more widely available. For example, peritoneal dialysis use in the USA has risen from 8% in 2009, to 10% in 2015, attributed principally to changes in reimbursement favouring use of peritoneal dialysis. Although this increase can be viewed enthusiastically, this 2% absolute increase could almost certainly be higher still if the culture of in-centre dialysis were less entrenched.

By providing kidney transplantation or home dialysis to a substantial fraction of patients, several nations use in-centre haemodialysis for fewer than a third of their patients with ESKD. These countries include Hong Kong (the lowest use of in-centre haemodialysis at 15%), Estonia, the Netherlands, New Zealand, and some Nordic countries (figure 2). By contrast, in many countries in eastern and southeastern Asia, at least 85% of patients with ESKD receive in-centre haemodialysis. Of these, Japan is notable because it has a large and mature ESKD treatment programme with excellent clinical outcomes, but very low use of transplantation and home dialysis. In-centre dialysis is favoured over home dialysis in Japan partly for historical reasons (many dialysis facilities are available and are easily accessible, with many placed explicitly near public transportation stops), and kidney donation rates are low, which might be because of spiritual or religious beliefs.

ESKD and dialysis mortality

Although most ESKD registries report incidence and prevalence data, survival data are preponderantly from higher-income countries. For those with ESKD onset from 2004 to 2008, unadjusted 5-year survival of all patients with ESKD (treated with dialysis or transplantation) was 41% in the USA, 48% in Europe, and 60% in Japan, despite patients being 2–3 years older on average in Europe and Japan than in the USA, and Japan having very few transplant patients.^{2,12–15} The survival difference between the USA and Europe is smaller than in previous years, because mortality has declined in both regions but to a greater extent in the USA. In 1996–2000, 5-year survival in patients with incident ESKD was 36% in the USA and 48% in Europe^{2,12,15} (in Europe, unadjusted survival was 47.6% in 2004 vs 48.3% in 2008; countries in the ERA-EDTA Registry differed slightly).¹⁶

Japan substantially outperforms other countries in survival of patients receiving dialysis. Unadjusted 5-year survival was 60% in Japan, 39% in the USA, and 41% in Europe for

patients starting dialysis in 2004–08.^{2,14,15} Where data are available, survival is good in other countries with populations of predominantly Asian ethnicity: unadjusted 5-year survival was 52% in Malaysia (2004–08)¹⁷ and 44% in Taiwan (2000–09).¹⁸ National dialysis outcomes data are, to our knowledge, not yet available from China or south Asian countries, although steps are underway to obtain such data.¹⁹

The reasons for international differences in the survival of dialysis populations are not completely understood. First, patients receiving dialysis in countries with the highest transplantation rates are relatively older and less healthy than those in countries with lower rates of transplantation, so these countries tend to have a lower dialysis population survival. The opposite is true for Japan, which has very few transplant patients and thus retains its healthiest patients on dialysis. However, differences between patient characteristics explain only part of the international variation in survival.^{10,20} A substantial part of the variability seems to be attributable to variation in cardiovascular²¹ and all-cause²² background mortality in the general populations. Investigations of the relative frequencies of types of stroke by ethnic origin showed a higher proportion of haemorrhagic versus thrombotic stroke in eastern and southeast Asian populations than in European and US populations,^{11,23} implying differences in vascular biology or pathophysiological responses to hypertension in different populations.

Intriguingly, adjusted survival on dialysis in Europe and North America is generally shortest in white individuals.^{2,24–26} In the UK, survival is longer in those of south Asian origin and those who are black compared with white patients. Similarly, in the USA, patients who are Asian, black, or Native American have longer survival than white patients, as do those of Hispanic origin than non-Hispanics. In the USA, nutritional status is healthier and muscle mass is greater in black than in white dialysis patients.²⁶ In the past 5 years, high ESKD incidence in black patients has been attributed to functional variants of the *APOL1* gene, which is most common in people of west African descent, and is believed to have evolved as protection from trypanosomal parasitic infections.^{27–30} Whether *APOL1*-associated ESKD has a role in explaining racial differences for survival of patients receiving dialysis in the USA is unknown.

International variation in dialysis practices

While international differences in dialysis outcomes derive in part from variation in patient characteristics, evidence over the years indicates that survival differences are, to some extent, affected by modifiable variation in dialysis practices. With regards to in-centre haemodialysis, many data supporting this assertion are from the Dialysis Outcomes and Practice Patterns Study (DOPPS), a series of consecutive, international, prospective cohort studies. The DOPPS is now in its 20th year and is still motivated by the hypothesis that differences in patient longevity, morbidity, and patient experiences are influenced by measurable differences in dialysis facility practices.^{31–52} The DOPPS studies a random sample of in-centre haemodialysis patients within a random sample of dialysis units in each participating country, stratified to represent facility types (eg, free-standing, hospital-based, or satellite facilities) and geographical regions in each country.^{53–55} The DOPPS was launched in the USA in 1996, and was expanded to Japan, seven European countries,

Canada, Australia, and New Zealand in 1998–2002, China in 2010, and Russia, Turkey, and six Gulf Cooperation Council countries in 2012.^{31–52,56–58}

Contrasting Japanese practices with those of other countries

Because haemodialysis mortality is much lower in Japan than most other countries in the DOPPS, many differences in practices and clinical measures have been studied (table 2). Anaemia management is less intensive, with lower erythropoietin stimulating agent doses and less intravenous iron use; targets for haemoglobin, serum ferritin, and parathyroid hormone are lower; dialysate composition is produced centrally without the chance to modify it at the bedside; dialysate water standards are stricter; and cardiovascular screening tests in the dialysis unit are routine. C-reactive protein concentrations, measured routinely in dialysis units outside the USA, are five times lower in Japan than in Europe, likely reflecting both genetic influences⁶⁰ and dialysis practices (eg, high use of surgical vascular access and ultrapure water). Although the previously stated differences are of interest, for many the causal associations with survival are uncertain, illustrating the dearth of definitive clinical trial data in the field.⁶¹ We discuss selected high profile practice areas with some support from higher-level evidence.

The crucial role of vascular access

Of haemodialysis practices, variation in vascular access is undoubtedly one of the most important determinants of patient outcomes.⁴² The native arteriovenous fistula (AVF) is widely recognised as the access of first choice for most patients, providing better outcomes than arteriovenous grafts or central venous catheters (CVCs). CVC use has been associated with substantially higher mortality, medical complications, and costs.^{42,62–69} Since joining the DOPPS more than 15 years ago, AVF use has been highest in Japan—at more than 90%—than any other country except for Russia, which had more than 90% AVF use at study entry in 2012–13 (table 2; figure 3).⁷⁰ (Of note, mortality in patients receiving haemodialysis in the Russian registry is very low at 7.2 deaths per 100 patient-years during 2009–13; although this mortality might reflect excellent practice, patient selection for dialysis could contribute, and greater understanding is needed.⁷¹) In the late 1990s to early 2000s, AVF use was lower in the USA (24% in 1997) than all other DOPPS countries.^{52,70} Shorter survival in the USA compared with Europe was explained largely by differences in vascular access use.⁴²

Because high AVF use is of crucial clinical importance and has been achieved in some countries for many years, practice guidelines, policy changes, and quality initiatives have been directed toward this goal in countries with lower rates of AVF use in the past 10–15 years.^{72–76} However, in 2013,⁷⁰ AVF use in prevalent haemodialysis patients varied from 49% to 92% across 20 countries, and catheter use ranged from 2% to 45% (figure 3A). In countries such as the UK and USA, changes spurred by policy interventions have had commendable effects. In the UK, CVC use declined from 28%^{70,77,78} to 16% after application of a tariff to CVC use in 2011–12.⁷⁹ In the USA, greater AVF use is largely attributed to the Centers for Medicare & Medicaid Services' (CMS) Fistula First Breakthrough Initiative (FFBI) launched in 2003. From 2003 to 2013, AVF use increased from 32% to 68%, arteriovenous graft use declined from 38% to 18%, and CVC use

declined from 27% to 15%.^{2,70} The FFBI spurred quality initiatives by dialysis companies, regional ESKD quality networks, and by the CMS.^{73,80} By contrast, fistula use has fallen and catheter use has risen in other countries.⁷⁷ CVC use is now 38% in Belgium and 45% in Canada, roughly three times higher than in the USA and some European countries.

Drivers of vascular access success, or underperformance, are complex. Social determinants and the dialysis unit culture might be a factor. Although some patients state a preference for CVCs—perhaps because surgical vascular access (AVF or arteriovenous grafts) requires large-needle venipuncture three times a week, often bleeds after dialysis, and can be physically disfiguring⁸¹—these preferences are more common in CVC users at dialysis centres with high CVC use, suggesting that these centres foster a culture of catheter use. Many additional observations and questions about current vascular access practice remain regarding: why differences in AVF failure rates between centres and countries are so large;³⁴ whether use of upper arm AVFs (now more common than forearm AVFs in the USA⁸²) accelerates loss of sites for future surgical vascular access; why vascular access procedure rates have risen dramatically, and the implications for AVF durability;⁸³ whether vascular access outcomes can be improved by better coordination of care between the dialysis unit, surgeon, and interventional suite; what are the best approaches to vascular access for dialysis patients with a very short life expectancy; and how patients' preferences can be honoured through the complex and frequently invasive processes associated with establishment and use of vascular access.

Dialysis adequacy and dialysis session duration

Dialysis session length for in-centre haemodialysis has received considerable attention because in the past decade sessions have become longer in most DOPPS countries, but have shortened in the USA (figure 3B). Reasons for these changes reflect interplay between clinical practice recommendations, reimbursement incentives, unit policies, and clinician and patient preferences, all in absence of definitive evidence from clinical trials. For many years, dialysis adequacy in everyday clinical practice has been measured primarily by dialytic clearance of blood urea, expressed typically as Kt/V_{urea} (a unitless measure representing clearance of urea [K] over the duration of a haemodialysis treatment [t], divided by the urea volume of distribution [V_{urea}]). Clinical trial data support achievement of single pool (unequilibrated) Kt/V_{urea} values of more than 1.2, but not necessarily a cutpoint greater than 1.2 for most patients.^{50,84,85} Kt/V_{urea} can be raised by increasing the dialyser size or blood flow rate through the dialyser (to increase K_{urea}), or by lengthening the dialysis session (ie, increase in treatment time).

In the absence of definitive clinical trial data, widespread opinion holds that longer treatment time confers clinical benefits beyond Kt/V_{urea} , including clearance of toxins substantially larger than urea (so-called middle molecules) and removal of target fluid volume while reducing haemodynamic instability (ie, intradialytic hypotension).^{86,87} Observational data indicate that longer treatment time is associated with longer survival, better volume management, better blood pressure control, better phosphorus control, and fewer cardiovascular events than shorter dialysis sessions.^{23,88–90} In this context, median dialysis treatment time in those patients receiving in-centre dialysis three times weekly is now 4 h

(total of 12 h per week) or longer in many high-income countries, despite the logistical challenges to management of dialysis shifts for health-care staff in busy dialysis units.^{35,48} Dialysis session duration of 4 h or more was tied to reimbursement measures in Japan in 2008, and Germany in 2009,⁹¹ and sessions in both these countries are now some of the longest in DOPPS countries (figure 3B).

By contrast, performance measures are not pegged to session duration in the USA, but instead to Kt/V_{urea} ⁷² achieved in dialysis units in the USA via short dialysis sessions, but high blood flow rate and large dialyser size (figure 3C). Shorter dialysis sessions yield many operational advantages for patient flow over three shifts a day in busy dialysis units. Although treatment time is nearly the shortest in the USA of DOPPS countries, average blood flow rate is roughly 50% higher than in Europe and double that used in Japan (table 2).³⁴ Japanese practice guidelines stress the importance of dialysis that is longer and gentler (ie, uses a lower blood flow rate), on the premise that this approach best ensures haemodynamic stability, despite greater likelihood of having Kt/V_{urea} values of less than 1.2.^{33,49,92} Uncertainty about optimum dialysis session length, and metrics for dialysis adequacy and fluid volume management in general, continue to merit research and policy attention. Results from an ongoing pragmatic trial in the USA of dialysis session duration in incident haemodialysis patients ([NCT02019225](#)), with randomisation at the centre level to standard session length or 4.25 h, will be of interest.

Use of haemodiafiltration for chronic dialysis has gained much attention with its rapidly increased use in many countries, spurred by the availability of on-line replacement fluid, dialysis machines that can be readily adapted to haemodiafiltration, and accompanying industry interests.⁸⁷ Haemodiafiltration use in the DOPPS countries is now 26% in Europe and 7% in Japan, but less than 1% in North America. Haemodiafiltration relies on convective dialysis, which might more closely mimic glomerular filtration than conventional diffusive-based dialysis. Despite widespread uptake of haemodiafiltration, comparative effectiveness studies have, so far, reported mixed results.

Extended duration dialysis

Haemodialysis is an intermittently delivered therapy, and thus an inherently unnatural approach to replacement of kidney function. Approaches to substantially extend haemodialysis duration—eg, from 4 h three times a week to a total of 15 h or more per week—include frequent dialysis (more than three sessions a week), long dialysis (> 5 h per session), or combinations thereof, provided during the day or overnight, and in the dialysis unit or at home. Despite the theoretical benefits of extended duration dialysis, supporting evidence is derived from observational data and from the relatively small, and logistically challenging, Frequent Hemodialysis Network (FHN) trials in the USA.^{93–96} The two trials^{6,94} in this network showed better composite outcomes for short daily (in-centre) dialysis versus conventional three times a week haemodialysis, and did not show a survival benefit for long-hours dialysis (predominantly home nocturnal dialysis). Higher mortality rates were reported for the long-hours dialysis group during the year after study completion.^{97,98} Although conclusive data are absent, use of extended duration haemodialysis is very common in countries experienced with this technique (eg, Canada, Australia, and New

Zealand; figure 2), where practitioners believe in its beneficial effects on dialysis outcomes and patients' everyday experiences.

For most patients with ESKD who are still undergoing standard dialysis three times a week, the once weekly 2-day interval between dialysis sessions (long gap) is now recognised to have increased risk of complications and mortality (often volume overload related).^{40,99} Beyond counselling patients to restrict salt and water intake at weekends, the practice of dialysing every other day, rather than three times a week, is physiologically appealing but rare due to scheduling challenges. A notable exception is Australia where 6–15% of haemodialysis patients receive dialysis on alternate days and predominantly in the home setting.¹⁰⁰

By contrast, some authorities now advocate incremental dialysis, typically twice a week, for people starting dialysis principally as a strategy to reduce dialytic complications and help preserve residual kidney function. Although residual kidney function is associated with increased survival and a favourable patient experience, the value of incremental dialysis is uncertain and controversial.¹⁰¹ Twice weekly dialysis is also common in countries with reduced access to dialysis or where patients have to pay for dialysis treatment. Use of dialysis twice weekly is less than 3% in Europe, Japan, and North America, but is 20% in China, and is more common in China among patients who report lower incomes.¹⁰²

Outcomes in the early dialysis period

Patients starting chronic haemodialysis are faced with very high mortality rates in the first few months (figure 4).^{33,103,104} As with overall dialysis mortality, mortality in the early dialysis period is lowest in Japan, and is higher in the USA than in many European DOPPS countries.³³ However, early mortality, if adjusted for age, is also especially high in Belgium and Canada. Catheter use by incident patients receiving dialysis is particularly high, and use of AVF is low in Canada, Belgium, and the USA (figure 5A).^{2,70}

Early and frequent pre-ESKD nephrology care is associated with improved patient preparedness, experiences, and survival in the early dialysis period. However, in many countries a high proportion of patients start dialysis within a few months of their first visit to a nephrologist—ie, too soon to establish surgical vascular access for use at dialysis initiation (figure 5B).^{45,105,106} And even early nephrological care does not guarantee readiness for dialysis. In the USA, AVF use at dialysis incidence is low (38%) even in patients who had seen a nephrologist 4 months or more before ESKD.^{2,70} This poor performance is partly due to disincentives in payment structure, as patients aged younger than 65 years become eligible for Medicare reimbursement at 90 days after ESKD onset.¹⁰⁷

Recognition that many patients are poorly prepared to start dialysis has led to scrutiny of estimated glomerular filtration rate (eGFR) at dialysis start. The IDEAL clinical trial,¹⁰⁸ corroborated by observational studies, demonstrated no clinical benefit in starting dialysis at higher or lower eGFR concentrations (ie, earlier *vs* later start).^{109–111} Yet the mean eGFR concentration at dialysis start rose in the USA and elsewhere in the first decade of this century, in part in response to practice guidelines (now altered), but perhaps in some places also driven by practitioners' desire to keep dialysis clinics operating at high capacity.¹¹²

Mean eGFR at dialysis start in the USA has been stable since roughly 2010,¹¹³ but the difference between DOPPS countries in mean eGFR at dialysis start of 3–4 mL/min per 1.73 m² in eGFR concentration at dialysis start (figure 5C, table 2) conservatively indicates that some patients might start dialysis 6 months earlier than needed or more. Multidisciplinary programmes to start dialysis when the patient is prepared, rather than on the basis of eGFR concentrations alone, might help reduce urgent or unnecessarily early dialysis starts and improve patient outcomes.^{114,115}

Future perspectives and conclusions

The upward trends in ESKD prevalence, and projections for the near future, support the need for expanded dialysis and kidney transplantation services to meet the disease's growing burden in much of the world. In some high-income countries progress is being made in slowing the development of kidney failure, an important public health achievement. At the same time, because patients with ESKD are surviving for longer and demand for transplantation is met by supply only in a few countries, the numbers of patients needing dialysis and transplantation will continue to rise even in countries with stable ESKD incidence. In many low-income and middle-income countries incremental increases in governmental support for chronic dialysis are positive developments. However, inequities in access to this life-saving therapy remain a major challenge in the context of competing priorities for resources.

In countries with universal access to ESKD therapies, large differences exist in the proportional use of transplantation or home dialysis (widely considered preferable to in-centre haemodialysis for many patients with ESKD). Overall survival of patients with ESKD is longer in Europe than in the USA, although this gap has been largely closed by incrementally greater improvements in the USA in the past few decades. Survival of patients receiving dialysis in Japan, and several other eastern or southeastern Asian countries with available data, substantially exceeds other regions partly due to lower background mortality and fewer transplant recipients. However, major differences in dialysis practices between countries highlight opportunities to improve outcomes. A commendable achievement is the exceptionally high use of surgical vascular access in Japan, some European countries, and some centres in countries with less favourable overall surgical access use, showing that excellence is a realistic expectation. Another laudable progression in some countries is the very common use of longer dialysis sessions, allowing for more gradual fluid removal and achievement of target weight with greater haemodynamic stability. By contrast, in countries where short dialysis sessions are the norm, complications of chronic volume overload remain a predominant concern. Mortality is especially high soon after onset of ESKD. Improved access to care and coordination of care to assure patients are adequately prepared to start dialysis are both feasible and necessary.

Modern dialysis is an expensive, intrusive, and physiologically inadequate treatment, and most uraemic toxins are only partly removed by the dialysers used. Nanotechnology and miniaturisation might simplify blood purification and bioengineered kidneys might provide restorative kidney functions, but these technologies are all in their infancy.¹¹⁶ Until game-changing innovations are successfully developed and become widely available dialysis will

remain life-saving but incredibly disruptive to patients' lives. A priority should be to improve patients' experiences by extending access to kidney transplantation, providing true choice between dialysis modalities, rehabilitating frail and poorly nourished patients, and aligning decision making with the wishes of patients and families, including the options to forego or stop dialysis if desired.

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Search strategy and selection criteria

We searched MEDLINE for articles published between Jan 1, 2006, and Jan 1, 2016, with terms related to specific content areas (including worldwide treatment end-stage renal disease [ESRD]; dialysis conservative care; APO L1 and kidney disease; haemodialysis treatment time; Frequent Haemodialysis Network; and HEMO trial). We also searched for relevant information in national ESRD or renal society registry reports, and for particular relevant health initiatives in some countries (UK: end of life planning; US Renal Physicians Association: shared decision making and dialysis withdrawal). We also cited selected publications from the Dialysis Outcomes and Practice Patterns Study, as this was a particular focus for this Series paper. We largely selected publications from the past 5 years, but did not exclude commonly referenced older publications. Reviews are cited to provide readers with more details and references than this Series paper has room for.

Key messages

- Although the majority of patients reaching end-stage kidney disease (ESKD) worldwide die because renal replacement therapy (RRT; eg, dialysis or transplantation) cannot be accessed, the incidence of ESKD treated with RRT is rising rapidly in many countries because of increased availability of these services and increasingly older populations with multiple comorbidities.
- ESKD incidence is stable or declining in many countries with long-standing access to RRT, presumably due, in part, to increased success in prevention of chronic kidney disease or slowing of its progression to avoid end-stage kidney failure.
- Transplantation or home dialysis are widely considered preferable to in-centre haemodialysis for many patients with ESKD, yet use of these modalities ranges from more than two-thirds of patients in some countries to fewer than 10% in many others.
- Worldwide survival is poor in most patients with ESKD who are treated with in-centre haemodialysis, but generally survival is improving, and is longest in some Asian countries.
- International variation in haemodialysis practices and outcomes highlights opportunities to improve care; commendable practice patterns include exceptionally high use of surgical vascular access in Japan and some European countries, and high use of longer or more frequent dialysis sessions in countries such as Germany, Australia, and New Zealand, allowing for more effective management of volume status.
- Mortality is especially high soon after onset of ESKD therapy, and improved preparation for ESKD is needed, including alignment of decision making (eg, modality selection, patient choice to decline or withdraw from dialysis, and timing of RRT initiation) with wishes of patients and their families.

Figure 1. Treated end-stage kidney disease incidence and prevalence by country in 2013

End-stage kidney disease (ESKD) incidence and prevalence calculated for patients using either maintenance dialysis or a kidney transplant for ESKD. Countries listed in order of lowest to highest incidence within each region. (A) Central and eastern Europe: Russia, Estonia, Bosnia and Herzegovina, Poland, Slovenia, Romania, Serbia, Croatia, Czech Republic, and Hungary; Nordic countries: Iceland, Finland, Norway, Sweden, and Denmark; and western Europe: Ireland, Scotland, UK (excluding Scotland), Netherlands, Spain, Austria, France, Belgium (French speaking), Belgium (Dutch speaking), Greece, and Portugal. (B) Eastern and southeastern Asia (gross national income <US\$25 000): Bangladesh, Philippines, Indonesia, Thailand, and Malaysia; eastern and southeastern Asia (gross national income ≥\$25 000): Hong Kong, South Korea, Japan, Singapore, and Taiwan; the Middle East: Iran, Qatar, Oman, Saudi Arabia, and Israel; South America: Argentina,

Uruguay, Brazil, and Chile; North America: Canada, USA, and Mexico (Jalisco). pmp=per million population. Data are from the US Renal Data System.²

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Figure 2. Renal replacement therapy modality used for patients with end-stage kidney disease, by country, in 2013

Modality use is shown for all patients reported in each country who received either chronic dialysis or a kidney transplant for treatment of end-stage kidney disease in 2013. Data are from the US Renal Data System.²

Figure 3. Selected practices or measures in prevalent haemodialysis patients, by country (2012–15)

(A) Type of vascular access used. Catheter is a central venous catheter. Data from Gulf Cooperation Council (GCC; Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates), Russia, Turkey, Belgium, Sweden, and China are based on vascular access at the initial cross-section of the Dialysis Outcomes and Practice Patterns Study (DOPPS) phase 5; data from remaining countries based on cross-section of haemodialysis patients in August, 2013. (B) Haemodialysis session duration (treatment time) in patients receiving dialysis three times a week; treatment time was defined as a categorical variable (<200, 200–225, 226–250, and >250 min). Because treatment time for most patients was at exactly 30 min intervals, these categories are labelled as 180, 210, 240, and 270 min, respectively. (C) Single pool Kt/V_{urea} in patients receiving haemodialysis three times a week, and receiving dialysis for at least 1 year. AV=arteriovenous. Kt/V_{urea}=a unitless measure representing clearance of urea (K) over the duration of an haemodialysis treatment (t), divided by the urea

volume of distribution (V_{urea}). Some countries are omitted from some figures because of missing data. Figure adapted from Pisoni and colleagues,⁷⁰ by permission of Elsevier.

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Figure 4. Mortality in time periods after the start of haemodialysis, by country in the Dialysis Outcomes and Practice Patterns Study (2002–15)

Countries ordered by mortality at 120 days. Error bars show 95% CIs, calculated with the Byar approximation. Data are of 86 886 patients at facilities participating in the Dialysis Outcomes and Practice Patterns Study, phases 2–5 (2002–15). Figure adapted from Robinson and colleagues,³³ by permission of Elsevier.

Figure 5. Selected practices or measures in incident haemodialysis patients, by country (2012–15)
 (A) Type of vascular access used in patients on dialysis 60 days at Dialysis Outcomes and Practice Patterns Study (DOPPS) enrolment. (B) Timing of first nephrology care before dialysis initiation in patients on dialysis 60 days at DOPPS enrolment; on the basis of responses to the question, "How many months before start of chronic dialysis did the patient first see a nephrologist?", collected at enrolment. (C) Estimated glomerular filtration rate just before patients started haemodialysis. Some countries are omitted from some figures because of missing data. Figure reproduced from Pisoni and colleagues,⁷⁰ by permission of Elsevier. AV=arteriovenous. GCC=Gulf Cooperation Council (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates).

Table 1:

Examples of factors affecting incidence and prevalence of treated ESKD

	Comments
ESKD incidence	Net trend in ESKD incidence varies (from strongly positive to weakly negative) across countries
Factors favouring higher incidence	
Increase in population size	Affects incident counts, not rate
Increase in population and age, and in prevalence of diabetes, hypertension, and obesity	Greater burden of risk factors for ESKD
Longer survival with chronic kidney disease	Yielding more people who can progress to ESKD
Increase in access to renal replacement therapy	In many low-income and middle-income countries
Larger percentage of gross domestic product spent on health care	Via effect on several other factors listed
Earlier start of dialysis therapy	Earlier as defined by higher eGFR at dialysis start
Factors favouring lower incidence	
Better treatment of diabetes and hypertension	Decreasing incidence of CKD or rates of CKD progression
Later start of dialysis therapy	Later as defined by lower eGFR at dialysis start
Greater use of conservative kidney management	Conservative kidney management is management without dialysis, for patients reaching ESKD
ESKD prevalence	Net trend in ESKD prevalence is increasing in nearly all countries providing data
Factors favouring higher prevalence	
Rising incidence of treated ESKD	Occurring in most countries
Increasing proportion of ESKD patients receiving a kidney transplant	On average patients with kidney transplant survive longer than dialysis patients
Longer survival for dialysis and transplant recipients	Documented in many countries
Fewer voluntary withdrawals from dialysis	Trends in dialysis withdrawals are uncertain in most countries
Factors favouring lower prevalence	
Stable or lower incidence of treated ESKD	Occurs in a few countries
Time-limited payment for dialysis	Occurs in some countries, where government support for payment is limited to, for example, 1 year of dialysis

ESKD=end-stage kidney disease. eGFR=estimated glomerular filtration rate. CKD=chronic kidney disease.

Table 2:

Haemodialysis practice areas and clinical measures that differ in Japan from Europe and the USA

	Japan	Europe*	USA
Vascular access			
Higher arteriovenous fistula use	91%	69%	68%
Anaemia			
Lower epoetin dose [†] (median units per week)	5000	7176	9000
Lower intravenous iron use [‡]	27%	69%	66%
Lower haemoglobin (g/dL)	10.5	11.3	10.9
Lower ferritin (ng/mL)	144	523	758
Mineral bone disorder			
Lower intravenous vitamin D use (vs USA)	36%	18%	60%
Lower parathyroid hormone (ng/L)	118	240	303
Dialysis prescription			
Lower blood flow rate (mL/min)	208	333	419
Lower Kt/V _{urea}	1.42	1.57	1.57
Longer dialysis session length (vs USA; min)	239	244	218
Dialysis routinely in supine position [§]	93%	53%	3%
Dialysate composition			
Higher dialysate sodium [¶] (mmol/L)	140	139	138
Lower dialysate bicarbonate [¶] (mmol/L)	29	34	36
Dialysate water			
JSDT standard for dialysis fluid is <0.050 EU/mL of endotoxin and a bacterial count <100 colony forming units per mL, the strictest in the world ^{15,59}	..	..	..
Cardiovascular factors			
Higher blood pressure (mm Hg)	146	138	145
Lower median CRP concentrations ^{**} (mg/L)	1.0	5.2	..
Use of tests			
Routine measurement of CRP ^{**} (% of facilities)	73%	70%	0
Routine chest radiographs ^{††} (% of facilities)	98%	59%	40%
Yearly screening for vascular calcification ^{††} (% of facilities)	38%	35%	7%
Patient preparation for dialysis^{‡‡}			
Higher proportion with pre-dialysis care ^{§§}	70%	76%	69%
Higher proportion with arteriovenous fistula use at haemodialysis initiation ^{§§}	84%	50%	28%
Lower estimated glomerular filtration rate at dialysis start ^{¶¶} (mL/min per 1.73 m ²)	6.8	9.5	10.1

Data are from the initial cross-section of patients enrolled in the Dialysis Outcomes and Practice Patterns Study (DOPPS) phase 5 (2012–15). Unless otherwise noted, values in the table represent the mean or prevalence weighted by the fraction of patients sampled in each participating facility. Kt/V_{urea}=a unitless measure representing clearance of urea (K) over the duration of a haemodialysis treatment (t), divided by the urea volume of distribution (V_{urea}). JSDT=Japanese Society for Dialysis Therapy. CRP=C-reactive protein.

* DOPPS phase 5 European countries were Belgium, Germany, Italy, Spain, Sweden, and the UK. France was excluded because of low DOPPS phase 5 enrolment at time of publication.

[†]Converted to intravenous epoetin equivalent dose; darbepoetin doses converted in ratio of 250:1; pegylated epoetin β (MIRCERA) doses converted in ratio of 208:1; subcutaneous doses converted in ratio of 1:15:1.

[‡]Prescription in the month before DOPPS enrolment.

[§]On the basis of DOPPS 3 (2006) enrolment data.

[¶]Excluding patients in whom dialysate sodium concentrations varied during treatment (sodium modelling or profiling).

^{//}Does not account for dialysate acetate concentration; median of 8.0 mmol/L for Japan, 3.0 mmol/L for Europe, and 4.0 mmol/L for the USA.

^{***}Restricted to facilities routinely measuring CRP at least once every 4 months for more than 75% of facility patients during DOPPS phase 5 follow-up.

^{††}Used data from DOPPS phase 5 year 3 (2014) medical director survey.

^{‡‡}4 months of prenephrology care.

^{§§}Among patients on dialysis $\geq$ 60 days at DOPPS enrolment.

^{¶¶}In patients enrolled in DOPPS within 120 days of starting dialysis; estimated glomerular filtration rate calculated with the Modification of Diet in Renal Disease (version 4) variable formulae, with variables of creatinine concentration, age, black ethnicity, and sex; qualitatively similar results obtained when also adjusting for Japanese ethnic origin.