# Beating kidney disease

## A joint agenda for research and innovation

nvn Dutch Kidney Patients Association

DUTCH KIDNEY FOUNDATION

NFN Dutch Federation for Nephrology

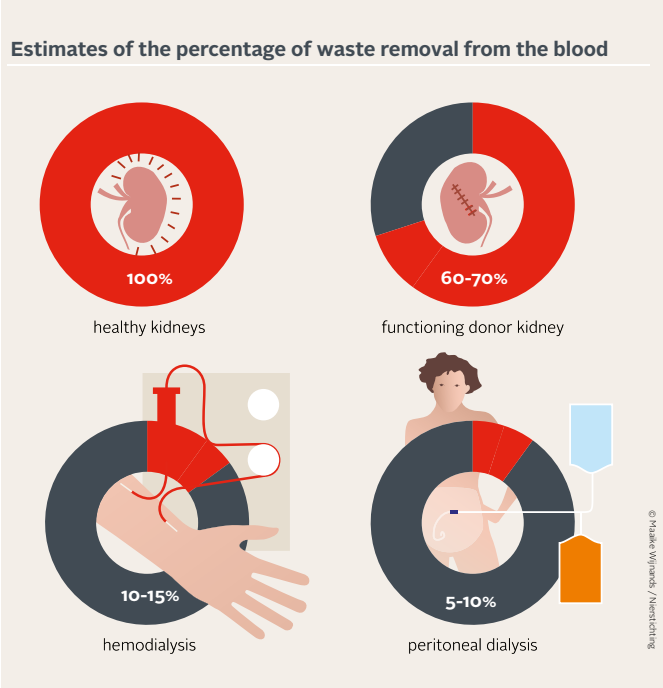
# Toward sustainable kidney health

The Dutch Kidney Patients Association, the Dutch Federation for Nephrology and the Dutch Kidney Foundation have jointly developed this strategic agenda for research and innovation. This agenda unites forces in order to put the great importance of kidney health firmly on the map. We wish to foster a general awareness of the serious negative impact of kidney damage and kidney disease on patients and on society as a whole. Our aim is to lay the foundation for a broad approach to chronic kidney disease that is aligned with the national science policy of the Netherlands. This strategic agenda is a starting point for further development, the next step will be to work out the agenda into a knowledge agenda for kidney health.

The Netherlands is facing a major challenge: we need to improve healthcare for kidney patients and people with kidney damage. The number of patients with kidney disease and kidney failure is increasing, with limited treatment options, poor outcomes and high cost. And the impact of kidney disease on the quality of life of patients and their families is immense. When compared with the general population, the rate of unemployment among kidney patients is high and participation in social, cultural and community activities significantly declines. The treatment is expensive while financial support within our healthcare system is limited. Thus, we need to find sustainable healthcare solutions for patients with kidney disease.

## Life style and ageing

Chronic kidney disease is never isolated – it is often accompanied by diabetes and/or cardiovascular disease. The number of kidney patients and people with chronic kidney disease will increase in the coming years due to, among other things, an ageing population and the rise in diabetes and cardiovascular disease. It is therefore of great importance that we put more effort in early detection and prevention of kidney disease. We need to develop the best treatments for kidney disease, to restore the highest quality of life possible for kidney patients and ultimately, find a cure for kidney disease.




The Netherlands boasts an advanced infrastructure for research and innovation and is internationally recognized as a leader in the field of renal research. These are strong ingredients for meeting the challenge and this strategic agenda fits well within the national policy for science and innovation. An essential component for success is intensive collaboration between scientists, healthcare providers, patients and other parties – as is already established within the Dutch renal field. All groups in the field are convinced that we need joint action for a better quality of life for patients with chronic kidney disease.

In order to write this strategic agenda, we held interviews and discussions with departmental heads and researchers of the nephrology departments in the university medical centres (academic research hospitals), and with scientists and healthcare providers in the field of chronic kidney disease. We also organized discussions with patient focus groups and representatives from the Dutch Kidney Patients Association, the Dutch Federation for Nephrology and the Dutch Kidney Foundation, and with the Scientific Advisory Board of the Dutch Kidney Foundation.

## Laying the foundation

We present a broad agenda covering four strategic themes for research and innovation and five underlying principles that are required for achieving optimal impact of research and innovation for kidney patients now and in the future. This agenda lays the foundation for developing a master plan for research and innovation in collaboration with many partners and with a firm embedding in Dutch science policy and the Dutch National Research Agenda. This is a starting point on the road towards sustainable kidney health in an vital society.

# Beating kidney disease

"How do we promote a healthy lifestyle and prevent illness?"
"How do chronic diseases arise and how can we detect them in an earlier stage?"
"What can I do myself?"

"How can we treat chronic kidney diseases individually?"
"What is the best combination of (anti rejection) medication?"
"How will knowledge about genetics play a role in understanding, screening and treating diseases?"
"What are the long term effects of medicines?"

"What are the psychological and physical consequences of chronic disease for quality of life and participation in society?"
"How can I deal with limitations such as fatigue?"

"How can we repair damaged tissues and organs by using (stem) cells and biomaterials?"
"What are innovative methods for growing organs for transplant?"

**THEME:**
*Preventing and controlling kidney damage*

Detect and tackle kidney damage at an early stage. Ultimately, prevent all kidney damage.

**THEME:**
*Personalised medicine*

Develop better forms of treatment, tailored to individual kidney patients.

**THEME:**
*Living with a kidney disorder*

Develop better support for patients to deal with the practical, psychological and societal effects of kidney disease.

**THEME:**
*Regenerative medicine*

Repair kidney damage and kidney function by stimulating the body's own repair mechanisms. Ultimately cure kidney disease.

**These five principles are required for achieving optimal impact of research and innovation for kidney patients now and in the future:**

*Patient perspective*
impact from the patient's perspective in research and innovation

*Economic perspective*
impact from an economic perspective in research and innovation

*Harness knowledge*
from fundamental research to tangible innovation for the patient

*Cooperation*
between all stakeholders and target groups

*Infrastructure and resources*
a strong infrastructure, stimulating environment and sufficient resources

***These questions are examples we derived from the Dutch National Research Agenda (NWA) and the research agenda from the Dutch Kidney Patients Association***

# Great urgency

## More people with kidney damage

Chronic kidney disease is a worldwide health burden with great economic impact. In the Netherlands alone, more than one in ten individuals has chronic kidney disease (Dutch Kidney Foundation 2016b). This number is expected to increase in both the short and long term, due to an ageing population and the rise in the number of patients with risk factors such as diabetes and cardiovascular diseases.
The most common causes of chronic kidney disease are diabetes, high blood pressure and narrowing of the arteries (arteriosclerosis). In turn, kidney disease can exacerbate conditions such as cardiovascular disease, bone disease (osteoporosis), high blood pressure and anaemia. Tackling kidney disease is therefore relevant to many patient groups.

## Late detection: missed opportunity

Most patients with early stages of chronic kidney disease have no symptoms, yet even these stages of reduced kidney function already increase the risk of morbidity and mortality. Patients may experience symptoms only when kidney function drops to around 30% – which can lead to late diagnosis. Unfortunately, by that time, chronic kidney disease is – as of now – irreversible (Dutch Kidney Foundation 2016a). In addition, multimorbidity (when a patient has two or more chronic conditions) and the natural decline in kidney function due to normal ageing also increase the complexity of diagnosis and treatment. Therefore, recognizing early stages of kidney disease may enable the implementation of preventative or treatment strategies that may delay or even stop the progression of kidney disease.

## Specific treatment is lacking

The exact mechanisms responsible for the development and progression of kidney disease are still unknown.
In almost a quarter of all cases, the cause of chronic kidney disease is unclear. In almost a fifth of all cases, there is a hereditary or congenital kidney defect, many of which are rare to extremely rare and can result in renal failure at a very early age. Currently, patients, even those with rare kidney diseases, are treated with more general strong, systemic drugs. There is a great need for specific treatments targeting the underlying mechanisms.

## Limited quality of life for patients with kidney failure

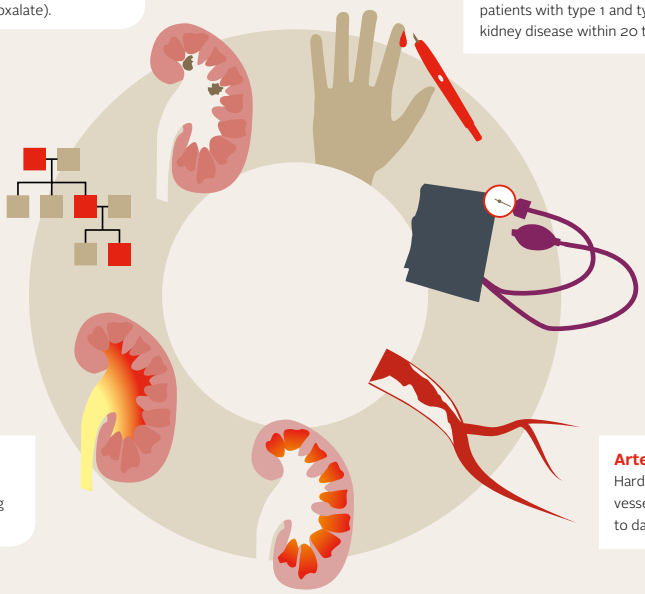
Chronic kidney disease may progress to kidney failure, which is fatal unless a patient receives renal replacement therapy – a kidney transplant or dialysis – which can extend their life expectancy. A kidney transplant is preferred because it generally results in a better quality of life and a higher life expectancy. There are more than 10.000 people with a functional donor kidney in the Netherlands (Dutch Kidney Foundation, 2016c). However, kidney transplantation is not a solution for all patients – for medical or personal reasons. Furthermore, there is a severe shortage of donor

## Frequent causes of damage to the kidney

**Kidney stones**
Stones develop when the urine contains more salts than it can hold in solution (for instance calcium oxalate).

**Diabetes**
This disease causes damage to the small blood vessels in the kidney filtration units (glomeruli). In the Netherlands, 25 to 40 per cent of the patients with type 1 and type 2 diabetes mellitus will develop chronic kidney disease within 20 to 25 years after first diagnosis.

**Hereditary kidney disease**
For example Alport syndrome or polycystic kidney disease.



**High blood pressure** (hypertension)
Directly injures the blood vessels and the kidney filtration units (glomeruli). About one in five hypertensive patients has chronic damage to the kidneys.

**Renal pelvis infection** (pyelonephritis)
Urine flowing back from the bladder to the kidney can cause renal infection. Frequent infection causes lasting damage to the kidney.

**Arteriosclerosis**
Hardening of the arteries and thickening of the vessel walls. Narrowing of the arteries can lead to damage to the kidneys.

**Inflammation of the glomeruli** (glomerulonephritis)
When the kidney filtration units are harmed by inflammation. Can be caused by for instance autoimmune disease.

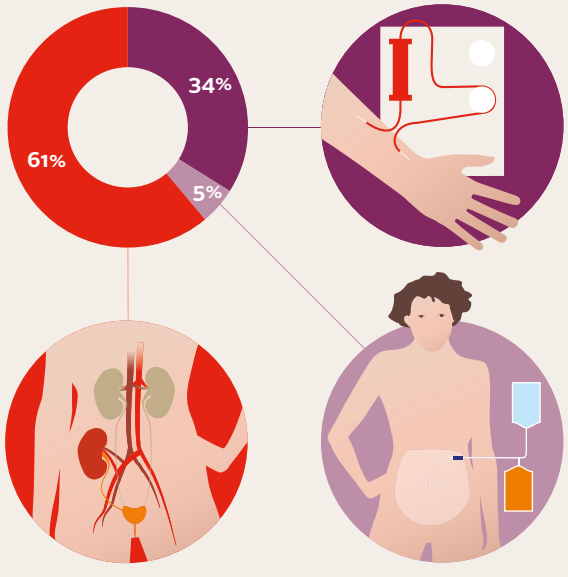
kidneys (both post-mortem and living donors) and a waiting list for transplants. More than half of the patients on this waiting list will wait over two years for a kidney from a post mortal donor – for a number of patients the waiting time will run up to five years or more (Dutch Kidney Foundation, 2016d). More than half of the renal transplants in the Netherlands are from living donors, these generally have a better outcome. Still, after transplantation every transplant patient requires lifelong anti-rejection medication that comes with numerous side-effects and these can negatively impact on the lives and welfare of patients and their families. Even then, the risk of organ rejection is always a concern: 10 years after a transplant, only 45% of post-mortem donor kidneys and 65% of living donor kidneys are still functional.

In the Netherlands there are about 6.500 patients on dialysis (Dutch Kidney Foundation, 2016e). A common misunderstanding is that dialysis completely replaces the kidney function so that a patient can lead a normal life. Sadly, dialysis only compensates for 5 to 15% of kidney function compared to healthy kidneys. There are several types and methods of dialysis (filtration through an artificial kidney via blood vessels in the arms; filtration through the abdominal cavity (peritoneum); at home or in a centre; during the day or at night), and for each treatment, the daily routine of all patients is affected as they must adhere to a strict diet and no more than half to one litre of fluids per day. Most haemodialysis patients undergo dialysis three times a week, with each session lasting four to five hours. Dialysis causes side effects such as fatigue, nausea, cramping and dizziness, and is stressful to the heart and blood vessels. Every year, one in six dialysis patients dies (Dutch Kidney Foundation, 2016e). Furthermore, many dialysis patients cannot maintain paid employment status and participating in social and cultural activities becomes more difficult. Dialysis is a last resort, yet it comes with a number of drawbacks and is a considerable burden on close relatives. Although dialysis is life-extending, it is certainly not an ideal treatment (Dutch Kidney Foundation, 2016c).

## High healthcare costs

The high cost of chronic kidney disease has a significant economic impact. The most recent *Costs of Illness in the Netherlands study (Kosten van Ziektenstudie)* was carried out by the Dutch National Institute for Public Health and the Environment (RIVM) in 2013. This study calculates the costs of healthcare in the Netherlands for different disease areas. They reported that in 2011, the healthcare cost of chronic kidney diseases in the Netherlands totalled 800 million euros (RIVM, 2011). The costs associated with renal replacement therapy are particularly high. According to an earlier study, the annual cost of dialysis is between 80,000 and 120,000 euros per patient and the one-time cost of a kidney transplant is about 80,000 euros. For transplant patients, there are also follow-up costs, for example, lifelong anti-rejection medication. As such, renal replacement therapies are among the most expensive treatments covered by health insurance in the Netherlands (Dutch Kidney Foundation, 2016c). In addition, there is also considerable budget allocated to patients with chronic kidney diseases who receive other forms of therapy. In order to attain sustainable and affordable healthcare for kidney patients, excellent research and innovation are essential (Vanholder, 2017).

**Distribution of renal replacement modalities in patients in the Netherlands (1 January 2016)**



# Now is the moment: opportunities for research and innovation

A Dutch physician, Professor Willem Kolff, invented the first working artificial kidney during World War II and used it to save a patient in 1945 – the first successful dialysis.
His invention has evolved into current dialysis machines and since then, we have been able to extend the lives of patients with kidney failure. This is one example of the many innovations and developments that have considerably improved the lives of people with kidney disease. Nevertheless, there is still an urgent need for research and innovation in the field of kidney damage and kidney disease, and the Dutch kidney research field is well-positioned to face this challenge.

## Highly regarded

Dutch scientists in the field of nephrology are internationally recognized. In terms of citations per publication, the Netherlands ranks among the top three of the countries with a large nephrology research output. Calculated over the last 20 years, the Netherlands even ranks first (Scimago, 2016). Dutch researchers are involved in major, multidisciplinary and public-private research consortia and work closely with private organisations. In particular, Dutch researchers, together with the Dutch Kidney Patients Association, are actively involved in developing and improving connections with patients, healthcare providers and other stakeholders. For instance, experiences of kidney patients have led to the establishment of outcome measures for clinical care. In addition, the various organisations are already working closely together to stimulate more innovation within the themes of this agenda; for example, the Dutch Kidney Foundation is working on the development of a portable artificial kidney. Data is systematically collected from the entire Dutch healthcare system by the quality control institute Nefrovisie, to improve prevention of kidney diseases and the quality of care. This nationwide system of quality control policy and registration of patients receiving renal replacement therapy serves as a good basis for introducing new advancements in clinical care (Registratie Nierfunctievervanging Nederland, Renine).

## Coordination with national policy

National policy for research and innovation is in motion with innovation as a leading theme. The connection between science and society, the basis of the Dutch National Research Agenda (Nationale Wetenschapsagenda NWA; OCW, 2014 & NWA, 2016), underlies important policy adjustments.
The academic hospitals have developed a vision for sustainable health (Dutch Federation of University Medical Centres, NFU, 2017); the Health Council of the Netherlands (Gezondheidsraad) proposes that the university medical centres reorient their research policies to a wider research spectrum that better addresses societal needs ('Onderzoek waar je beter van wordt', Health Council 2016); the Union of Collaborating Universities (Vereniging van Samenwerkende Universiteiten) aims to put the Netherlands on the map as a pioneer in research and innovation for people-oriented information technology (VSNU, 2016). These initiatives have a significant influence on the organization of science and innovation in the Netherlands and are also aimed at fitting well with the research policy of the European Union.
The latter strongly advances valorisation of research, interdisciplinary collaboration and partnering with companies (Horizon 2020).

## Greater impact

The theme of kidney health fits perfectly within the national and international landscape. There is an urgent need to develop innovative clinical care solutions for patients, which requires cohesive cooperation between all stakeholders, from patients to professionals, and a strong scientific infrastructure. Together, we can develop a united approach for the prevention, diagnosis, treatment and sustainable care of patients with chronic kidney disease and this should become firmly embedded in the overarching policy for research and innovation. Because chronic kidney disease is complex and stands in a reciprocal relation with other diseases like diabetes and cardiovascular disease, addressing kidney health is relevant to a broader patient community. By extending and intensifying collaborations, interacting closely with patients and responding promptly to national and international policy developments, we aim to achieve a greater impact with research and innovation for existing and future kidney patients, and to reduce the burden on society.

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# Four themes for research and innovation

### 1. Preventing and controlling kidney damage

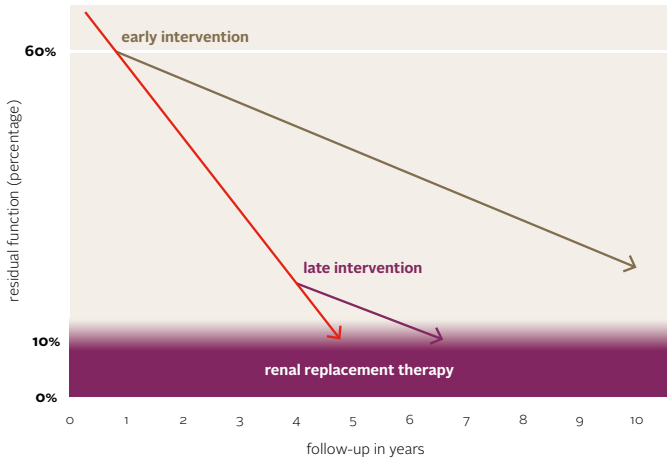
**The aim of this theme is the better detection and treatment of kidney disease in its early stages. It concerns the wider target audience of people with or at risk of kidney damage as well as existing patients with a specific kidney disease. Through prevention, early detection and the slowing down of kidney disease, we aim to tackle the high individual and societal costs of kidney disease at its roots. Ultimately, we want to prevent kidney disease from happening.**

The early signs of chronic kidney disease often go unnoticed. The first symptoms are usually non-specific and difficult to identify. In most cases, patients display symptoms when kidney function has fallen to approximately 30%, and consequently, chronic kidney disease is often diagnosed late. Having started, kidney damage will slowly and irreversibly progress. Moreover, the risk of other conditions and complications, especially due to cardiovascular disease, is already increased in early stages. As kidney function declines, so does the patient's quality of life, while the costs of treatment steadily increase (Vanholder, 2017).

Prevention focuses on stopping or controlling kidney damage through early detection, a healthy lifestyle and treatment. There is growing evidence that with minor kidney damage, early preventive measures such as blood pressure medication and a healthy lifestyle can be beneficial. The identification of kidney damage and interventions targeting risk factors are therefore crucial, not only at an early stage, but at each stage of kidney disease, in order to prevent the exacerbation of kidney damage. The combination of screening and early treatment, not only in high-risk groups but also in the general population, may be a valuable approach.

Kidney damage caused by diabetes, high blood pressure or arteriosclerosis appears later in life. It is possible to detect kidney damage long before the symptoms appear, and thus treating early stages of kidney disease must be incorporated into standard clinical care. Although technological advancements and pharmaceutical therapies are valuable, we must also consider novel interventions that focus on social factors. A person's perceived or actual health is often linked to factors in their physical and social surroundings, such as their education level and income, which may influence disease and treatment management.

**Improved health through early intervention**

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*"How do we promote a healthy lifestyle and prevent illness?"*
(Source: NWA, 2016)

*"How do chronic diseases arise and how can we detect them in an earlier stage?"*
(Source: NWA, 2016)

*"What can I do myself?"*
(Source: Dutch Kidney Patients Association, 2016)

We call for a broad approach that requires examining all factors that influence a person's lifestyle, including knowledge and motivation; social interactions and physical environment; organization of care, education, economy, politics and society. Integrating these will paint a picture of the therapeutic effectiveness and cost-benefit of all possible interventions within the entire spectrum, from mild to severe kidney disease, as well as the value of an intervention from the perspective of each patient.

The Dutch kidney field has extensive experience in developing new interventions. In 2006, a campaign called "Stop early kidney disease" was launched, based on the scientific study Prevention of Renal and Vascular End-stage Disease (PREVEND) which examined a cohort of more than 7,500 patients. In order to increase awareness of kidney disease prevention and identification, the Niercheck (kidney check) was established and more than 1.2 million people participated in a simple urine sample home test. It is estimated that the Niercheck identified several thousand new patients: 200 people with kidney disease, 300 with diabetes, 1,600 with high blood pressure and 3,200 with kidney damage (NIVEL, 2007). This indicates that with certain early detection measures, we have a chance to interrupt and possibly stop the progression of kidney disease. In 2018 the Dutch Kidney Foundation – together with UMCG, KPN E-zorg and healthy.io – starts a project to investigate whether screening for kidney damage in the general population yields health benefits and is cost effective.

## 2. Personalised medicine

**The aim of this theme is to develop better forms of treatment, tailored to individual kidney patients. We are striving towards treatments and innovations that focus as closely as possible on a patient's individual genetic properties and underlying disease mechanisms as well as their personal preferences, requirements, lifestyle and environment.**

*Personalised medicine*, also known as *precision medicine*, has the potential to provide more focused care and customized treatments to patients with kidney disorders. Previous research into similarities in symptoms and the course of disease among patients with kidney disease has led to guidelines and protocols that greatly improved treatment, including better genetic diagnostics. Nevertheless, treatment is often still not optimally tuned to the individual patient.

*"How can we treat chronic kidney diseases individually?"*
(Source: NWA, 2016)

*"What is the best combination of (anti rejection) medication?"*
(Source: Dutch Kidney Patients Association, 2016)

*"How will knowledge about genetics play a role in understanding, screening and treating diseases"*
(Source: NWA, 2016)

*"What are the long term effects of medicines?"*
(Source: Dutch Kidney Patients Association, 2016)

There is a strong need for more in-depth knowledge about the molecular differences among groups and subgroups of patients with certain kidney disorders, as well as non-genetic risk factors such as lifestyle and behaviour. This will enable us to better stratify patients in order to develop more accurate therapies and encourage therapy compliance. It is therefore important to properly unite biomedical and social sciences.

Big data collection and analysis is becoming essential for understanding the efficacy and safety of therapeutics. This is particularly promising given the rapid advancement of computational and analytical capacities (VSNU, 2016). Personalised medicine combines quantitative approaches with individual needs of patients in order to determine the optimal treatment regimen for each patient.

Personalised medicine will greatly benefit patients who currently do not fit into a more general therapeutic category. Such patients include the elderly, children and patients who suffer severe side effects from treatment. Over time, a more customized approach will also achieve better results for more patients.

In order to fully capitalize on the potential of personalised medicine, we need more comprehensive research and innovation. As future technological and pharmaceutical innovations enrich and broaden current treatment options, it is important to ensure that these align closely with the patient's wishes, requirements and characteristics. It is therefore necessary to connect to and include insights from patients as early as possible in the research process. Proper development of effective treatments will also reduce the cost of healthcare.

One example of this is the Dutch DOMESTICO (Dutch Nocturnal and Home Dialysis Study to Improve Clinical Outcomes) study, a joint project with healthcare insurers. DOMESTICO aims to remove barriers to home dialysis and to identify which patients would benefit from dialysis at home. This would provide patients with more continuous dialysis in the comfort of their own home and afford them more flexibility in their daily routine. By combining data from a large patient cohort (to look retrospectively) and a new clinical trial, the project examines benefit to the patient (patient choice and clinical outcomes) and society (cost-effectiveness). The goal is to find the right balance between optimal quality of life for the patient at minimal cost.

### 3. Life with a kidney disorder

**The aim of this theme is to develop better support for the patient when dealing with the practical, psychological and societal effects of kidney disease. For patients, kidney health is a much broader issue than proper renal function alone. We want to turn patients' questions into a scientific approach, research and innovations that make a real difference.**

Living with a kidney disease means much more than dealing with a physical illness. Therefore, research into the practical, psychological and social factors that affect patients is of great importance. Research among patients shows that issues like fatigue, mood changes, therapy compliance, depression, side effects of medication, itching, self-management and lifestyle often result in very practical questions. We aim to increase awareness and research into such questions in order to understand how patients and their families can improve their quality of life.

*"What are the psychological and physical consequences of chronic disease for quality of life and participation in society?"*
(Source: NWA, 2016)

*"How can I deal with limitations such as fatigue?"*
(Source: Dutch Kidney Patients Association, 2016)

To do this, we must first turn the questions asked by patients and their families into relevant research questions. Findings from other chronic conditions serve as examples for kidney disease. This theme requires close interaction between scientists and patients, with a focus on how patients perceive their own experiences with respect to treatment and quality of life. The resulting research fits in well with de advice from the Health Council of the Netherlands (Health Council 2016).

The Dutch kidney field is currently developing and translating Patient Reported Outcome Measures (PROMs) – self-reporting methods, such as questionnaires – for all Dutch kidney patients. We participate in the International Consortium for Health Outcomes Measurement (ICHOM), which strives to create a standard set of measurements and clinical outcomes as perceived by patients and patient representatives, and our input is reflected in both the questionnaire research and as members of the steering committee.

In addition, we are involved in the Standardised Outcomes in Nephrology (SONG) initiative. In collaboration with all stakeholders, SONG is developing sets of core outcomes and outcome measures for specific treatment methods, such as haemodialysis and transplantation. These are based on shared priorities of all stakeholders to ensure that they are meaningful for patients and their caregivers.

## 4. Regenerative medicine

**The aim of this theme is the repair of kidney damage and restoration of kidney function by stimulating the body's own repair mechanisms. This promising field is rapidly developing with good long-term prospects. We want to remain at the forefront of regenerative medicine so that kidney patients can quickly and fully benefit. Our ultimate aim is to cure kidney disease.**

Regenerative medicine focuses on the functional repair of damaged tissues and organs by making use of the inherent properties of our own organs and cells. A key approach is the use of our body's own stem cells, which can be cultured into new kidney cells. In the future, we hope that stem cell-based treatments will be able to restore renal function for patients suffering from kidney failure, thereby creating a solution for stressful dialysis treatment and the shortage of kidney donors.

*"How can we repair damaged tissues and organs by using (stem) cells and biomaterials?"*

(Source: NWA, 2016)

*"What are innovative methods for growing organs for transplant?"*

(Source: Dutch Kidney Patients Association, 2016)

At present, renal transplant patients have to take immunosuppressant drugs to mitigate the risk of organ rejection. New tissue grown form a person's own stem cells, however, will not be rejected by that person's immune system. Research into this area includes, for example, the construction of a new, functional kidney by prompting stem cells to differentiate into kidney tissue which can be grown in a kidney-like structure (*scaffold*). Our long-term goal is to grow a kidney derived from an individual patient's own cells for transplantation.

Another application is the use of organoids: miniature organs grown from stem cells. We already use organoids to screen drug candidates and to predict a patient's response to treatment and organoids may also help reduce the numbers of animals needed for testing. Organoids show great promise for customized therapies and regenerative medicine.

We're also focused on stimulating or helping the body's own natural regeneration capacity to reduce local kidney damage or stop the progression of damage. In addition, bio fabrication enables the automated production of three-dimensional structures that combine synthetic materials and living cells. We can therefore envision the bioprinting of artificial renal tubules, which may lead to the development of functional bioartificial kidneys that can be transplanted back into the patient. Ultimately, we want to reverse the process of kidney damage.

Regenerative medicine is quickly advancing and holds great potential. RegMed XB, an international public-private research consortium, was established in 2016 and contains an important 'moon shot' aimed at the kidney with a focus on the development of a bioartificial kidney. Researchers in the Netherlands also participate in international consortia for regenerative nephrology, including Stellar (Stem cell based Therapy for Kidney Repair) and RECORD KID (RECellularizing ORgan Donors for KIDney bioengineering). In order to accelerate future innovations to the patient, it is essential that we collaborate internationally and strive for important advancements in science and technology.

# Principles for impact

Sustainable kidney health and care is the ultimate goal of everyone involved in renal care, from outstanding scientists and committed patients to dedicated healthcare providers and other stakeholders. Together, we are developing an integrated approach that includes early detection, prevention of kidney damage, better dialysis and transplantation and ultimately, possible cures for kidney disease.
Our chances of success increase considerably if all stakeholders work together towards creating the optimum environment for research and innovation.

The following principles will guide us through the future development of this agenda to ensure that research and innovation have the greatest possible impact on the lives of kidney patients.

## Patient perspective

For patients, it is important that the term 'health' is widely interpreted. The impact of kidney diseases goes far beyond a reduction in renal function, and patients often experience the effect of the disease and treatment differently than healthcare providers. For patients, it is not just about medical outcome measures but about a better quality of life and about the ability to adapt and self-manage in the face of physical, emotional and social challenges (Huber, 2011). This demands the recalibration and enrichment of the outcome measures of treatment and care as well as an integrated approach for patients with kidney conditions. New interventions will need to be measured against existing and developing Patient Reported Outcome Measures (PROMs). This demands close cooperation between scientists and patients. Our ultimate aim is care that takes into account what a patient considers worthwhile treatment (value-based healthcare).

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The importance of including the patient's perspective in scientific research is growing. The early involvement of patients in research is key to the success of innovations. We need patients to participate in the development and implementation of this research agenda, and for patients to contribute to activities such as the evaluation of proposals for research and innovation and the design of clinical trials, and to give their perspective in research studies. The Netherlands is already a leader in this area and will continue to stimulate and support all stakeholders in these joint efforts.

## Economic perspective

Healthcare costs are rising and there is growing attention to the sustainability and affordability of healthcare. It is therefore essential that we consider the economic impact when investigating new treatment options.
Renal replacement therapy now has high costs, innovations and the emergence of personalised medicine ideally result in more individual choices for the patient with lower costs. Finding the right balance between sustainable high-quality care and the economic burden to both individual patients and society is challenging. If we integrate the scientific, social and economic perspectives into the research process, we will increase our chances of bringing new interventions to the market.

## Harness knowledge

It is important to recognise that research is needed across the whole spectrum: from fundamental to applied research and from physiological to social science research. There is high-quality kidney research in the Netherlands that produces results that are promising for new patient interventions. However, it is not easy to turn research results into tangible innovations that can be used in standard care.

We therefore need to properly align each step of the process from idea to innovation and we need to foster great interactions between research, healthcare practice and the patient. Our ultimate goal is to make innovations available to all relevant patients at affordable prices.

In order to successfully harness expertise, we need an environment that supports and promotes the process of valorisation. This ecosystem for innovation is a key element in the Dutch national research policy. Other stakeholders such as the healthcare industry and health insurers are vital to delivering innovations to patients and financial support for public-private cooperation is available from the Dutch Top Sectors policy and European Union funding. The development of this strategic agenda focuses on generating and sharing new expertise as well as on transforming expertise into practice.

As an example, the NeoKidney project holds great potential in bringing a portable artificial kidney to the market.

The Dutch Kidney Foundation, researchers, health insurers and companies are working together on this project to create a new, improved and more affordable dialysis model.

### Cooperation

A broad yet integrated approach is essential, and includes cooperation between scientists, healthcare providers, patients and other stakeholders such as companies, health insurers, policy makers and financiers.
This starts with a well-developed cooperation within the field of nephrology itself. The Dutch Kidney Patients Association, the Dutch Federation for Nephrology and the Dutch Kidney Foundation are already collaborating strongly for getting good quality and access of renal care. Another success factor is interdisciplinary research as there are significant links between kidney disease and other disorders such as diabetes, cardiovascular disease, high blood pressure, rheumatoid arthritis and metabolic syndrome.

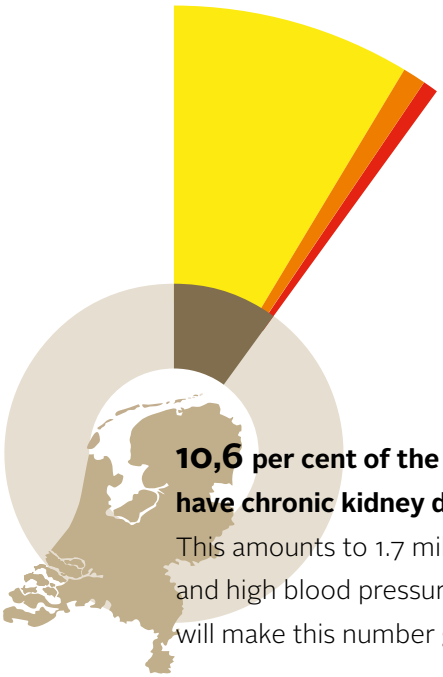
Successful cooperation must be flexible, self-driving and self-sustaining, and we must recognize that different levels of cooperation may exist. We need to build an environment that encourages and rewards collaboration in research and innovation. Connecting the various stakeholders involved will promote the cross-pollination of ideas and foster better cooperation. The stakeholders involved in this strategic agenda understand the importance of this and are integrating cooperation opportunities into their own plans.

There are also joint international alliances for research, innovation and sustainable kidney health. The Kidney Health Initiative in the USA, Canada (Hemmelgarn, 2017) and the United Kingdom (UKKRC, 2016) advances the scientific understanding of kidney health; and the European Kidney Health Alliance, a network of professional groups, patients and health charities, makes recommendations for sustainable kidney care in Europe (EKHA, 2015). The Dutch renal field is represented both in the EKHA and KHI. Together, these initiatives form the basis for more cross-border cooperation between top international groups, between larger patient target audiences and among international funding agencies. This enables us to achieve much more than with national cooperation alone.

### Infrastructure and resources

Internationally, science in the Netherlands is highly ranked (Scimago, 2016) and it is an opportune time to intensify it. The stakeholders in this field and the creators of this strategic agenda are investing in the infrastructure of Dutch renal research to ensure excellent research and innovation. However, to maintain and further develop this, the government must continue to guarantee the quality of the entire biomedical research system: the way it is organized, the working environment of researchers, their perspectives in science, development of talent, available materials and equipment, and the necessary financial resources. However, total spending by the Netherlands on research and innovation lags behind comparable European countries (OECD, 2017). Of note, the Netherlands are strongly advised to improve on this situation (AWTI, 2016).

## Chronic kidney disease in the Netherlands



**10,6 per cent of the population of the Netherlands have chronic kidney damage.**
This amounts to 1.7 million people. The increase of diabetes and high blood pressure and ageing of the population will make this number grow.

This 1.7 million people have a risk of kidney failure and of death from cardiovascular disease as follows:

- **87%** have a moderate risk (1,5 million people)
- **10%** have a high risk (170,000 people)
- **3%** have a very high risk (50,000 people)

The system of science itself seems under mounting pressure. Competition between scientists is increasing and resources and time are not spent optimally. Science in the Netherlands is flourishing, yet it takes more and more time to get research funded. This is at the cost of the researcher doing research. In addition, the uncertainties in the position and perspectives of young scientists is growing – while maintaining quality in research depends on drawing in talented young researchers. Furthermore, the modern academic working environment has as a consequence that medical specialists find it increasingly difficult to combine their clinical duties with doing research.

The link between the laboratory and the clinic is of great importance to our success and leaders in the field of nephrology are already active in talent management. They are also engaged in promoting cooperation between the laboratory and the clinic. The Dutch Kidney Foundation for example, awards research grants for young researchers through the Kolff Programme, and provides funding to consortia through the Consortium Programme for translational research. The challenge lies in creating a sustainable system and this is the responsibility of all stakeholders within this field. Within the borders of the international system, scientists, financiers and research organisations need to find more effective arrangements.

Within the Netherlands, the research policies of the university medical centres (academic research hospitals) are varied. Although nephrology may be an independent focus, it is often part of broader themes such as cardiovascular disease, regenerative medicine or healthy ageing. In order to bring it into the spotlight, renal research must get a clear position within the policies of the university medical centres. Traditionally, university medical centres' research agendas focus more on curative treatments rather than prevention, early detection and sustainable care. Thus, it is important that the university medical centres broaden the scope of their policies, and also include the development of research within primary care practices and at the larger non-university hospitals ("top clinical hospitals"). Both have proven to be of added value for renal research in the Netherlands, but advancing these areas of research still requires extra attention.

Finally, there is the quantitative evaluation of scientific quality. The H-index, impact factors, citation indices and a track record of successful grant applications are important but they are not the only assessment factors. Creating a more extensive evaluation process demands a change in policy, which was recently endorsed by the Health Council of the Netherlands (Health Council, 2016). In addition, Science in Transition, a Dutch initiative, calls for a reform in how research quality is measured and evaluated through the inclusion of the added social value of research (Science in Transition, 2013).

# Finally

Quality of life is inferior for many people with kidney damage and kidney disease  As kidney damage progresses, the burden of disease exerts an immense impact on patients and their families. In addition, this complex disease is often associated with or accompanied by other chronic conditions such as diabetes and cardiovascular disease. The kidney patient is a complex patient and treatment is expensive. Therefore, the approach to relieve the burden of kidney damage has a central meaning and wide reach.

Equally important is the lack of awareness of the severity and impact of kidney disease. A focus on chronic kidney disease can deliver important benefits for patients and society and has the potential of driving innovation with a strong economic perspective. More research and innovation and a collaborative effort to improve quality of life and achieve sustainable healthcare are needed.

This is why we are joining forces in the renal field with this agenda. We want to create a foundation for a broad scientific and social approach to finding solutions for patients with kidney damage and kidney disease. What we strive for is sustainable kidney health for all.

Now is the time to take action. The Netherlands has the critical components to move the field of kidney research and innovation forward. The quality of research is internationally recognized and there is strong cooperation between relevant stakeholders. A national registration of all patients receiving renal replacement therapy and a nationwide policy on quality of care are established. There is a serious societal need and great innovative potential.

To be successful we must have powerful collaboration not just in the kidney field itself. It is essential to involve other players in society, businesses and industry, government and policy makers, and funders of research and innovation. Also, we need to embed the agenda firmly within the Dutch national research policy.

The Dutch Kidney Patients Association, the Dutch Federation for Nephrology and the Dutch Kidney Foundation have set a starting point with this agenda. We will further develop the four themes of the agenda and seek the cooperation and embedding required to meet our objectives.

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# Colophon


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**Dutch Federation for Nephrology**

The Dutch Federation for Nephrology (NFN) is the professional interest organisation and the scientific association of nephrologists, trainee nephrologists and researchers in the field of kidney disease. The NFN concentrates on the collective interests of its members, the development and execution of the profession and science. Their aim is to guarantee high quality healthcare for patients with kidney disease and promote the further development of clinical and experimental nephrology.

**Dutch Kidney Patients Association**

The Dutch Kidney Patients Association (NVN) is an association run by and for people with chronic kidney disease, their families and kidney donors. With 7,500 members, the NVN is a strong, leading representative of the interests of those suffering from a renal disorder. The NVN's mission is to help kidney patients maintain and/or improve the quality of their life and care.

**Dutch Kidney Foundation**

As a health fund, the Dutch Kidney Foundation is committed to preventing kidney damage, to improve treatment of kidney diseases and a better quality of life for kidney patients and their families. Its ultimate dream is to be able to cure kidney disease. Research and innovation are crucial to this. For this reason, the Dutch Kidney Foundation funds research and projects in addition to encouraging collaboration between patients, researchers and healthcare providers so that people suffering from kidney disease regain or sustain their passion for life.