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## **The value of dialysis and conservative care for older patients with advanced chronic kidney disease**

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## **General introduction**

## INTRODUCTION

### Box 1: case

Today, you are seeing an 80-year-old man with advanced chronic kidney disease for a routine check-up; you are his nephrologist. He was referred by the cardiologist about a year ago because of his deteriorating kidney function. His medical history includes a myocardial infarction, a coronary artery bypass grafting procedure, and heart failure since recent years. Despite an increasing need for diuretics to control his heart failure, he is still able to perform his daily activities, including walking and playing the clarinet. He is married, has four children, and ten grandchildren. Over the past year, his estimated glomerular filtration rate (eGFR) gradually dropped from 18 mL/min/1.73 m<sup>2</sup> to 15 mL/min/1.73 m<sup>2</sup> today. If his kidney function continues to decline at this rate, he might need to start dialysis treatment during the next year. You both wonder what to do. Should he start dialysis once needed, or what would be the best treatment plan? What would fit best in his goals of care?

### Dialysis treatment

Much has changed for patients with kidney failure since the development of the first artificial kidney by the Dutch internist Willem J. Kolff about 75 years ago. Kolff commenced his search to find “*other ways for excretion of retention-products*” in patients without diuresis several years earlier after being confronted with the death of a 22-year-old man due to acute kidney failure [1, 2]. His goal was to develop an artificial kidney based on the principle of dialysis. Dialysis involves the shift of molecules from one solution to the other using a semipermeable membrane. Kolff succeeded in building the first dialysis machines to be used in human beings with kidney failure in a hospital in Kampen, The Netherlands, under difficult circumstances during the Second World War [2]. It was not until two years later, in 1945, that the first of his seventeen patients successfully survived to recovery with dialysis treatment [1]. The invention of the artificial kidney became a major technological achievement in medicine.

Initially, dialysis treatment offered a life-saving therapy for patients with acute kidney failure who would otherwise have died. An important breakthrough came in 1960

with the development of the Scribner shunt, allowing repeated vascular access [3]. Maintenance treatment with dialysis now became feasible for patients with chronic kidney failure as well. Due to rationing, special selection committees were appointed to allocate dialysis treatment to the most suitable patients [4, 5]. Next to criteria as the patient's age and level of comorbidity, these so-called God Committees sometimes used subjective selection criteria such as “social worth”, which received much criticism [6]. Rationing based on some form of criteria-based selection, however, remained widespread for many years, with most older and comorbid patients being excluded from dialysis treatment [7]. Following expansion in dialysis provision and after recognition of unwarranted undertreatment of specific patient subgroups [8, 9], exclusion of eligible patients gradually disappeared. Nowadays, dialysis treatment can be offered to each eligible patient in many countries and has become an established practice, also in older patients and patients with comorbid conditions.

### **Changing patient population**

Over the last decades, the global burden of advanced chronic kidney disease has risen considerably [10]. This rise has been driven by factors as population growth, aging, and the increased burden of obesity, diabetes, and hypertension [11, 12]. Advanced chronic kidney disease involves a chronically and severely reduced kidney function, in which the often gradual progressive loss of kidney function could result in the need for kidney replacement therapy such as dialysis. Advanced chronic kidney disease is defined as stages G4 (eGFR 15–29 mL/min/1.73 m<sup>2</sup>) and G5 (eGFR <15 mL/min/1.73 m<sup>2</sup>) of chronic kidney disease, based on the classification by Kidney Disease: Improving Global Outcomes (KDIGO) [13]. Alongside the increasing number of patients, the characteristics of the patient population with advanced chronic kidney disease have changed substantially as well. Older patients now represent the largest and fastest growing group, including patients aged of at least 70 or 80 years old [10, 14]. Among older patients, dialysis has become the most common treatment for advanced chronic kidney disease and is nowadays often considered the default treatment pathway in this setting [15–17]. The majority of patients starting with dialysis is nowadays older than 65 years in countries like the United States, the United Kingdom, and The Netherlands [18–20]. Compared to younger patients, older patients are more often frail, have more comorbid conditions, and have more functional impairments [21]. These changes have led to concerns about the appropriateness of dialysis treatment in the older patient population [11, 16, 22]. Will dialysis, while being technically feasible in the vast majority,

always be of benefit in the lives of older patients with advanced chronic kidney disease? Dialysis is an intensive therapy that older patients and healthcare professionals might consider as too burdensome, outweighing its potential benefits.

### **Conservative care: a viable alternative?**

Conservative care has been proposed as a potential alternative to dialysis treatment in older patients with advanced chronic kidney disease [23-25]. Conservative care involves ongoing multidisciplinary care and active medical treatment including all interventions needed, except for dialysis [23]. The main goal of conservative care is to preserve quality of life with adequate symptom control rather than life prolongation per se. A conservative care pathway is intended to be provided until death (not just to postpone dialysis). Common elements are medical and dietary interventions to control fluid and electrolyte balance, treat anemia, and minimize symptoms such as pain and pruritus, as well as provision of palliative and end-of-life care. Estimates indicate that up to 15% of older patients decide to forego dialysis and choose a conservative care pathway instead [26-28].

Data on outcomes in both treatment pathways are needed to evaluate whether conservative care is a viable alternative to dialysis in older patients and, if so, to help inform the decision-making process on treatment plan by the patient and healthcare professional. Robust data are, however, limited available. The few studies that compared outcomes between older patients on either a dialysis or conservative care pathway so far were all observational and generally determined survival only [29, 30]. Furthermore, most of these studies included small and heterogeneous study populations, were performed in the United Kingdom only, and defined considerably different time points for survival analysis (*e.g.*, from treatment decision, or based on a threshold eGFR) [31]. Patients consider outcomes other than survival to be important as well, such as health-related quality of life and treatment burden [32-34]. Hence, more adequate data on survival as well as data on more patient-relevant outcomes are needed to evaluate whether conservative care is a viable treatment alternative to dialysis in older patients. This need for more patient-relevant outcome data on both treatment pathways has been recognized as research priority by patients, healthcare professionals, and organizations like KDIGO [23, 35, 36]. Furthermore, comparative data on treatment costs are needed next to patient-relevant outcome data to evaluate the value of both treatment pathways for society as well.

**How to decide which treatment plan is best?**

Shared decision-making is recommended as the model for all decision-making, including for decision-making about possible treatment for advanced chronic kidney disease in older patients [37, 38]. The main goal of shared decision-making is to enable decision-making by the patient and healthcare professional working together on a treatment plan that is consistent with the patient's values and preferences and also professionally acceptable. Its fundamental idea is that the patient is the expert on what matters in their life and the healthcare professional is the expert on biomedical evidence. Hence, shared decision-making aims to combine the unique expertise of both the patient and healthcare professional, in order to come to an individualized treatment plan that is of benefit in the patient's life.

Despite efforts to implement shared decision-making and improve patient involvement, shared decision-making appears to be not yet routine in clinical practice [37, 39-41]. Studies found patients describing poor decision-making experiences, particularly patients who chose the most intensive treatment pathway: dialysis [32, 33, 42, 43]. In current practice, for instance, patients often indicate to experience a lack of power, despite being informed about the possible treatment options [44, 45]. At the same time, studies also observed that a substantial part of older patients with advanced chronic kidney disease still doubts or even regrets their treatment decision afterwards, especially if the decision was more driven by the healthcare professional's preference [46-48]. Evaluation is needed how decision-making on treatment plan for advanced chronic kidney disease could be improved and become more shared. Specifically, reconsideration is needed what conception of shared decision-making is best in this chronic care setting, involving older and often frail patients with multiple comorbid conditions who approach the end of life [49, 50].

Therefore, the central questions of this thesis are:

1. What is the value of dialysis and conservative care for older patients with advanced chronic kidney disease?
2. How could shared decision-making be improved to enable older patients with advanced chronic kidney disease to decide which treatment plan is best?

Together, more insight could help to improve clinical care for older patients with advanced chronic kidney disease, such as the 80-year-old man described above.

## OBJECTIVES AND OUTLINE OF THESIS

The first main objective of this thesis is to determine the value of dialysis and conservative care for older patients with advanced chronic kidney disease. Specifically, our aim is to compare a combination of patient-relevant outcomes and treatment costs in older patients who chose either dialysis or conservative care after a shared decision-making process.

To support the shift towards measuring outcomes relevant to patients with chronic kidney disease in general, **Chapter 2** describes the development of a standardized minimum set of patient-relevant outcomes for chronic kidney disease care by an international multidisciplinary working group, initiated by the International Consortium for Health Outcomes Measurement (ICHOM). Defining a consensus recommendation on the outcomes that matter most to patients and other stakeholders is needed to enable standardization of health outcome measurement in different settings. Standardized health outcome measurement may help to improve the quality of chronic kidney disease care, support the shift towards value-based healthcare, and could inform shared decision-making. In this chapter, we describe the development of a standardized minimum set of health outcomes that are deemed most important to patients with chronic kidney disease, including patients treated with dialysis or conservative care, and that is targeted for integration into routine clinical practice.

To determine the value of dialysis and conservative care, we retrospectively identified a single center cohort of older patients with advanced chronic kidney disease (stages G4/G5). We included all patients aged  $\geq 70$  years old who had made an explicit decision in favour of dialysis or conservative care after a shared decision-making process. Shared decision-making on preferred treatment plan was initiated as part of standard care when the patient's eGFR gradually decreased  $< 20 \text{ mL/min/1.73 m}^2$ . An experienced and multidisciplinary team of nephrologists, nephrology nurses, social workers, and dieticians was involved in the shared decision-making process. Patients on a dialysis pathway comprised all patients who chose dialysis, irrespective whether or not dialysis was started during follow-up. In patients choosing conservative care, active medical treatment and multidisciplinary care were continued.

**Chapter 3** describes the results on survival in our retrospective cohort of older patients ( $\geq 70$  years old) who chose either a dialysis or conservative care pathway after a shared decision-making process. We assessed survival outcomes from multiple time points, including time of treatment decision (main time point; being most informative to patients during decision-

making) and three time points based on a threshold eGFR ( $<20$ ,  $<15$ , and  $<10$  mL/min/1.73 m<sup>2</sup>). **Chapter 4** includes a value-based evaluation of survival, health-related quality of life, treatment burden, and treatment costs in an extended patient cohort of older patients ( $\geq 70$  years old) who chose either a dialysis or conservative care pathway. This evaluation is based on the concept of value-based healthcare in which value of delivered care is defined as the benefits on health outcomes achieved per monetary unit spent (value = outcomes/cost) [51]. Value-based healthcare is promoted as strategy to improve care quality by monitoring, comparing, and acting on patient-relevant outcomes in combination with costs [52]. Using a value-based perspective, we compared the value of dialysis and conservative care for: (1) older patients with advanced chronic kidney disease in terms of survival and health-related quality of life versus treatment burden; and (2) society in terms of patient-relevant outcomes per monetary unit spent. An addendum to Chapter 4 (**Chapter 4a**) contains a critical appraisal of two outcome measures on health-related quality of life described in Chapter 4, since several different scoring algorithms appeared to be used in similar studies. **Chapter 5** describes a systematic literature review of all studies published so far that compared health-related quality of life outcomes and symptoms among patients who chose either a dialysis or conservative care pathway for advanced chronic kidney disease. **Chapter 6** provides further evaluation of hospital utilization and costs in our retrospective cohort of older patients ( $\geq 70$  years old) who chose either a dialysis or conservative care pathway, including a comparative analysis of hospital utilization and costs near the end of life.

The second main objective of this thesis is to evaluate and improve shared decision-making regarding treatment plan for advanced chronic kidney disease in older patients. **Chapter 7** describes older patients' experiences with their shared decision-making process on choosing dialysis or conservative care, providing insight in barriers and facilitators. Following these results and based on wider observations, **Chapter 8** includes a reconsideration how decision-making might become more shared. For this complex chronic care setting, we describe the need for a person-centered conception of shared decision-making, which aims to come to a treatment plan that fits best in the patient's goals of care by focusing on all that matters to the patient, as person.

Finally, **Chapter 9** contains a summary and general discussion of the main findings in this thesis, including our concluding remarks on the value of dialysis and conservative care for older patients with advanced chronic kidney disease, and future directions for research and clinical care.



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