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Funding kidney research as a public health priority: challenges and opportunities

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ABSTRACT

Medical societies have a social responsibility to disseminate knowledge and inform health authorities on threats to public health posed by various diseases. Advocacy for health protection programmes and for medical research funding is now embedded into the missions of most scientific societies. To promote kidney research funding in Europe, the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA), rather than acting as an individual society advocating for the fight against kidney disease, has actively helped to create an alliance of national associations centred on kidney diseases, the European Kidney Health Alliance (EKHA), and joined the Biomedical Alliance (BMA). The ERA-EDTA is fully committed to supporting its working groups (WGs) and consortia of its members to allow them to produce valuable kidney research. The framing and formalization of projects, and the

regulatory issues related to submission to the European Commission, are complex. To help WGs to gain expert advice from agencies with specific know-how, the ERA-EDTA has adopted a competitive approach. The best research projects proposed by WGs and consortia of other European investigators will receive seed funding to cover the costs of consultancy by expert agencies. Via its broader platforms, the EKHA and the BMA, the ERA-EDTA will strive towards broader recognition of kidney disease and related clusters of non-communicable diseases, by European and national agencies, as major threats to the qualities of life of their populations and their economies.

Keywords: CKD, funding, kidney, research, scientific societies

Historically, the advancement of science has been supported by affluent individuals or families, and investigators have rarely been self-sustaining. Galileo's discoveries were funded mainly

by wealthy individuals while Darwin's voyage to the Galapagos islands was, in part, paid for out of his own pocket. Today, over \$1 trillion per year are spent worldwide on sustaining research [1] and medicine is one of the most financially demanding research areas. In 2014, health research absorbed about 45% of the US government's total investment in research and development [2]. In general, health projects of public interest are mainly sustained by governments and foundations, while research into treatment is conducted almost exclusively by industry. In 2018, drug companies spent \$44.2 billion on funding for clinical trials [3], which was about one-third of the whole health budget of the National Health Service in the UK in the same year [4].

On a worldwide scale, the prevalence of chronic kidney disease (CKD) is 9.1% (Figure 1) [5, 6]. In 2017, 1.2 million deaths from CKD were registered and mortality increased by 41.5% between 1990 and 2017 in the face of a stable background mortality rate [5]. CKD is one of the most rapidly advancing diseases on the list of the world's most deadly conditions, and mortality associated with it is expected to rise by a factor of two, advancing CKD from number 16 in 2016 to number 5 by 2040 [7]. Over the last 27 years, the prevalence of CKD worldwide has hardly declined, in contrast to many other important non-communicable diseases (NCDs) [5]. Unfortunately, the global burden of kidney disease has long been overlooked by the World Health Organization (WHO) and no specific goals to limit the CKD epidemic have been established by this organization so far [8]. NCDs as a whole are health conditions with the largest imbalances between disability-adjusted life years and research investment [9]. Among NCDs, scientific advancements in biotechnology and in 'omic' sciences have produced breakthroughs in oncology and cardiology, but basic and clinical research on kidney disease has lagged behind over the last decade [10]. Nephrology is probably the specialty that produces the lowest number of randomized clinical trials and quality concerns have been expressed regarding trials focusing on kidney diseases [11]. Europe lacks Clinical Trial Service Units (CTSUs) that could coordinate network-based clinical studies and

support clinicians. Such CTSUs exist in other parts of the world such as Australia, Canada and the USA, and have already contributed to our understanding of treatments for NCDs. Clearly, at this time juncture, there is a need to maximize efforts aimed at promoting effective collaborations between kidney investigators involved in clinical and translational research to sustain the growth of the specialty (Box 1). Gaps in therapeutic advancements in nephrology have been made clear in analyses made by CenterWatch [10]. In 2019, investment in research from the National Institutes of Health (NIH) in the USA amounted to \$11.1 billion for cancer, \$3.0 billion for Human Immunodeficiency Virus and \$5.2 billion for cardiovascular disease, but only \$680 million for kidney diseases [12]. Solving the problem of adequately funding kidney research is crucial if we are to effectively counter the CKD epidemic, as well as acute kidney injury, which is a frequent cause of CKD [13] and is considered by some to represent a continuum with CKD [14]. The coronavirus disease 2019 (COVID-19) pandemic has painfully exposed a number of weaknesses in our current medical research funding models. While allotting adequate funding for the development of a vaccine against the group of coronaviruses would have had a high cost, it would have prevented the present financial crisis, which will cost much more. Of course, the financial impact of CKD is less dramatic, but it is still costly, and is continuous rather than temporary.

IMPORTANCE AND COMPLEXITY OF MEDICAL RESEARCH FUNDING

Scientific discoveries are a product of the intellectual capital of society. Funding is fundamental to nurture such capital. For medicine, decisions about research funding are extraordinarily complex because financially demanding resources need to be allocated for the production of knowledge related to human health at all levels, from basic science to clinical science and prevention (Box 2). In 2012, \$119 billion was spent on medical research in the USA and \$82 billion in European countries, and most of this investment came from industry, 59% in the USA



FIGURE 1: Key numbers relating to CKD and CKD research.

Box 1

Multicentre interventional studies with better trial design, and therefore a higher probability that the measured outcomes will align with measurable differences to patient care:

- Development of novel tests and technologies for improved patient care, e.g. artificial intelligence.
- Ability to achieve translation from ‘bench to bedside’ more quickly.
- Expansion of the nephrology workforce with better training.

Box 2

- Decisions about research funding in medicine are difficult because financially demanding resources need to be allocated for the production of knowledge related to human health at all levels, from basic science to clinical science and prevention.
- Public research funding should have adequate time projections and be prioritized on the basis of the present and future (predicted) epidemiological impact of diseases on human health, at a national or international level.
- The actual investment in research and its distribution over time should be calibrated against the complexity of the research goals.

and 65% in Europe [15]. To effectively support scientific advancements in biomedicine, medical research funding should have adequate time projections and should be prioritized on the basis of the present and future (predicted) epidemiological impacts of diseases on human health, at national or international levels, and the potential impacts of the resulting products on outcomes, quality of life and societal costs. Indeed, whereas almost all other research products are subject to liberal rules of price-setting regulated by supply and demand, for therapies a third party, i.e. social security, and as a consequence society at large, is often involved. The actual investment in research and its distribution over time should be calibrated against the complexity of the research goals. These factors (robustness of the investment, duration of funding and complexity of the questions being investigated) will dictate the organization of the research and the sizes of the networks needed. For example, nanotechnology is needed to produce nanostructured materials for drug delivery and therefore clinicians, pharmacologists in particular, need to establish strong collaborations with nanotechnology experts. Bioartificial organ development, which is now being actively pursued to find more efficient alternatives to traditional dialysis treatment, necessitates close collaboration between cell

biologists and polymer chemists to generate the scaffolds on which cells will be seeded [16].

Public research funding

Globalization has broken down national barriers. There is now a highly mobile population that travels all continents, which is exposed to and may spread old and new pandemics, as in the case of COVID-19. Health disasters do and will continue to occur, while environmental problems including pollution are on the rise. Therefore, society as a whole should be prepared to face such threats to human health by funding appropriate research programmes to predict and prevent pandemics, for timely responses to health disasters and to mitigate environmental pollution (Box 3). Public models of research funding, like those provided by the NIH or by the European Commission and various corresponding national agencies, supply most of the funding needed to tackle major health threats. These institutes and agencies divert substantial economic resources to biomedical research that would be very difficult to obtain by alternative sources. However, the public model, which is based on periodic research calls, depends on economic cycles, with funding being increased during periods of economic growth and vice versa. These mechanisms are based on intense competition for financial resources, whereby not all relevant proposals are funded. Negative economic cycles produce even more uncertainty and instability in medical research [17]. Furthermore, in the past, funding for clinical research has been squeezed out of general healthcare provision [18] rather than a separate source. If medical research is the intellectual capital infrastructure for healthcare systems, it needs to be directly funded because no improvements to human health can be realized without research. Investment in infrastructure is the inescapable prerequisite for the stimulation of the economic growth of states and public prosperity. Likewise, the intellectual infrastructures of health systems need to be nurtured to improve human health. Therefore, it is fundamental that we cushion the effects of economic cycles and prejudicially eliminate competition for funding in medical research and healthcare if we are to maximize the health returns of medical research. In this respect, the California model stands out as being uniquely innovative. In 2004, an effective communication plan was launched to explain the need for innovative medical research funding strategies to the public [17]. In the same year, bonds totalling \$3 billion for the funding of medical research and \$3 billion to pay interest on the same bonds over 35 years were issued. This was a farsighted and successful programme, with long-term projections that have insulated research funding from fluctuating economic cycles in California [17].

In European countries, healthcare systems are funded by national governments, while the medical research is funded both by national governments and, increasingly so, by the European Commission. Over the last 6 years, the European Union (EU) has provided almost €80 billion in funding for the Horizon 2020 research programme (2014–20). Such European framework programmes have grown to over four times the amount provided in 2006 [19], and are planned to grow further in the eighth programme, called Horizon Europe [20]. Over the same period of time, the amount of internal research funding committed by

Box 3

- Society should be prepared to face threats to human health (e.g. environmental pollution and epidemics) by funding appropriate research programmes for the prediction and prevention of epidemics, for timely responses to health disasters and to mitigate environmental pollution.
- Public models of research funding, like those provided by the US NIH or by the European Commission and the various corresponding national agencies, supply most of the funding needed to tackle major health threats.
- The public model, which is based on periodic research calls, depends on economic cycles, with funding being increased during periods of economic growth and vice versa.
- Cushioning the effect of economic cycles on medical research is essential to ensure the continuity of scientific advancement.

national governments has either remained stable or dwindled. For example in Italy, global medical research funding (including private funding) in 2016 totalled just €2.6 billion [21].

Private research funding

The development of a basic understanding of a disease or of biochemical pathways that are disrupted in disease states is a prerequisite to drug development. In addition to investigations conducted in academic institutes, many such studies in research laboratories are funded by industry. Furthermore, pharmaceutical companies fund the bulk of clinical trials. This kind of industrial funding is fundamental to provide the evidence upon which medical practice is based, but has the inherent problem of conflict of interest. Understandably, the main interest of the pharmaceutical industry is the ability to achieve financial returns, a goal that may not always coincide with the of provision of robust scientific underpinning. At least 40 primary studies, and a variety of systematic reviews and meta-analyses, have documented the fact that industry-favouring results are more likely in trials funded by pharmaceutical companies [22]. The problem is in the public domain and is openly discussed in the media. Safeguards like adaptations in the training of ethics committees, and improved scrutiny by regulatory bodies like the US Food and Drug Administration or the European Medicines Agency, regarding the ethical implications of clinical trials being sponsored by industry are increasingly applied. On the other hand, it should be recognized that investigator-initiated clinical trials are not immune to problems such as adequate funding, regulatory issues and trial oversight, and suboptimal expertise in statistics and data management [23]. In addition, in recent years, we have seen a rise in the availability of overly expensive drugs for orphan diseases [24], for which (for obvious reasons) it is difficult to provide a solid evidence base. This practice imposes increasing pressure on regulators, forcing them to withdraw resources from sometimes more justified

interventions. If not reimbursed, an additional risk of inequity is imposed, whereby some people may be able to gain access to a therapy and while others may not (for example, because of better income or a better social network allowing crowdfunding).

Thus, there is a need for independent (i.e. not industry-sponsored) health economic research to be conducted on every drug entering the market that stringently assesses societal benefit and cost-effectiveness. Furthermore, regulators, supported by ethicists and health economists, need to open up conversations with industry to provide a sound ethical framework.

Foundations

With the exception of large charitable institutions like the Bill and Melinda Gates Foundation, support to research by foundations tends to focus on the domains of organ-specific institutions. In the area of kidney disease, foundations like the US National Kidney Foundation [25] represent an independent source of research funding in the USA. Such foundations are sparse in Europe and, in general, pursue limited goals. In this respect, The Netherlands is a notable exception. Indeed, since 1968 the Dutch Kidney Foundation (DKF) (Nierstichting Nederland) has achieved effective funding of selected research programmes conceived by kidney disease investigators in its country [26]. In 2018, the DKF launched Beating Kidney Disease (Nierziekte de Baas), involving a variety of stakeholders that included kidney patients, to develop an ambitious national strategic agenda to the improve outcomes and quality of life of kidney patients [27]. Based on four main pillars (prevention, patient quality of life, personalized medicine and regenerative medicine), it is now being considered for presentation to the Directorate-General for Health of the European Commission, to be rolled out, after adjustment, in the coming years throughout the EU.

SCIENTIFIC SOCIETIES: AT THE INTERFACE BETWEEN INVESTIGATORS AND FUNDING BODIES

Mechanisms of research funding by major governmental and philanthropic organizations are diverse, poorly defined and are often not transparent [28]. Medical societies have the social responsibility of disseminating knowledge about the threats to public health posed by various diseases and informing health authorities of the risks posed by the same diseases (Box 4). These societies produce analyses and documents that are useful for interactions with health agencies, and governmental bodies, concerning general or particular aspects of human health that require priority attention. These documents represent an important source of knowledge and a sound basis for the lobbying of governments to promote research programmes that may advance the field, and improve general and/or particular aspects of human health. As alluded to before, the global burden of CKD is an increasing concern in both economically developed and developing countries [5]. For this reason, the International Society of Nephrology has begun an important initiative to persuade the WHO of the urgency of including CKD in the 2030 global action plan for the prevention and control of NCDs [8].

Box 4

- Medical societies have the social responsibility of disseminating knowledge regarding the threats to public health posed by the various diseases and informing health authorities of the risks posed by them.
- Advocacy for health protection programmes and for medical research funding is now embedded into the mission of most scientific societies.

In the USA, kidney research funding reached an all-time low in 2013 [29]. About 20 years ago, the American Society of Nephrology (ASN) initiated advocacy activities to promote kidney research and public funding for CKD in the USA. From 2010 onwards, the costs of these activities by the ASN gradually increased to \$200 000 in 2019 [30]. Thanks to the ASN's actions, in March 2018 Congress approved an increase in funding of over \$2 billion for kidney research [31], and last July President Trump signed an executive order to reform the US End-Stage Kidney Disease treatment industry. This order is expected to create new payment models and facilitate kidney transplantation and home dialysis [32]. Furthermore, in 2012, the US Food and Drug Administration (FDA) and the ASN created the Kidney Health Initiative (KHI), a public-private partnership that aims to stimulate innovative approaches to the optimization of drugs and devices to improve the future of kidney patients, including their safety [33], by bringing together regulators, patients, academic and non-academic nephrologists, and other governmental agencies [10]. The KHI now includes five government partners—the Centers for Disease Control, the FDA, the NIH, Veterans Affairs and the Center for Medicare—11 foundations and patient associations, 31 drug companies, 19 device manufacturers, 7 dialysis providers, 10 research organizations, and 4 not-for-profit, digital health and artificial intelligence companies. In 2018, the KHI launched a technology roadmap for innovative approaches to renal replacement therapy to stimulate an internationally oriented, multidisciplinary approach to solution development for kidney patients. The KHI aims to realize the possibility of a portable/wearable and ultimately regenerated kidney [34].

The European Renal Association – European Dialysis and Transplant Association

The European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) operates in the geopolitically complex EU, which includes 27 member states, but also serves non-EU countries in Europe or bordering Europe and the Mediterranean. While in the USA—a true federation of states—the Federal Government has access to a broad array of tax revenues, the EU is largely dependent on what the member states contribute, which is only about 1% of their Gross Domestic Product. As a consequence, the EU's yearly budget is only a fraction of that of the USA. Thus, the potential for the EU to fund research is inherently limited compared with the situation in the USA. In Europe, public research largely relies on funding provided at country level. Mainly due to the negative

economic cycle that started in 2007, government budget allocations for research and development as percentages of state expenditures declined quite substantially from 2000 to 2014 in the Netherlands (−0.9%), Belgium (−1.1%), France (−1.3%), the UK (−3.7%), Italy (−5.2%) and Spain (−5.3%) [35].

In this difficult environment, since 2005 the ERA-EDTA has invested over €3 million in seven research projects selected via a competitive process, some of which are still ongoing. Among these projects, the Validation of the Oxford classification of IgA (VALIGA) study [36] has had a major impact on the way the most common form of glomerulonephritis, IgA nephropathy, is diagnosed histologically and has provided unique information on the prognostic value of kidney histology for kidney outcomes. The Cardiovascular Morbidity in Children with Chronic Kidney Disease (4C) study [37], a project focusing on cardiovascular disease in children based on data from 54 academic institutions, has generated unique information on this fundamental issue and published over 30 papers in major nephrology and internal medicine journals. However, due to the current financial climate, no additional investments of this kind are likely to be made by the society in the foreseeable future. Therefore, to promote kidney research funding in Europe, the ERA-EDTA has explored alternative possibilities (Figure 2). Rather than acting as an individual society to advocate for the fight against kidney disease, it is actively helping to create an alliance between national and international associations focused on kidney diseases, the European Kidney Health Alliance (EKHA), and has joined the Biomedical Alliance (BMA). These alliances are key for advocacy at the level of the European Commission and the European Parliament on the urgency of funding kidney research. Furthermore, the ERA-EDTA, via its Scientific Advisory Board (SAB), offers competitive fellowships to stimulate its working groups (WGs) to develop research networks that will initiate valuable projects focusing on priority themes that can be submitted for funding by the European Commission and other funding bodies.

The EKHA. The EKHA, created in 2007, is an association that includes as full members the ERA-EDTA and three other international and national societies focusing on kidney diseases, namely the European Kidney Patients' Federation (EKPF), the European Dialysis and Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA) and the DKF, in addition to a number of affiliated members, which are national stakeholder organizations representing not only nephrologists but also patients and foundations [38]. The EKHA works on the principle that the prevention and treatment of kidney diseases should be based on a shared vision at European level, and strives to achieve optimal quality of care and patient quality of life at affordable societal cost, with outreach to all valid candidates. The EKHA has established links with 19 Members of the European Parliament (MEP) that form the MEP Group for Kidney Health, a group of European politicians from 10 countries that is committed to improving policy responses to the growing burden of kidney disease in Europe. Interaction with the European Commission and the European Parliament has been quite successful and, starting from 2015, in early spring of each year the EKHA has organized 'the

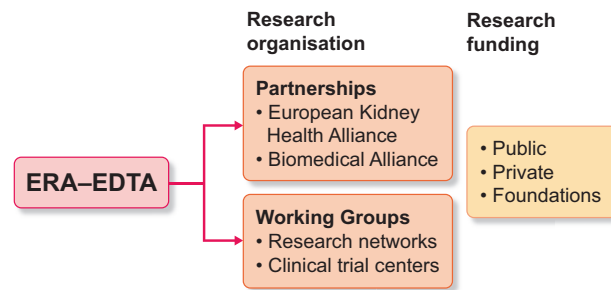


FIGURE 2: The ERA-EDTA and research organization and funding.

European Kidney Forum’ event held at the European Parliament. At this event, EKHA members, the MEP Group for Kidney Health, other MEPs, European and national administrators, and other stakeholders openly discuss priority kidney care issues. The EKHA has published recommendations that aim to help European and national policy makers understand and design kidney health policies [39], including prevention and early detection, choice of treatment, access to transplantation and treatment, and reimbursement strategies [38]. The EKHA has also contributed to several publications on policy and regulatory measures related to kidney disease [40–42]. A proposal by the EKHA, the ‘Effect of Differing Kidney Disease Treatment Modalities and Organ Donation and Transplantation Practices on Health Expenditure and Patient Outcomes (EDITH)’, a project including 15 European countries, has been awarded €1 million [43] and is approaching its conclusion together with the disclosure of its first results. The project is assessing disparities in access to renal replacement therapy throughout Europe and the reasons for them. Finally, the EKHA was commissioned by the EU to convene a Thematic Network of stakeholders to offer recommendations to the European Commission on how to improve organ donation and transplantation throughout the EU, which resulted in a Joint Statement on the issue [44]. To provide information to the EKHA Board on perceived research needs regarding CKD in Europe, the ERA-EDTA has created a Nephrology and Public Health Committee, and this Committee recently formulated a series of proposals to stimulate research collaboration on CKD in adults and children in Europe [45]. The EKHA is also a member and currently holds the chair of the European Chronic Diseases Alliance (ECDA), an EU advocacy platform of 11 societies involved with the broad spectrum of interrelated NCDs, which affect about 75% of the adult European population [46]. The ECDA’s focus is essentially on prevention and lifestyle measures.

The BMA. In 2019 the ERA-EDTA joined the BMA. This is a large alliance of over 30 leading European medical societies covering almost the full range of medical specialties, and aggregating >400 000 investigators and clinicians [47]. The mission of this association is to speak with a common voice to help the

growth of biomedical research in Europe. The BMA facilitates the training and mobility of investigators and clinicians in Europe, and aims to improve public understanding of medical research in Europe. The alliance is a strong advocate for increased funding in favour of biomedical research to promote excellence and improve health in European countries. The BMA calls on the European Institutions to increase the total Horizon Europe budget to at least €120–125 billion, and to dedicate 25–30% of the Horizon Europe budget to biomedical and health-related research. The alliance also aims to develop a long-term vision and strategy through the creation of a European Council for Health Research. Furthermore, the BMA is a European Medicine Stakeholder and, as such, it is consulted by the European Medicines Agency on themes related to the specific expertise of its member societies. The richness of competencies and knowledge among BMA medical societies is vast and includes the European Society of Cardiology, the European Association for the Study of Diabetes, the European Association for the Study of Obesity, the European Society of Endocrinology, the European Federation of Immunology societies, the European Respiratory Society and other societies that may share a proximate interest in kidney diseases with the ERA-EDTA. Thus, within the BMA, unique opportunities for large-scale collaborations and ambitious projects exist for investigators of various origins that are interested in kidney research.

The ERA-EDTA WGs and seed funding. To stimulate scientific collaboration among its members, in 2009 the ERA-EDTA created WGs in various areas of kidney research, from glomerulonephritis to diabetes, nutrition, metabolic bone disorders and cardiovascular risk in CKD. These WGs are transnational networks overseen by the SAB that share common interests in themes related to kidney diseases, and that pursue common research and educational activities in their area of expertise. There are currently eight WGs [48] that have produced a continuous flow of publications in major journals including *The Lancet*, *Nature Reviews Nephrology*, the *Journal of the American Society of Nephrology*, *Kidney International*, *Nephrology Dialysis Transplantation* [49–52] and other nephrology journals. The ERA-EDTA is fully committed at supporting its WGs and consortia of European kidney disease

investigators to allow them to produce valuable research on these diseases. To facilitate interaction, in October 2019 a special event was organized in Vienna, the Scientific Educational and Interaction Day, where the WGs had the opportunity to discuss issues related to the development of shared research projects and set the basis for the creation of effective research consortia. The framing and formalization of projects, and the regulatory issues related to submission to the European Commission are complex. Therefore, WGs need expert advice from agencies with specific know-how on how to frame project-related administrative issues. With this in mind, the ERA-EDTA council has decided to provide seed funding to cover the costs of consultancy from expert agencies. This novel approach has facilitated the creation of two large research consortia composed of institutions and investigators with diverse expertise. The first is a project that aims investigating the complex links between the kidneys and the brain. Understanding these links is a priority if we are to reduce cognitive problems related to CKD. Consequently, in March 2020 the European Commission decided to fund the project as a Cooperation in Science & Technology (COST) Action. COST funding enables researchers to set up interdisciplinary research networks, thereby enabling the establishment of synergies with EU-funded research projects. The second consortium aims to improve the identification and clinical management of CKD using real-world data from European healthcare agencies, registries and cohorts. Using a comparative health systems approach, it is using machine learning algorithms and artificial intelligence programmes to investigate the patient trajectory from primary to specialist care in different settings. Thus, the provision of seed funding to WGs and consortia of European investigators has the potential to stimulate research on kidney diseases and maximize the channelling of funds towards kidney research. Within the budgetary limits fixed by the ERA-EDTA Council, a yearly, competitive call will be made for investigators to submit research projects that are potentially fundable by the European Commission to the SAB. The SAB will evaluate these projects and the most meritorious will be awarded the seed money needed for expert consultancy on submission-related issues to the European Commission by the Council.

CONCLUSION

Funding patterns and mechanisms of funding by major health organizations remain poorly defined. Transparency and prioritization issues need to be addressed. Raising the awareness of governmental bodies and agencies responsible for health research funding about the burdens of various diseases is of paramount importance for improvement of the allocation of funding. In this respect, kidney research remains largely underfunded in Europe, as it was in the USA until 2 years ago. Scientific societies can play an important role in interacting with funding bodies in order to optimize the allocation of research funding in Europe. In this respect, initiatives based on solid epidemiological data about the burdens of diseases via large multispecialty alliances are more likely to be successful than efforts by single scientific or patient associations. In addition, societies dealing with NCDs including CKD should join

forces in advocacy and research planning when their aims overlap. In the case of kidney disease, diabetes, hypertension and cardiovascular disease traditionally come to mind, but cancer, liver disease and even pulmonary disorders are also linked to kidney disease [35]. Efforts should not be restricted to traditional basic and clinical research topics, but also to health economics, patient quality of life and prevention. The ERA-EDTA has already adopted this approach to help increase the funding of kidney research in Europe. In addition, the ERA-EDTA will support meritorious proposals with the initial seed funding needed to optimize how projects are framed prior their submission to the European Commission.

Via its broader platforms, the EKHA and the BMA, the ERA-EDTA will also strive to achieve broader recognition by the EU and national agencies that kidney disease, and a related clusters of NCDs, are major threats to the qualities of life of their populations and economies. Whereas acute problems, like the current COVID-19 epidemic, necessitated immediate and transnational action, it should be noted that those most severely affected by COVID-19 have been those with comorbid conditions, namely NCDs as a whole [53], but also more specifically patients with CKD [54]. Thus, for the reasons explained in this article, it is essential that these diseases gain the attention that they deserve.

CONFLICT OF INTEREST STATEMENT

None declared. All authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest.

REFERENCES

1. Costs of scientific research/Dr.M on Science, Research, & Scientists [Internet] [cited 3 March 2020]. <https://dr-monsrs.net/tag/costs-of-scientific-research/>
2. R&D in the FY 2014 Omnibus: The Big Picture/American Association for the Advancement of Science [Internet] [cited 3 March 2020]. <https://www.aaas.org/news/rd-fy-2014-omnibus-big-picture>
3. Clinical Trials Market Size & Share/Industry Trends Report, 2019–2026 [Internet] [cited 31 January 2020]. <https://www.grandviewresearch.com/industry-analysis/global-clinical-trials-market>
4. NHS Finance. The NHS budget and how it has changed/The King's Fund [Internet]. *Department of health budget*, 2017 [cited 2 February 2020]. <https://www.kingsfund.org.uk/projects/nhs-in-a-nutshell/nhs-budget>
5. Bikbov B, Purcell CA, Levey AS *et al*. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2020; 395: 709–733
6. Jager KJ, Kovesdy C, Langham R *et al*. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. *Nephrol Dial Transplant* 2019; 34: 1803–1805
7. Foreman KJ, Marquez N, Dolgert A *et al*. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. *Lancet* 2018; 392: 2052–2090
8. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. *Bull World Health Organ* 2018; 96: 414–422C
9. Allen L. Non-communicable disease funding. *Lancet Diabetes Endocrinol* 2017; 5: 92
10. Archdeacon P, Shaffer RN, Winkelmayr WC *et al*. Fostering innovation, advancing patient safety: the Kidney Health Initiative. *Clin J Am Soc Nephrol* 2013; 8: 1609–1617
11. Chatzimanouil MKT, Wilkens L, Anders HJ. Quantity and reporting quality of kidney research. *J Am Soc Nephrol* 2019; 30: 13–22

12. NIH Categorical Spending -NIH Research Portfolio Online Reporting Tools (RePORT) [Internet] [cited 21 April 2020]. https://report.nih.gov/categorical_spending.aspx
13. Hsu RK, Hsu C-Y. The role of acute kidney injury in chronic kidney disease. *Semin Nephrol* 2016; 36: 283–292
14. Vanmassenhove J, Vanholder R, Lameire N. Points of concern in post acute kidney injury management. *Nephron* 2018; 138: 92–103
15. Medical Research - Wikipedia [Internet] [cited 31 January 2020]. https://en.wikipedia.org/wiki/Medical_research
16. Schophuizen CMS, De Napoli IE, Jansen J *et al.* Development of a living membrane comprising a functional human renal proximal tubule cell monolayer on polyethersulfone polymeric membrane. *Acta Biomater* 2015; 14: 22–32
17. Klein R. A new paradigm for funding medical research. *Stem Cells Transl Med* 2012; 1: 3–5
18. United States. Congress. Senate. Committee on Appropriations. Subcommittee on Departments of Labor, Health and Human Services, Education, and Related Agencies. Clinical Research: Hearing Before a Subcommittee of the Committee On Appropriations, United States Senate. One Hundred Fourth Congress, Second Session, Special Hearing. [Corr. print.] Washington: U.S. G.P.O., 1996.
19. Hines P. *Why fund research?*, 2017. <http://sciencebusiness.net/OurReports/DownloadFree>
20. Horizon Europe - the next research and innovation framework programme/European Commission [Internet] [cited 31 March 2020]. https://ec.europa.eu/info/horizon-europe-next-research-and-innovation-framework-programme_en
21. La ricerca di punta è senza lucro/Scienza in Rete [Internet] [cited 31 January 2020]. <https://www.scienzainrete.it/articolo/ricerca-di-punta-è-senza-lucro/luca-carra-sergio-cima/2019-03-18>
22. Doucet M, Sismondo S. Evaluating solutions to sponsorship bias. *J Med Ethics* 2008; 34: 627–630
23. Konwar M, Bose D, Gogtay NJ *et al.* Investigator-initiated studies: challenges and solutions. *Perspect Clin Res* 2018; 9: 179–183
24. Phillips MI. Big Pharma's new model in orphan drugs and rare diseases. *Expert Opin Orphan Drugs* 2013; 1: 1–3
25. Research Grants/National Kidney Foundation [Internet] [cited 2 March 2020]. <https://www.kidney.org/professionals/research/awards>
26. Dutch Kidney Foundation (www.narcis.nl) [Internet] [cited 2 March 2020]. <https://www.narcis.nl/organisation/RecordID/ORG1238896/Language/en>
27. Beating kidney disease A joint agenda for research and innovation. https://www.nierstichting.nl/media/filer_public/4d/6d/4d6d6b4e-ce56-4a4b-8ba2-f5ac957d0df8/beating_kidney_disease_-_joint_agenda_for_ri_june_2018.pdf
28. Viergever RF, Hendriks T. The 10 largest public and philanthropic funders of health research in the world: what they fund and how they distribute their funds. *Health Res Policy Sys* 2016; 14: 12
29. Bryan L, Ibrahim T, Zent R *et al.* The kidney research predicament. *J Am Soc Nephrol* 2014; 25: 898–903
30. American Society of Nephrology Lobbying Profile • OpenSecrets [Internet] [cited 3 February 2020]. <https://www.opensecrets.org/federal-lobbying/clients/summary?id=F200220>
31. Budget Boosts Funds for Kidney Disease Research, Prevention/Kidney News [Internet] [cited 3 February 2020]. <https://www.kidneynews.org/kidney-news/current-issue/budget-boosts-funds-for-kidney-disease-research-prevention>
32. Jost TS, Lazarus S. Trump's executive order on health care—can it undermine the ACA if congress fails to act? *N Engl J Med* 2017; 376: 1201–1203
33. Wieringa FP, Sheldon M. The Kidney Health Initiative innovation roadmap for renal replacement therapies: building the yellow brick road, while updating the map. *Artif Organs* 2020; 44: 111–122
34. Bonventre JV, Hurst FP, West M *et al.* A technology roadmap for innovative approaches to kidney replacement therapies a catalyst for change. *Clin J Am Soc Nephrol* 2019; 14: 1539–1547
35. Reale E. The PREF study – Analysis of national public research funding - European Commission [Internet] [cited 4 February 2020]. <https://rio.jrc.ec.europa.eu/en/library/pref-study---analysis-national-public-research-funding>
36. European Validation Study of the Oxford Classification of Iga Nephropathy (VALIGA) [Internet] [cited 31 March 2020]. <http://web.era-edta.org/uploads/valiga-report-2018.pdf>
37. The Cardiovascular Morbidity in Children with Chronic Kidney Disease (4C) Study [Internet] [cited 2020 Mar 31]. [http://web.era-edta.org/uploads/4c-study-report\(1\).pdf](http://web.era-edta.org/uploads/4c-study-report(1).pdf)
38. Home/EKHA - European Kidney Health Alliance [Internet] [cited 2 March 2020]. <http://ekha.eu/>
39. Recommendations for Sustainable Kidney Care/EKHA - European Kidney Health Alliance [Internet] [cited 31 March 2020]. <http://ekha.eu/accomplishments/recommendations-sustainable-kidney-care/>
40. Vanholder R, Annemans L, Brown E *et al.*; on behalf of the European Kidney Health Alliance. Reducing the costs of chronic kidney disease while delivering quality health care: a call to action. *Nat Rev Nephrol* 2017; 13: 393–409
41. How to Increase Kidney Transplant Activity Throughout European Advocacy Review by the European Kidney Health Alliance [Internet] [cited 31 March 2020]. https://pubmed.ncbi.nlm.nih.gov/30629203/?from_single_result=Vanholder%2C+NDT%2C+34%2C+1254-1261%2C+2019
42. van der Tol A, Stel VS, Jager KJ *et al.* A call for harmonization of European kidney care: dialysis reimbursement and distribution of kidney replacement therapies. *Nephrol Dial Transplant* 2020; 35: 979–978
43. Jager KJ, Stel VS, Branger P *et al.* The effect of differing kidney disease treatment modalities and organ donation and transplantation practices on health expenditure and patient outcomes. *Nephrol Dial Transplant* 2018; 33: 560–562
44. Updated final version of the Joint Statement on Organ Donation and Transplantation now available/EKHA - European Kidney Health Alliance [Internet] [cited 31 March 2020]. <http://ekha.eu/blog/updated-final-version-of-the-joint-statement-on-organ-donation-and-transplantation-now-available/>
45. Massy ZA, Caskey FJ, Finne P *et al.* Nephrology and Public Policy Committee propositions to stimulate research collaboration in adults and children in Europe. *Nephrol Dial Transplant* 2019; 34: 1616–1616.
46. European chronic disease alliance – European chronic disease alliance [Internet] [cited 31 March 2020]. <https://alliancechronicdiseases.org/>
47. BioMed Alliance - Home [Internet] [cited 6 March 2020]. <https://www.biomedeuropa.org/>
48. ERA-EDTA Scientific Working Groups - Homepage [Internet] [cited 6 March 2020]. <http://www.era-edtaworkinggroups.org/en-US/homepage>
49. Coppo R, D'Arrigo G, Tripepi G *et al.* Is there long-term value of pathology scoring in immunoglobulin A nephropathy? A validation study of the Oxford Classification for IgA Nephropathy (VALIGA) update. *Nephrol Dial Transplant* 2018; 32: 1002–1009
50. Bellur SS, Roberts ISD, Troyanov S *et al.* Reproducibility of the Oxford classification of immunoglobulin A nephropathy, impact of biopsy scoring on treatment allocation and clinical relevance of disagreements: evidence from the VALidation of IGA study cohort. *Nephrol Dial Transplant* 2019; 34: 1681–1690
51. Lerch C, Shroff R, Wan M *et al.* Effects of nutritional vitamin D supplementation on markers of bone and mineral metabolism in children with chronic kidney disease. *Nephrol Dial Transplant* 2018; 33: 2208–2217
52. Wuttke M, Wong CS, Wühl E *et al.* Genetic loci associated with renal function measures and chronic kidney disease in children: the Pediatric Investigation for Genetic Factors Linked with Renal Progression Consortium. *Nephrol Dial Transplant* 2016; 31: 262–269
53. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 Cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323: 1239–1242
54. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol* 2020; 52: 1193–1194

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