Reducing the costs of chronic kidney disease while delivering quality health care: a call to action

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Abstract | The treatment of chronic kidney disease (CKD) and of end-stage renal disease (ESRD) imposes substantial societal costs. Expenditure is highest for renal replacement therapy (RRT), especially in-hospital haemodialysis. Redirection towards less expensive forms of RRT (peritoneal dialysis, home haemodialysis) or kidney transplantation should decrease financial pressure. However, costs for CKD are not limited to RRT, but also include nonrenal health-care costs, costs not related to health care, and costs for patients with CKD who are not yet receiving RRT. Even if patients with CKD or ESRD could be given the least expensive therapies, costs would decrease only marginally. We therefore propose a consistent and sustainable approach focusing on prevention. Before a preventive strategy is favoured, however, authorities should carefully analyse the cost to benefit ratio of each strategy. Primary prevention of CKD is more important than secondary prevention, as many other related chronic diseases, such as diabetes mellitus, hypertension, cardiovascular disease, liver disease, cancer, and pulmonary disorders could also be prevented. Primary prevention largely consists of lifestyle changes that will reduce global societal costs and, more importantly, result in a healthy, active, and long-lived population. Nephrologists need to collaborate closely with other sectors and governments, to reach these aims.

Renal replacement therapy (RRT), including dialysis and kidney transplantation, is the only available life-prolonging treatment for end-stage renal disease (ESRD). RRT prevents death from uraemia and helps to maintain a reasonable quality of life, but at a substantial financial cost to society, particularly for haemodialysis[1,2]. The various types of RRT differ greatly in terms of their costs and associated benefits, with transplantation imposing the lowest societal cost while offering the highest quality of life, in-hospital haemodialysis imposing the highest cost and providing the lowest quality of life, and at-home dialysis (haemodialysis and peritoneal dialysis) generally considered to provide intermediate quality of life with medium-level costs. In most Western countries, the incidence of ESRD has stabilized. However, the prevalence, and consequently the financial burden, of ESRD is still rising, in part owing to improved survival[1,3,4]. Although most of the cost per patient in the chronic kidney disease (CKD) population is related to ESRD, earlier stages of the disease also generate costs, mainly by inducing cardiovascular events[5]. Ageing of the general population will exacerbate this trend. Alarmingly, the burden of both incident and prevalent CKD and ESRD continues to rise in low-to-middle-income countries (LMICs), creating disparity with the Western world[6]. CKD of unknown origin, such as Mesoamerican nephropathy[7], imposes an additional burden, particularly to LMICs, because prevention and therapy become possible only when the cause has been ascertained.

In this in-depth Review, we discuss the economic aspects of CKD and ESRD, with an intentional focus on the prevention of conditions that lead to CKD or its progression. We summarize the existing analyses in this field and build a paradigm of how to curtail the costs associated with CKD and ESRD based on the "Recommendations for sustainable kidney care" published by the European Kidney Health Alliance in 2015 (REF. 8). These recommendations are not limited

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Key points

- The treatment of chronic kidney disease (CKD) and of end-stage kidney disease (ESRD) has a high societal cost
- Insufficient efforts are being made to promote the use of cost-effective renal replacement therapies (RRT), such as transplantation and home dialysis (including peritoneal dialysis)
- In CKD and in many other chronic diseases, the time has come to decrease investment in curative approaches and to focus on prevention
- The relative costs and benefits of each approach should be carefully analysed before a preventive or curative method is favoured
- A need exists for more health-economic studies of primary and secondary prevention in CKD to be conducted, and for the quality of such research to be improved

to kidney disease *per se* but encompass the broad spectrum of chronic disorders that both cause and are caused by CKD. We describe options to maintain quality of care for patients with CKD without increasing costs or decreasing access to services.

CKD is associated with other chronic diseases, including diabetes mellitus, hypertension, chronic liver disease, cardiovascular disease, and cancer. As median survival is continuously improving for all these chronic diseases, an increasing proportion of patients survive until they need RRT[9]. CKD is also associated with several life-threatening or concurrent complications (BOX 1), which overlap with and amplify the effect of chronic diseases[10], resulting in exponentially worsening outcomes and cumulative costs. Despite the low absolute incidence of ESRD (FIG. 1a) relative to other stages of CKD, and even if the absolute cost of RRT per capita decreases, the total worldwide cost of RRT will increase because of ageing of the population, the rise in frailty, prolonged survival among people with chronic diseases, the shortage of organs for transplantation, and the high additional costs of CKD[1,11].

Opportunity costs
The health benefits that could have been achieved had the money been spent on the best alternative option.

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Nondemographic factors, such as the increasing costs of health technology, diagnostics, and medication; increasing demand for advanced services; and increasing incomes of health-care professionals and of the population at large, also affect the societal cost of CKD[12]. Other costs, such as patients' out-of-pocket expenses, loss of productivity due to unemployment, costs of patient time and of unpaid care by next of kin, psychological and physical stress, and lost opportunities for travel or social contact, should also be considered.

The proportion of patients with CKD who do not receive dialysis exceeds 10% of the global population[13]. By comparison, those who benefit from RRT comprise ~0.15% of the global population[14,15] (FIG. 1b). Yet, this small group absorbs 2–4% of the health-care budget of some countries[5,16–19], generating problems of prioritization and opportunity costs[20,21]. Owing to a lack of funds, many patients with kidney failure, particularly in LMIC, are not treated, and health systems that choose to fund RRT might have to forego health-care programmes for other conditions. Differences in uptake for each RRT modality exist between countries, even in a structured and homogeneous entity like the EU[15]. The total number of patients who receive RRT per million people (pmp) differs by a factor of 3.2 between EU countries (Bulgaria: 541 pmp versus Portugal: 1,749 pmp)[15] (TABLE 1). Analysis conducted using worldwide data from the US Renal Data System[22] (TABLE 2), discloses even larger discrepancies than those in Europe with the number of patients who receive RRT differing by a factor of 28.5 between the countries with the highest (Taiwan: 3,219 pmp) and the lowest (Bangladesh: 113 pmp) patient numbers.

These differences cannot be explained by medical factors alone, but also depend on lifestyle, the efficacy of prevention, the predisposition, incidence of and survival rates for CKD, and the availability of RRT. These factors are a matter of concern, if the aim is to procure optimal therapy for every patient. Multiple solutions have been proposed, but few have been sufficiently explored, and no concerted global approach exists to address the growing economic burden of ESRD. Unfortunately, in the political sphere, health issues are often discussed in terms of cost reduction, and not how global health could be improved with adoption of efficacious and cost-effective interventions.

From an epidemiological point of view, adopting a lifetime perspective of the risk of disease is important[23]. Lifetime health economic research focuses on how conditions observed at a specific life stage influence future health[24]. The Canadian population health model simulates individual risk factors and disease states, which enables projected estimates of outcomes, including health-care costs[25]. Health economic studies based on this model have already informed decisions about colorectal cancer screening[26]. Furthermore, studies reporting lifetime risk could help patient education and screening. Lifetime risk of CKD and ESRD has been studied sporadically[27]. For people without ESRD at the age of 40 years, the average lifetime risk of developing CKD is 2.66% for men and 1.76% for women, but with increasing risk at lower baseline estimated glomerular

Box 1 | **Complications associated with chronic kidney disease***

Cardiovascular
- Cardiac decompensation
- Fluid overload
- Hypertension
- Vascular damage

Endocrine
- Dyslipidaemia
- Hyperaldosteronism
- Hyperparathyroidism
- Insulin resistance

Gastrointestinal
- Anorexia
- Malnutrition
- Constipation

Haematological
- Anaemia
- Hypercoagulability
- Hyperkalaemia
- Inflammation
- Metabolic acidosis
- Susceptibility to infection

Nephrological
- Progression of kidney failure

Osteoarticular
- Bone fractures
- Osteodystrophy
- Osteomalacia

Stomatological
- Periodontitis

*These are the major complications; the list is not exhaustive[9].

filtration rate (eGFR)[27]. Unfortunately, lifetime modelling to assess health-care costs has not been undertaken in the field of nephrology. Such analyses could be used to estimate the economic impact of an unhealthy lifestyle and other events at early stages of life that affect health status in older age. This analysis would include the impact of fetal stage, childhood, and adolescence on the later evolution of kidney function, and factors such as maternal smoking, which seems to be a risk factor for childhood proteinuria[28].

Considering this lifetime perspective, we include diseases that are associated with an increased risk of kidney failure (FIG. 2) in our discussion. We propose several options on how to decrease costs when RRT is needed and assert that prevention (particularly primary prevention) is likely to provide the optimum balance between quality of life and survival within an affordable budget. For this sustainable approach to CKD and other chronic diseases to succeed, the active involvement of many stakeholders, including regulators and administrators, industry, the medical community, the lay public and patients, will be needed. Considering the scarcity of good quality health-economic studies and studies upon which health-economic analyses can be based, a substantial effort is required to provide additional data. We begin with the discussion of RRT to emphasize the high cost of these therapies, and to justify strengthening primary and secondary prevention of CKD as an alternative. The potential economic benefits of primary and secondary prevention of CKD are then discussed extensively in the second part of this Review.

Renal replacement therapy

Kidney transplantation

Kidney transplantation is by far the most cost-effective treatment for ESRD, particularly beyond the first year after surgery, owing to the combination of prolonged survival, improved quality of life, and reduced costs[1,29–32]. Yet only in a very few European countries, such as Norway and Iceland, does the number of patients with a functioning kidney graft exceed 60% of the RRT population (TABLE 1). In most other countries, <50% of patients who receive RRT have a functioning transplanted organ. In eight of the of 31 European countries considered, this figure is ≤20% (TABLE 1). Worldwide, the statistics are similar (TABLE 2) to those in Europe. In addition, even if the preference for transplantation would be high, the rising number of very old or frail patients with ESRD and the shortage of suitable organs for donation hinders the use of this strategy.

The marked differences among countries in numbers of prevalent patients on RRT who have undergone transplantation suggest there is room for improvement. In some countries (for example, Austria, Belgium, France, and Spain), transplantation from a deceased organ donor is the primary approach, whereas in others (for example, Iceland, the Netherlands, Turkey, and the UK) there is more focus on donation from a living donor[15]. In both cases, increasing the use of the alternative donation method might improve the overall transplantation rate[33,34].

A potential barrier that could lead to low rates of transplantation is a lack of patient education. In a survey of 3,867 patients from 36 countries, 39% stated that they had not been informed about options for RRT alternative to their current modality[35]. The lack of such essential steps in the care pathway means that transplantation is underexploited worldwide. Importantly, however, care should be taken to prevent commercial organ trafficking for transplantation from either living or deceased kidney donors[36].

Organs from deceased donors. The proportion of deceased and living donor transplantations varies widely between countries. In general, deceased donation prevails in countries that use an opt-out as opposed to an opt-in policy of presumed consent for donor allocation. In addition, transplantation procedures as a whole (deceased plus living donation) seem to be more frequent in countries with opt-out policies[37].

Proactive measures to increase donation of kidneys from deceased donors could include changes to donor registration systems, extension of the involvement of the donor families, reimbursement of expenses for hospitalization or funeral costs, or a formal recognition of donation. Such measures were suggested by investigators from Australia who assessed patient and community preferences using discrete choice experiments[38].

Although most data indicate that opting out is the most favourable solution for increasing transplantation rates from deceased donors[39], many countries are reluctant to implement this strategy for political, philosophical, social, practical, or religious reasons[40]. In 2016, a motion in favour of opting out of organ donation was passed with a majority of one in the lower house of the Dutch Parliament, demonstrating the difficulties involved in changing existing legal framework. The bill awaits a confirming vote from the upper house[41]. By contrast, many countries have already adopted an opt-out system[39]. In Singapore, the transition to an opt-out system in 2007 was accompanied by a striking rise in yearly organ transplantations[42]. The same effect was observed in Croatia, although several other measures, such as the appointment of transplant coordinators, other changes in legislation, educational initiatives, and enrolment in

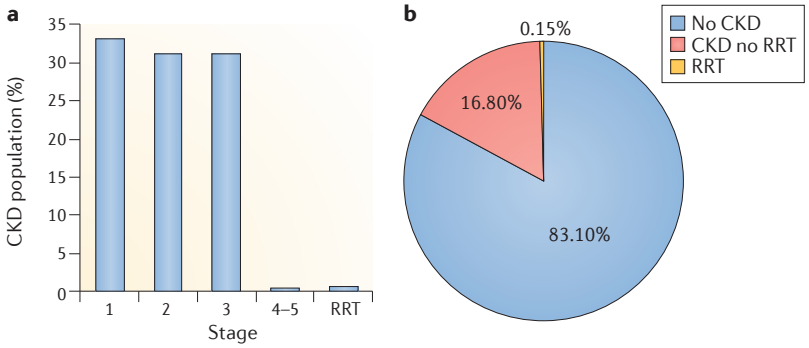

Figure 1 | **The burden of chronic kidney disease (CKD)*. a** | Percentage distribution of the various stages of CKD. **b** | CKD in the global population. The fraction of patients who undergo renal replacement therapy (RRT) is very small. *Global approximations, extracted from various databases[5,12–18].

an international cooperation network (Eurotransplant) were implemented at the same time[43].

Organ shortage is an important barrier to the expansion of transplantation programmes. Extending donor criteria (such as the use of organs obtained after cardiac death and an "old for old programme" — assigning organs from ageing donors to older recipients) might increase transplantation rates[44], but these approaches should be based on carefully explored scientific evidence to avoid increased risks to organ recipients and additional costs to society[45].

Organs from living donors. Transplantation of kidneys from living donors is almost non-existent in some, mainly Western, countries, whereas it is essentially the only source of donor kidneys in other, often low-income countries[15,37,46]. In addition, living donation is more prevalent in countries with opt-in policies[37].

Pre-emptive kidney transplantation from a living donor should be encouraged[45], as outcomes are better than for organs from deceased donors[47]. Obstacles to living donation, such as donor inconvenience and expenses linked to the donation[34], could in part be absorbed by the implementation of social measures. Other barriers, such as insufficient education of the patient population, are among the responsibilities of the nephrological community and are unfortunately not always optimally addressed. Lack of dialysis capacity as a bridge to transplantation is more difficult to overcome as it depends on geographical, economical and political conditions. Yet, ways exist to circumvent these problems, for example, by placing more emphasis on pre-emptive transplantation or on the use of peritoneal dialysis. In addition, inconsistencies in donor acceptance criteria among transplantation programmes should be minimized by providing a clear evidence base for selection[48].

Dialysis

In many Western countries, at-home haemodialysis, peritoneal dialysis, and self-care dialysis are more cost-effective than in-hospital haemodialysis[1,49]. With the sporadic exception of assisted home care, transportation costs are almost always highest for dialysis outside the home. Organizing transport to and from the place of dialysis can be challenging for health-care systems and individual patients[50]. Dialysis performed away from a hospital environment is the preferred choice of patients irrespective of the modality they receive[51]. However, in Europe, 89% of patients undergoing dialysis are treated in hospital with striking discrepancies among countries[15] (TABLE 1). Worldwide, the region with the highest proportion of patients undergoing peritoneal dialysis (Hong Kong: 72% of the total dialysis population) has a rate that is 36-fold higher than the country with the lowest rate (Bosnia-Herzegovina: 2% of the total dialysis population; TABLES 1,2). With a few exceptions, countries with a high proportion of patients undergoing peritoneal dialysis also have a high transplantation rate.

Reimbursement for the use of at-home dialysis varies widely between countries[49], and is not always high enough to cover real costs, discouraging physicians and patients from considering this mode of RRT. Applying one reimbursement rate for all methods of dialysis, as in Portugal, the USA, and some regions of Canada, could partially solve this problem. Uniform reimbursement for all dialysis strategies in the USA resulted in increased uptake of peritoneal dialysis[52]. Another option could be to reimburse only 'real costs' as made by the hospital or dialysis unit (as is the case in Austria and several Scandinavian countries), or to buy dialysis materials nationwide in tenders, which could limit inflation and avoid the use of expensive alternative materials that show no obvious benefit in terms of outcome or quality of life.

Possible barriers to the widespread use of peritoneal dialysis include differences in incentive systems for doctors and hospitals (for example fee-for-service versus capitation systems[53]), and the costs of labour[1] and of the disposable materials used in dialysis. Other factors potentially preventing the use of peritoneal dialysis include the high percentage of patients with diabetic nephropathy, higher health-care expenditures, the share of private-for-profit haemodialysis facilities, and cost of consumables relative to those of staffing[54]. In LMICs, disposable materials need to be transported over long distances and paid for in foreign currency. Such costs can be substantially decreased through the local production of disposable items[55,56].

The use of home-based therapies could be further hindered by inadequate patient information, which as mentioned above, is ultimately the responsibility of medical professionals. Respondents in a large survey of patients in Europe reported that the amount of education they received was markedly lower for at-home haemodialysis and peritoneal dialysis than for in-hospital haemodialysis and transplantation[35]. Furthermore, economic barriers to at-home dialysis from a patient perspective include loss of productivity associated with changes in employment, the necessity for personal subsidization of financial costs related to home dialysis, and socioeconomic disadvantages, such as living in a house unsuitable for home therapies[57].

Redirection to the least expensive forms of dialysis is not optimally exploited. Purely financial incentives favouring home-based treatments are not always effective, as demonstrated in Germany[58,59] and in Ontario,

Benefit
Any intervention for which the results offer added financial or health-related value.

Canada[60]. By contrast, in countries where RRT is developing, the choice by health services to promote the use of home-based treatments has been very effective in increasing access to RRT, as demonstrated in Hong Kong and Thailand[58,61]. However, these initiatives should be strictly limited to political directives of preferences and not include financial stimuli.

In most countries, the use of peritoneal dialysis declines with increasing patient age, and in-hospital haemodialysis is usually the only modality suitable for frail, elderly patients[62]. However, this approach reduces quality of life because of the necessity for frequent travel and, in contrast to peritoneal dialysis, the associated adverse effects such as haemodynamic instability and intradialytic hypotension[63]. When patients are given information and involvement in choice, >50% choose a home-based treatment[64], including elderly individuals. Assisted peritoneal dialysis, which involves support from trained staff or family members for patients unable to perform their own peritoneal dialysis, is a valid alternative to in-hospital haemodialysis[65]. Even among elderly patients, quality of life and hospitalization rates were the same for assisted peritoneal dialysis as for in-hospital haemodialysis, but with greater satisfaction with therapy[66] and no additional costs[67]. These findings underscore the need for free informed choice, especially among elderly patients with ESRD[68].

Late referral to a nephrologist for RRT compromises outcomes among patients with CKD and increases therapeutic costs[69–71]. Reasons for negative outcomes include the absence of planned prevention for progression of CKD and its complications, the inability to educate patients and to allow sufficient time for informed choice, the lack of appropriate access to dialysis, predominant use of hospital-based dialysis strategies, longer and more frequent hospital stays compared to those of individuals who are referred earlier, and low rates of transplantation, especially pre-emptive transplantation. The reversible causes of late nephrology referral are linked to education — either of the general population, patients with CKD, or the medical profession — and the lack of access to general or specialized care[72].

Ageing and conservative treatment

Exponentially increasing financial stress on societies can be expected in the coming years, owing to ageing of the general population[73,74], and the need to provide medical care for people with multiple morbidities. As kidney function declines with age, the prevalence of CKD is higher in older people[75]. The average age of patients receiving RRT increases year-by-year, owing to improved survival in the general and ESRD populations worldwide[76]. Quality of life with haemodialysis is perceived to be lower by elderly patients (aged >75 years) than by younger patients[76]. Unsurprisingly, therefore, a rising number of elderly patients withdraw from dialysis[77], although not enough to taper the overall prevalence of older people on haemodialysis. Almost all the survival time gained by elderly patients through dialysis is spent in hospital, either for dialysis itself or for other indications[78].

Elderly patients recieving dialysis, regardless of modality, have a high burden of age-related medical conditions, high mortality, and a high rate of frailty requiring social support within a few months of starting dialysis[79]. Frailty is itself related to both mortality

Table 1 | **Renal replacement therapy (RRT) in Europe**

Country	All RRT (pmp)*	Tx (%)‡	All dialysis (pmp)*	PD (%)§
Albania	341	19	275	7
Austria	1,054	51	521	10
Belgium	1,247	42	720	9
Bosnia-Herzegovina	747	8‖	691	2‖
Bulgaria	541	13	472	3‖
Croatia	800	20‖	620	6
Czech Republic	1,034	41	613	8
Denmark	877	49	449	22¶
Estonia	572	60¶	226	15
Finland	826	59¶	335	20¶
France	1,175	44	646	7
Georgia	385	10‖	345	6
Greece	1,172	20	933	6
Iceland	686	67¶	226	33¶
Israel#	735	NA	735	6
Italy**	752	NA	NA	NA
Latvia	600	54	276	20¶
Lithuania	719	32	491	3‖
Montenegro	305	54	139	4‖
Norway	901	72¶	252	14
Poland	822	34	541	5
Portugal	1,749	36	1,117	6
Romania	817	8‖	753	10
Serbia	839	14‖	718	9
Slovakia#	609	NA	609	3‖
Slovenia	1,008	33	680	4‖
Spain	1,126	52	544	13
Sweden	940	57	400	21¶
Switzerland#	382	NA	382	8
The Netherlands	945	59¶	387	15
UK	1,020	53	407	14

Data extracted from the Registry of the European Renal Association–European Dialysis and Transplantation Association for 2013 (REF. 15). The total number of patients receiving dialysis was calculated as the sum of patients receiving haemodialysis (HD) and those undergoing peritoneal dialysis (PD). NA, not available. *Number of patients per 1 million people (pmp). ‡Percentage of patients with a functioning kidney graft. §Percentage of patients undergoing dialysis who are receiving PD. ‖The lowest scoring countries for tranpslantation (Tx) and PD. ¶The highest scoring countries for Tx and PD. #Israel, Slovakia, and Switzerland provided only data on dialysis. **Data from Italy obtained from C. Zoccali (personal communication), and only data on dialysis (HD plus PD) were available.

and hospitalization[80]. Mortality is particularly high in the first month after the start of dialysis[81], especially if patients have multiple comorbidities[82]. Only those with few or no comorbidities survive longer with dialysis than with conservative treatment[82]. Nevertheless, dialysis is presented as the standard life-prolonging option even in very elderly patients with a high comorbidity index[83].

Given this experience and the observation that dialysis might not extend life in very elderly individuals, or in those with multiple comorbidities or poor physical function[82], the choice to pursue conservative care (no dialysis, but active supportive care) among such patients is unsurprising[68,84]. A change to the classical paradigm might be beneficial, such that conservative treatment is offered as the first line approach for frail, elderly patients. Such a strategy should involve interventions to delay the progression of kidney disease and minimize complications, and involve planning of care in advance, improved communication, and the provision of psychological and family support to improve patient quality of life[85]. The option for conservative care should be offered to all patients as one of the potential approaches to treatment. Shared decision making should involve the patient, their family and the caregiver, and conservative care should be based on validated risk prediction models, and include the possibility to revise the decision at any time[86]. Indeed, for all RRT options, decisions should be actively re-evaluated at regular intervals. Although conservative care for elderly patients is less expensive than dialysis, ethically the decision to treat cannot be based on economic considerations and should only be based on the patient's well-being.

Table 2 | **RRT worldwide (excluding Europe)**

Country	All RRT (pmp)*	Tx (%)‡	All dialysis (pmp)*	PD (%)§
Argentina	856	22	665	6‖
Australia	944	46¶	513	20
Bangladesh#	113	NA	104	7
Brazil#	773	NA	549	7
Canada	1,291	41¶	757	19
Chile	1,301	16	1,094	6‖
Colombia	604	18	493	29¶
Hong Kong	1,248	39	759	72¶
Indonesia#	134	NA	130	3‖
Iran	617	43¶	323	6‖
Jalisco (Mexico)	1,568	38	979	47¶
Japan	2,505	3‖	2440	4‖
Kuwait	963	58¶	403	11
Malaysia	1,219	5‖	1,157	10
New Zealand	962	38	598	31¶
Philippines	289	1‖	285	5‖
Qatar	689	52¶	331	27
Republic of Korea	1,572	20	1,260	11
Russia	241	20	194	7
Saudi Arabia	771	33	513	9
Singapore	1,891	20	1,529	12
South Africa	178	16	151	16
Taiwan	3,219	4‖	3,093	10
Thailand	1,208	9‖	1,097	30¶
Turkey	870	14	747	8
Ukraine	590	28	139	15
Uruguay	1,122	33	756	9
USA	2,076	30	1,498	10

Data extracted from the database of the US Renal Data System for 2014 (REF. 22). The total number of patients receiving dialysis was calculated as the sum of patients receiving haemodialysis and those undergoing peritoneal dialysis (PD). NA, not available, RRT, renal replacement therapy. *Number of patients per 1 million people (pmp). ‡Percentage of patients with a functioning kidney graft. §Percentage of patients undergoing dialysis who are receiving PD. ‖The lowest scoring countries for transplantation (Tx) and PD. ¶The highest scoring countries for Tx and PD. #Bangladesh, Brazil, and Indonesia supplied only data on dialysis.

Timing of RRT initiation

The IDEAL study[87] showed that the decision to start dialysis early (eGFR 10–14 ml/min/1.73 m^2) or late (eGFR 5–7 ml/min/1.73 m^2) did not affect patient outcomes. Therefore, European Renal Best Practice (ERBP) guidelines recommend that the timing of dialysis should be based on the patient's clinical condition rather than on their eGFR[88,89]. This approach might result in a stabilization, or even a decrease, in the number of patients receiving RRT. A cost analysis undertaken alongside the IDEAL study showed that, for the majority of patients, early dialysis would lead to higher costs and lower quality of life[90]. These data suggest that waiting to start dialysis until symptoms develop might have a societal benefit without loss of quality of life. In a pay-for-performance health system, authorities might consider adopting a 'planned' late start to dialysis below a well-defined eGFR in a well-justified proportion of patients requiring dialysis, the percentage of whom should be defined from the available evidence[91]. Notably, patients enrolled in the IDEAL study[87] were all followed up by a nephrologist for at least 1 year, and the majority had functioning vascular access for dialysis. A strategy of delayed dialysis is, therefore, only likely to succeed if accompanied by nephrology monitoring.

Summary

In most reimbursement systems, in-hospital dialysis is favoured over at-home dialysis, transplantation, or conservative treatment. To remove this bias, a common reimbursement fee for all patients who are close to requiring RRT or currently receiving RRT (for example, those with an eGFR of <15 ml/min/1.73 m^2) would favour patient choice to a greater extent than existing systems. The rationale behind this theory is that financial pressure would be taken away from hospital management and providers of RRT driving them to favour financially rewarding options, and providng the liberty necessary for patients to choose the treatment that suits them best.

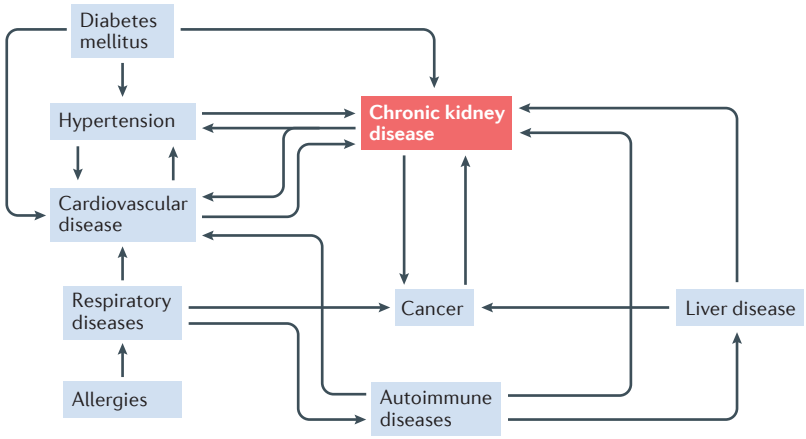

Figure 2 | **The network of chronic diseases and their mutual influences.** Almost all chronic disorders impact each other in various ways. Chronic kidney disease is often one of the end points in this cascade, but can also cause several chronic conditions, leading to a vicious cycle.

Prevention

Targeting the development of kidney disease and its major causes (primary prevention), or progression of kidney disease and its complications (secondary prevention), is hugely underexploited in spite of its potential to greatly reduce societal cost. However, preventive initiatives seem to be scattered, inadequate, and incongruent[92]. Governments tend to invest the majority of health-care budgets (often >95%) in treatment rather than prevention[93,94], even though if applied judiciously, preventive measures, including those that target the social determinants of health[94], may be associated with a lower cost per additional unit of benefit (quality-adjusted life year (QALY))[95], than purely curative measures. Although treatment for chronic diseases is vital, preventive measures are often inexpensive to implement, as demonstrated in Belgium where the addition of iodine to bread was highly effective in the prevention of thyroid nodular disease[96]. Admittedly, the prevention of CKD might be more complex than that of thyroid disease, but reducing the salt content of bread is a very similar measure that could well have a health-economic benefit[97–99].

The benefits associated with preventive interventions take a long time to accrue and might not be as cost-effective as expected. One explanation for this reduced cost-effectiveness is the effect of discounting. Future costs, such as those for treatment, and savings (cost offsets) are discounted at 3–6% and future health effects at 1.5–6.0% per year of waiting time, whereas early costs such as those for prevention often accrue at the onset and are, therefore, only modestly discounted[100]. Discounting is justified by financial economic theory (short-term benefits are valued higher than long-term benefits), but disfavours preventive measures with mainly long-term benefits. To mitigate the impact of discounting, a gradual decrease in discounting with every year of waiting time has been suggested[101]. Decreasing discounting of benefits leads to an increasing preference for preventive over curative interventions.

A gradual shift in focus from treatment to prevention could help keep global health care financially sustainable, while contributing to the overall health of the population. In the sections that follow, we describe potential measures to increase the impact of preventive care, and discuss their socioeconomic impact (see Supplementary information S1,S2 (table, box)).

The ultimate goal of prevention was initially to improve the health of the population, rather than to save money[102]. However, this statement was made at the end of the 20th century when financial restrictions and the task of weighing expensive therapies against each other were less preponderant than they are now, and before the use of thresholds for cost-effectiveness. Although improving health and saving money are both worthwhile aims, the ratio between health consequences and costs are currently weighed against each other before treatments are made available and the surplus costs of more expensive treatments may be compensated for by disinvesting in less cost-effective interventions. In addition, interventions do not necessarily need to be cost saving to be considered good value for money, provided that they deliver guaranteed health benefits.

Notably, health-economic studies on preventive measures that consider costs related to CKD and ESRD are very rare. An urgent need exists for studies on the cost-effectiveness of prevention of kidney diseases in the global population, and studies on the role of lifestyle factors and their modification on the development of costs associated with CKD.

Primary prevention

Noncommunicable diseases (NCDs) are major causes of death worldwide, and their prevalence is rising, particularly in LMICs and in high-income countries among people of low socioeconomic status[103–105]. NCDs also impact economic productivity, for example owing to 'sick leave' from employment[106]. Many of the reversible causes of NCDs are related to lifestyle, diet, or environmental factors and are preventable by measures that are simple to take on an individual basis, but might be difficult to implement from a global, societal perspective[103,107,108]. The investigators of an analysis undertaken in 2005 concluded that preventive efforts would result not only in the avoidance of a substantial number of deaths from chronic diseases, but also in substantial cost savings[109]. Although much progress has been made since the publication of this paper, NCDs are still a major challenge for health systems worldwide. The most effective strategy is likely to be primary prevention through changes in lifestyle. The costs of such strategies are usually minimal[110,111], although uncertainty exists about the optimal method of primary prevention and whether gains can be sustained. By improving the general health of the population, primary prevention could also enable health resources (personnel and infrastructure) to be redirected towards activities such as telemedicine, or supportive care for the elderly or disabled, rather than the curative therapies for which they are currently used.

Lifestyle factors, such as tobacco smoking[112–114], obesity[115], and lack of exercise[116] are all linked to the

Quality-adjusted life year (QALY) A life year adjusted for its utility. The plural (QALYs) is a measure of the utility of individual life years lived multiplied by duration (survival).

Discounting The reduction in the value of a future cost or benefit at a prespecified 'discount rate', which depends on its temporal distance from the starting point.

Cost-effectiveness An economic evaluation in which the incremental costs of an intervention are compared with the incremental benefits.

development and progression of CKD. Addressing these modifiable factors could have a major impact on the incidence of CKD and on health in general[116]. Unhealthy diet, including a high intake of salt, fats, *trans* fats, red meat, or alcohol, has been linked to an increased risk of chronic diseases[108,117]. Health-care expenses associated with these factors increase over time[97]. In an observational cohort study, both the incidence of CKD and mortality were reduced with increasing scores indicating a healthy lifestyle[116]. In patients with diabetes, lack of a social network (for example, established friendships) as well as other lifestyle factors increases the risk of mortality and CKD[118]. Environmental factors have an impact on the development of chronic diseases that is often neglected. Specific environmental risk factors for CKD are heavy metals, industrial and agricultural chemicals, elevated ambient temperatures, contaminants of foods or drinking water, other ingested substances such as medicines, and infectious diseases propagated by environmental conditions[119].

Concern could be raised that primary prevention might increase societal costs by increasing longevity. However, long life does not impact cumulative health-care costs for healthy elderly people (aged >70 years)[120]; these individuals enjoy good quality of life, remain productive, and fulfil social roles (such as caregivers)[121]. Most health-care costs are incurred near the end of life, irrespective of age[122,123]. Nevertheless, a substantial proportion of elderly people have NCDs and so primary prevention is especially important in settings where the population is long lived.

Dietary intervention. Overconsumption of salt contributes to one in ten cardiovascular deaths, predominantly in those aged <70 years[124], and is linked to the development and progression of CKD. Restricting salt intake prevents the progression of CKD by enhancing renin–angiotensin–aldosterone system (RAAS) blockade[125–129], but remains a controversial intervention in the healthy population[130–132]. Of interest, a high salt intake has been attributed to the sodium content of purchased foods rather than to behavioural choices by consumers (such as adding salt in food preparation)[133]. A health-economic study of salt intake reduction to decrease systolic blood pressure by 2 mmHg showed that costs related to stroke and myocardial infarction could be reduced by US$118 million[99]. A health-economic model assuming salt intake reduction by 9.5% through collaboration with the food industry demonstrated potential savings of $32.1 billion with the addition of 2.1 million QALYs[98]. The impact of a salt tax was lower, but still reduced medical costs by $22.4 billion. Combining sodium reduction in processed foods with a sodium tax had an additive effect[98]. In another analysis, reducing sodium intake from processed foods by 1,840 mg per day led to a decrease in blood pressure of 5.06 mmHg systolic and 2.70 mmHg diastolic, saving $430 million in health-care costs alone[134]. These results illustrate the potential benefits of concerted public policy aimed at primary prevention of NCDs. In June 2010, the Employment, Social Policy, Health and Consumer Affairs Council of the EU started action to reduce population salt intake by voluntary initiatives, such as setting limits to added salt in bread and mass-catering products[135].

Extending the analysis to a broad spectrum of food products, the health-economic impact in Germany of a reduction of salt, sugar, and saturated fat intake to the recommended quantities was investigated[97]. The effects on cardiovascular disease, CKD, cancer, diabetes, Alzheimer disease, sleep apnoea, hypertension, osteoarthritis, obesity, and obstructive pulmonary disease were considered. The decrease in total health costs was calculated at €16.8 billion per year. The cost impact of a reduction in sugar intake exceeded that of salt or fat. Only direct health benefits (not productivity, or societal or economic impact) were assessed; therefore, the true gains might have been larger than those projected[97].

Nondietary, lifestyle interventions. If interventions are effective in the long term (which remains to be proven), an increase in activity levels of sedentary people seems to be favourable from a health-economic perspective. Studies suggest that the incremental cost-effectiveness ratio (ICER) of increased physical activity is €348–86,877 per QALY, depending on type of intervention and the perspective taken in analysis[136]. The most substantial benefits were seen in a randomized controlled trial of instructor-guided exercise programmes[137]. However, follow-up was fairly short (1 year) given the long periods of time involved in NCD prevention and control.

Direct medical costs and indirect medical costs related to obesity and overweight in Canada in 2006 were $6 billion, 4.1% of overall health expenditure[138]. In Switzerland, obesity and overweight accounted for 2.3–3.5% of total health costs[139]. In a study conducted in Belgium, the health-economic impact of reducing BMI by one unit was calculated at €15.9 billion over a 20-year period[140]. Of note, the costs of CKD were not considered in any of these analyses.

The broad economic impact of smoking cessation has been highlighted in the literature, encompassing direct health costs as well as loss of productivity and costs related to passive smoking and to fires caused by smoking[111]. The health costs of smoking increase over time, especially among women[141]. In 2003, smoking-related societal costs in Germany were calculated at €21 billion[141]. In other analyses, the suggestion has been made that the direct economic benefits of smoking cessation might be negated by prolonged survival[142,143]. In one study, health costs were lowest among smokers, intermediate among individuals who were obese, and highest in the healthy population because of their high life expectancy and supplementary costs related to longevity[143]. In these studies, however, essential factors such as productivity and quality of life were neglected, and the health consequences of passive smoking, and of active smoking on CKD or hypertension were not included[142,143].

Secondary prevention

In established CKD, secondary prevention should include slowing down progressive kidney dysfunction and prevention of complications to improve life

Incremental cost-effectiveness ratio
The difference between costs of two interventions divided by the difference in the outcomes.

Direct medical costs
Costs of resources in the health-care sector (for example, drugs).

Indirect medical costs
Medical costs that arise from the life years gained.

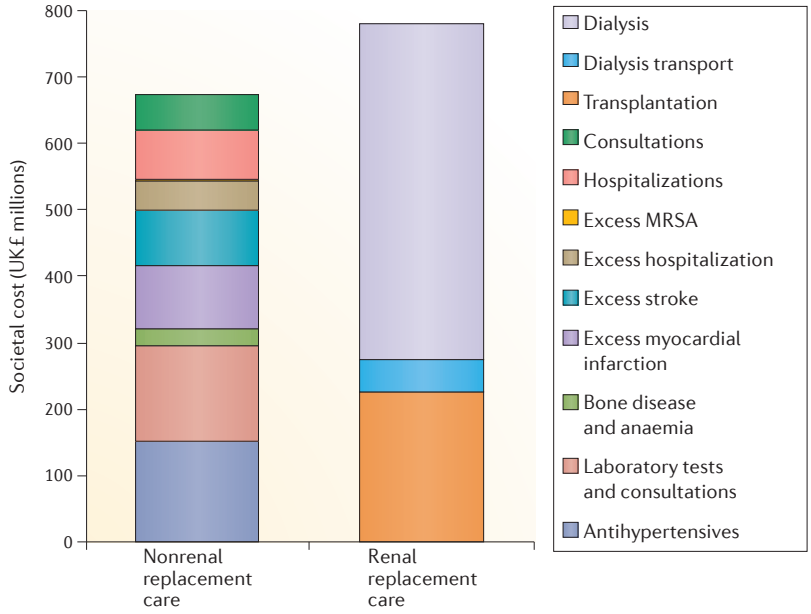

Figure 3 | **Societal costs for the care of patients with chronic kidney disease in the UK.** During the period 2009–2010, the costs involved in nonrenal replacement care almost equalled those for renal replacement care. MRSA, methicillin-resistant *Staphylococcus aureus*. Modified from Kerr, M. *et al.* Estimating the financial cost of chronic kidney disease to the NHS in England. *Nephrol. Dial. Transplant.* **27** (Suppl. 3), iii73–iii80 (2012) by permission of the European Renal Association–European Dialysis and Transplantation Association.

expectancy[27]. Despite the high incidence of cardiovascular events in patients with CKD[10,144–147], cost-effectiveness studies of secondary prevention including both cardiovascular events and CKD are scarce. Even the most conservative of estimates show that the risk of cardiovascular events and death begins to rise at an eGFR of 60 ml/min/1.73 m^2 (REFS 144–146). CKD causes an array of pathophysiological disturbances[10], necessitating medical consultations, drug therapies, surgical interventions, and hospitalizations, all of which generate costs. During 2009 and 2010, the yearly expense to the National Health Service in the UK for patients with CKD not requiring dialysis almost matched that for RRT[5] (FIG. 3). In addition, the per-patient cost of follow-up tends to increase as CKD progresses[148].

In the placebo-controlled IRMA 2 trial of patients with hypertension, type 2 diabetes, and microalbuminuria, the renoprotective effect of the angiotensin receptor blocker (ARB) irbesartan was demonstrated[149]. Based on a lifetime Markov model to calculate the impact on life expectancy and health-care costs in this population, early intervention (initiation of irbesartan at the stage of microalbuminuria) resulted in an estimated yearly cost reduction culminating at 25 years[150] (FIG. 4a). Net cost savings were realized after 10 years (FIG. 4a), while with later intervention at the stage of macroalbuminuria the balance resulted in lower net cumulative savings[150]. Early initiation of irbesartan added 1,500 ± 270 undiscounted life years per 1,000 patients[150].

The use of angiotensin-converting-enzyme (ACE) inhibitors was found to be cost-effective in patients with a serum creatinine level >265.3 µmol/l (>3 mg/dl), proteinuria and hypertension, but without diabetes or severe heart failure[151]. A comparison of antihypertensive treatments in patients with CKD showed a quick and growing return of investment with the ACE inhibitor benazepril[152]. Based on data from the PREVEND IT[153] and PREVEND[154] studies, screening the general population in the Netherlands for albuminuria, and treating those who tested positive with the ACE inhibitor fosinopril to prevent cardiovascular events and progression of CKD to ESRD was cost-effective when compared with no screening[155]. The investigators, however, emphasized the limited time frame of their study and the necessity for the results to be confirmed in other studies[155]. Although the practice of screening the general population for CKD is debated[156], this preventive approach might be cost-effective and would perhaps be even more so if screening is limited to populations at risk of CKD[155,157,158]. Indeed, another analysis of data from the PREVEND study showed improved cost-effectiveness when screening was limited to older individuals (aged ≥50 years, and even more so in those aged ≥60 years)[159]. In addition, the cost-effectiveness of antihypertensive agents, particularly RAAS antagonists, improved with increasing baseline albuminuria[160]. Yet other studies suggest that no clear evidence exists for a protective role of RAAS blockade in patients with CKD from causes other than diabetes[161] or in patients >70 years of age[162].

The CAP-KD trial suggested a nephroprotective effect of the oral adsorbent AST-120 in Japanese patients with CKD (serum creatinine concentration <442 µmol/l (<5 mg/dl) and not undergoing dialysis)[163]. This agent was proposed to be cost-effective in the subgroup of patients with diabetes[164]. Subsequent randomized controlled trials did not, however, confirm the nephroprotective effect of this drug[165,166]. The SHARP[167] randomized, placebo-controlled trial, demonstrated that lowering cholesterol with simvastatin plus ezetemibe in patients with CKD decreased the incidence of major atherosclerotic events. This approach was established to be cost-effective, especially in patients at the lower end of the cardiovascular risk spectrum, and those with stage 3 CKD[168]. The investigators speculate that less costly cholesterol lowering regimens might be even more cost-effective[168]. The results of SHARP[167] highlight the need for trials that could provide evidence of the efficacy of less costly medications.

Savings to the US health-care budget were modelled for a decrease in the progression of CKD (reducing the decline in eGFR by 10%, 20%, or 30%)[168]. A 30% reduction in the rate of eGFR decline for an intervention initiated at a GFR of 30 ml/min/1.73 m^2 would have resulted in $33 billion savings between 2000 and 2010. The amount saved would have been almost twice as much if the intervention was initiated at 60 ml/min/1.73 m^2 (REF. 169) (FIG. 4b). Even a <30% decline in the rate of disease progression was projected to result in substantial savings[169,170].

The studies discussed above indicate that secondary prevention measures are cost-effective. By contrast, a study based on the results of the TEMPO trial suggested that tolvaptan might reduce loss of kidney function in

Markov model
A decision model that enables transitions between different health states over a period of time (often defined as life long).

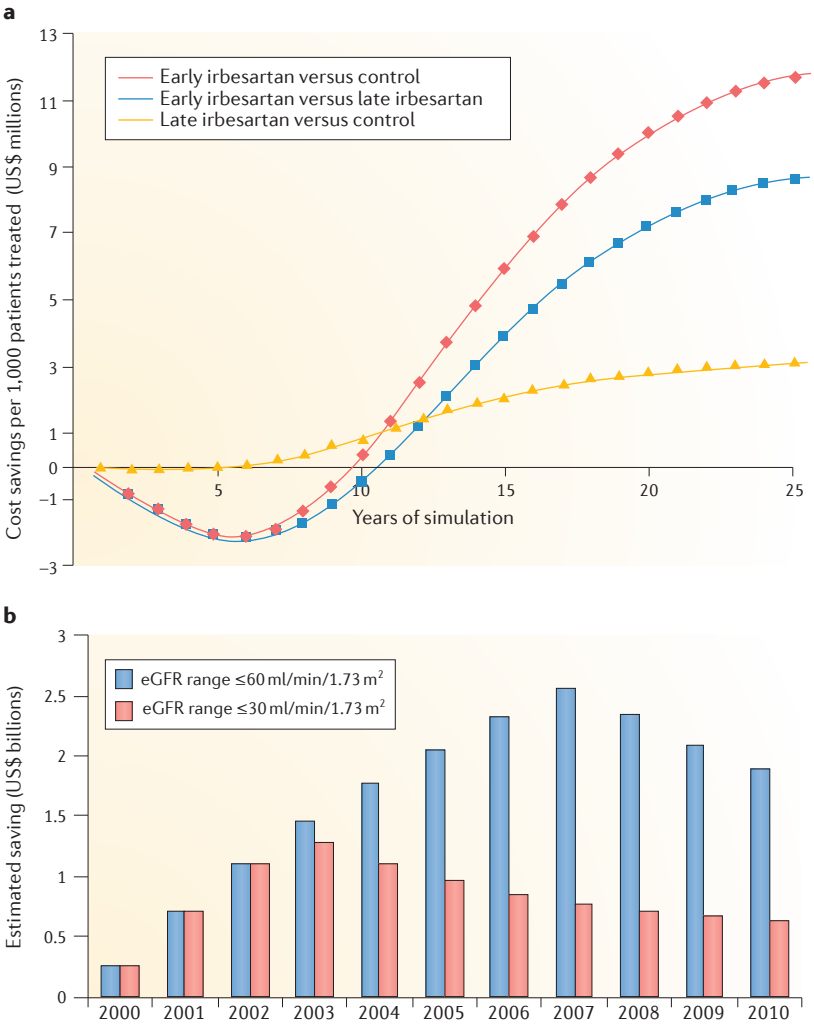

Figure 4 | **Savings in societal costs through secondary prevention of chronic kidney disease (CKD). a** | Effect of irbesartan in patients with diabetes and microalbuminuria on costs per 1,000 patients treated over a period of 25 years. Early intervention is most cost saving, although the curve goes through a negative phase during the first 2 years. **b** | Estimated cost savings if the decline in estimated glomerular filtration rate (eGFR) is decreased by 30%, starting from an eGFR of 60 ml/min/1.73m² or 30 ml/min/1.73m². Part **a** modified with permission from the American Diabetes Association © Palmer, A. J. *et al.* Cost-effectiveness of early irbesartan treatment versus control (standard antihypertensive medications excluding ACE inhibitors, other angiotensin-2 receptor antagonists, and dihydropyridine calcium channel blockers) or late irbesartan treatment in patients with type 2 diabetes, hypertension, and renal disease. *Diabetes Care* **27**, 1897–1903 (2004). Part **b** modified from Trivedi H. S. *et al.* Slowing the progression of chronic renal failure: economic benefits and patients' perspectives. *Am. J. Kidney Dis.* **39**, 721–729 (2002) with permission from the National Kidney Foundation.

patients with autosomal dominant polycystic kidney disease (ADPKD), but at an ICER of $744,100 per QALY gained[170], which exceeds any threshold of societal willingness for gaining QALYs specified to date. The ICER of tolvaptan was highest for patients with slowly progressing ADPKD[170]. Subsequently, a reduced price for tolvaptan was negotiated by regulatory authorities and payers in the UK and other western European countries, leading to ICERs that matched the upper acceptable range (£23,500–43,500 in the UK, as calculated by The National Institute for Health and Care Excellence)[170,171]. Future price setting strategies based on high acceptable ranges of ICERs might impose a progressively greater burden on health-care systems, and all stakeholders (including the pharmaceutical industry) should be aware of this threat. If not corrected, the disparity will increase between societies or patients who can and cannot afford a certain treatment. These considerations have led to the recommendation that tolvaptan be restricted to patients with documented or likely fast disease progression[172]. Of note, if a difference in the cost of a drug is observed between countries, prices might be based on what the market will sustain, rather than on production costs. On the other hand, several agencies use well-defined strategies for price negotiations that include factors such as health benefits to patients, as well as sequence of entrance to the market (first agent or not), the likelihood of off-label use, or support to local industry.

Who should be evaluated for CKD and who should be treated? The cost-effectiveness of screening the global population for CKD versus screening only those with diabetes or hypertension was evaluated in a systematic review[156]. Albuminuria was assessed in eight out of the nine selected studies, whereas eGFR was measured in only two studies. No uniform cost advantage was found for albuminuria screening in the general population. By contrast, ICERs of $5,000–55,000 and $23,000–74,000 per QALY were estimated for patients with diabetes and hypertension, respectively. Screening the general population was only cost-effective when included in health check-ups or with rapid progression of CKD and was, in a sensitivity analysis, strongly influenced by the preventive impact of RAAS inhibition on cardiovascular risk[156]. The finding that screening and monitoring was most effective in those at risk, for example, in patients with proteinuria and diabetes or cardiovascular disease, has been confirmed in other series[173,174]. In addition, screening of the general population could also lead to false positives that alarm healthy individuals and result in unnecessary treatment[175]. Finally, currently available screening tests are not specific[176,177] so care must be taken to confirm single positive results, which increases costs.

These data in favour of screening at-risk patients only relate to diabetes and hypertension[156,173,174] and not to the other risk factors for CKD (BOX 2). Screening for CKD in people with obesity or a family history of CKD, those of low socioeconomic status, and the elderly, warrants further investigation[175,178]. On the basis of a meta-analysis of studies published up to November 2011 (REF. 179), the US Preventive Task Force recommended against screening for CKD in asymptomatic adults without risk factors, and also against testing for proteinuria in adults with or without diabetes who are currently taking an ACE inhibitor or an ARB[175]. The task force remarked that there is "very limited evidence about whether knowledge of CKD status in patients with isolated hypertension helps in making treatment decisions" (REF. 175). This negative statement was criticized by the nephrological community for focusing on the existing uncertainties

Box 2 | **Risk factors for chronic kidney disease (CKD)**

Published evidence of health-economic benefit with preventive intervention

- Diabetes mellitus
- [Hypertension]*

No published evidence of health-economic benefit with preventive intervention

- Cardiovascular disease
- Infectious diseases
  - Hepatitis B
  - Hepatitis C
  - HIV
- Low socioeconomic status
- Smoking
- Sedentary lifestyle
- Acute kidney injury
- Known kidney damage or condition with potential to damage the kidneys

Nonmodifiable risk factors

- Age >60 years
- Family history of CKD

*Parentheses used as the health-economic impact of preventing hypertension on CKD is less well-documented than for diabetes.

rather than on who should be screened[180–182]. Additional studies are needed to determine the populations who should be screened for CKD and to estimate the cost-effectiveness of a range of early detection policies at a population level. As the need for additional medical consultations seems to be a financial barrier, coupling the test to other mass screening initiatives, such as those for colorectal cancer, could be an option.

When analysing the cost-effectiveness of case-finding strategies, the prevalence of the risk factors and the incidence of potentially avoidable events have a central role. As the number of individuals to be considered for early prevention is much larger than those to be treated by RRT, detection and prevention at the earlier stages of CKD must be substantially less expensive than RRT to be economically attractive[183]. Whether this is the case is uncertain, particularly in LMICs. However, most of the available cost-effectiveness studies are based only on the prevention of RRT, whereas screening for CKD and effective treatment of those who test positive will also result in prevention of cardiovascular events. This additional benefit should be included in future cost-effectiveness studies.

Several drugs have been marketed to prevent progression of CKD, despite insufficient economic evaluation[170,184]. Reimbursement should, therefore, be restricted to drugs of proven benefit, and populations who will benefit the most from the drug need to be identified. This approach should prevent waste and maximize opportunities for health gains from other, less-costly strategies[185]. Personalized medicine could help to limit the use of drugs to patients who will benefit the most. Several novel drugs have been developed specifically for rare kidney diseases. Owing to the small number of cases, assessing the specific health-economic impact of such diseases is difficult. Although the absolute cost might seem negligible, if several of these drugs come to the market, financial pressure on governments will be substantial and may clash with societal pressure to provide those drugs to affected patients. Health-economic assessment should, therefore, focus on cost per patient. Changes to health service payment models could also be considered, such as reimbursement based on achieved health outcomes rather than for delivered interventions.

To avoid unnecessary investment in expensive drugs, guideline committees must place additional emphasis on health-economic evidence when making recommendations. Such regulatory bodies have a duty to include explicit statements if costs are not justified by demonstrated benefits[186]. For example, ERBP has stated that tolvaptan should be restricted to patients with ADPKD of documented or likely fast disease progression, as the evidence of the health-economic benefit of the drug was not sufficiently strong for it to be recommended for those with slowly progressive disease[171,172].

The impact of acute kidney injury. Acute kidney injury (AKI) is a common clinical condition that affects up to 1% of the general population and 8–15% of patients hospitalized for any reason[187]. The worldwide incidence of AKI is increasing[188]. In the AKI-EPI study[189], AKI was found to be present in 57.3% of patients admitted to an intensive care unit in a 1 week period. The global increase in AKI is likely to be attributable to greater recognition of this condition and a reduction in the thresholds of diagnostic criteria. However, ageing of the general population; the increasing incidence of comorbidities; greater use of high-risk interventions resulting in increases in risk factors such as sepsis; and exposure to radiocontrast agents or other nephrotoxins, also conribute to the increase in AKI incidence[190]. In the UK, the annual cost of AKI-related inpatient care was estimated at UK£1.02 billion, approximately 1% of the National Health Service budget[191]. Prevention of 20% of AKI cases could represent savings of £200 million per year, equivalent to 0.2% of the health budget[191].

Over the past few years, observational studies have suggested that AKI and CKD are linked (one condition being a risk factor for the other) and that both can lead to cardiovascular disease[192]. Observational evidence suggests that even mild in-hospital AKI with full recovery might lead to CKD[193]. These associations might not be causal, however, but rather the result of residual confounding or ascertainment bias[194]. If AKI were an important mechanism through which CKD occurs and progresses, the need to prevent AKI would be compelling, for the health of individual patients as well as to reduce health-care costs.

Severe AKI, such as in the setting of septic shock, is difficult to prevent. The focus for prevention should, therefore, be on mild AKI in the community or on general hospital wards; these cases are more prevalent and easier and less expensive to prevent than severe

AKI[195]. Prevention of AKI can be achieved by careful and vigilant use of radiocontrast agents and nephrotoxins, rapid intervention for infection, and by maintaining kidney perfusion. Patients with AKI should be followed up either in specialized AKI clinics[196] or by primary-care physicians, which might be the more cost-effective option.

A call to action

The utility and potential economic benefits of primary and secondary prevention of CKD are underutilized. In the examples given below we outline some potential strategies by which efficiency in this field could be increased. The focus is on dietary intervention, but other lifestyle factors are also considered.

Many processed foods can jeopardize health[197] as they do not conform to the recommended thresholds of nutrients[133,198], perhaps because of concern by manufacturers and the retail sector that they will not be appealing to consumers[199]. Consumption of processed foods has been linked to the rising prevalence of obesity[200]. The public interest would be better served if increased efforts were made by the food industry to produce, promote, and sell healthy food[198]. In an ideal world, everyone would prepare healthy food from fresh ingredients rather than buying processed foods, but this aim is difficult to achieve under current socioeconomic conditions. However, opportunities exist to reduce the salt, sugar, and fat content of processed food[198].

Processed food is often less expensive than fresh food[201], and low income is linked to the purchase of unhealthy foods[202]. Cost is, therefore, a potential barrier to NCD prevention and control, especially as chronic diseases are most common in groups of the lowest socioeconomic and educational status[203]. Policy interventions are required to decrease the price differential between healthy, fresh and unhealthy, processed foods. A roadmap for action on food product improvement was developed under the auspices of the Dutch EU presidency (1st January to 30th June 2016). This plan describes pathways to improve food product quality and promote healthy food intake by decreasing salt and calorie sources, including sugar and saturated fats, in food products[204]. This initiative is similar to measures recommended by the US government[205].

Labelling

Nutritional labels are now available on most food products, but are rarely displayed in prominent locations using sufficiently large font size and are often difficult to read and interpret[206,207]. Nevertheless, correct use of food labels helps consumers to identify healthy foods and improve their diet[208]. From a public health perspective, good reasons exist to improve and simplify food labelling[207].

Although simple, front-of-package labels are used in several European countries, they are not universal within Europe, which has four different simplified labelling systems for food. The UK label, which consists of a three-colour code (green, orange, and red) indicating a scale from safe (green) to unsafe (red), for levels of salt, fat, and sugar was heavily criticized by European food producers[209]. One of the arguments against this system was that overall survival in countries such as Italy is higher than in the UK despite the absence of simplified food labels and high intakes of foods that are unfavourably labelled in the UK, an advantage that was attributed to the 'Mediterranean diet'. A Mediterranean diet *per se* is likely to have a positive effect on health[210]. However, survival is also linked to many other factors, such as environmental conditions or a genetic predisposition to longevity. In Australia, Iceland, Japan, and Singapore, survival is similar to that in Italy, although a Mediterranean diet is unlikely to be commonplace in these countries. In Australia, a five-star rating for foods is used, ranging from zero stars for unhealthy food to five stars for very healthy food[211]. In May 2016, the FDA announced a new Nutrition Facts label for packaged foods, which highlights information on calories and 'servings per container' based on revised guidelines for serving size[212]. Manufacturers will need to implement the new label by July 2018. The Choices International Programme uses an evidence-based system for the profiling of food products according to their health-promoting properties[213]. The 'Healthy Choice' label is used to mark food products that conform to specific criteria. In a modelling study considering the everyday dietary habits of young adults in the Netherlands (aged 19–30 years), sole consumption of foods with the 'Healthy Choice' label led to theoretical reductions in the intake of salt, *trans* fats, and carbohydrates of 23%, 62%, and 16%, respectively, and an increase in fibre intake of 28%[214]. Of note, a decrease in salt intake by 20% starting from 10 g per day would decrease net salt intake by 2 g per day; that is, at least twice as much as in a study that showed a substantial reduction in the financial cost of cardiovascular disease with reduced salt intake.

Education to improve health literacy

According to a survey conducted in 2009, >50% of people in the USA are unaware of the existence of food labels, and only 30% use them to inform decisions about purchase and consumption[215]. The presence of an NCD risk factor (for example, hypertension, diabetes, overweight, heart disease, and hypercholesterolaemia) had little influence on an individual's use of food labels[215], suggesting that interventions could be initially targeted at these populations who, arguably, have most to gain. In a European study, only 16.8% of shoppers looked at food labels and the degree of consumer understanding differed markedly between countries[216]. Many opportunities exist to improve, simplify, harmonize, and increase knowledge about food labelling. Correct use of food labels will be difficult to achieve without education of the general public[202]. Lack of health education is an important problem among patients with CKD and many patients receiving dialysis have difficulty understanding dietary and fluid restrictions[217]. In a study of patients stratified by the stage of CKD, the percentage with poor health literacy rose with the severity of renal disease[218]. In the CRIC study[219], which involved

Utility
The measure of the preference or value that an individual or society attribute to a health state. This is a quality of life score that ranges from 0 for death to 1 for perfect health, with negative scores being allowed for states considered worse than death.

a population with mild-to-moderate CKD, eGFR was lower and prevalence of hypertension, diabetes, and vascular disease were higher in the group with limited health literacy. A clear association exists between general education and mortality[94]; the assumption could, therefore, be made that low health literacy, low overall education, and low income occur together. However, in one study no correlation between eGFR and income or degree of general education was found, whereas health literacy seemed to be the only factor with a significant correlation to eGFR[218]. These findings may be due in part to a lack of statistical power. However, all evidence seems to underscore the importance of health education in all members of society, including those with a high educational level and income. Educational measures should include all aspects of a healthy lifestyle — diet, exercise and smoking cessation[220–222]. Endeavours should begin at school age[220,222] and continue into adulthood, through cookery and lifestyle magazines or television programmes, and the involvement of healthy food and lifestyle ambassadors creating health-based role models. Programmes should be specifically developed to target people of low socioeconomic status, who might require different modes of communication than the rest of the population.

Regulation

Controversy exists as to whether governments should formulate policies aimed at improving lifestyle factors through regulating industry, retailers, and the public. Although exercise cannot be directly regulated, public policy aimed at encouraging exercise (for example, promoting pedestrian-friendly cities, or employing exercise coaches in the workplace) is underused. By contrast, strict regulation of food industry is more straightforward than regulation of exercise. Adversaries emphasize the importance of individual liberty. However, as healthy food is increasingly difficult and expensive to obtain, governments are duty-bound to improve public health by regulations aimed at promoting the consumption of this food. Such regulation is of tangible benefit, as illustrated by the example of road traffic accident prevention; imposing speed limits and blood tests for alcohol level helped reduce the number of deaths and injuries.

In the last two decades, the food industry has adopted various self-regulatory initiatives — including restrictions on sales of sugary beverages in schools and of marketing of foods to children, and the introduction of Smart Choices labels[223] — perhaps aimed at reducing the need for government intervention. Whether these interventions are sufficient to improve public health at large is unproven and leaving regulation to the discretion of industry is a high-risk approach. The tobacco industry has applied self-regulation for many years, but this approach has resulted in little or no effective action[223].

Another option for governmental action is the introduction of health taxes. This concept was heavily criticized in Denmark after its introduction in 2011, with some suggesting that taxation would increase government revenue rather than improve health[224]. The project was abandoned after 15 months. However, an analysis published in 2016 showed an association between the Danish health tax and nutritional purchase attitudes, resulting in an estimated 123 lives saved per year[224]. In 2015, the British Medical Association called for a 20% sugar tax in the UK to subsidize the cost of fruit and vegetables[225]. However, additional evidence that health taxes are effective is needed.

Conclusions

Here we have summarized current understanding of the substantial costs associated with CKD and its treatment. In particular, RRT for patients with ESRD imposes a substantial financial burden on societies and individuals and could be decreased through a more rational approach to RRT by favouring transplantation and home-based dialysis modalities.

Approaches to prevent CKD and address the conditions that lead to CKD as an alternative option to investing in curative interventions have been insufficiently explored. Such preventive approaches could be more effective than therapeutic approaches, leading not only to reduced costs, but, more importantly, to a healthier population with a better quality of life.

Several approaches to facilitate the prevention of CKD have been analysed from a health-economic perspective (Supplementary information S1 (table)). However, high quality health-economic studies of primary and secondary prevention in CKD are scarce, and we urge the scientific and medical communities to increase their efforts in this domain.

Prevention of CKD has the potential to complement the societal benefits achieved by investment in treatments, at a reasonable cost. We are convinced that a renewed focus on preventive strategies would be timely and appropriate given the huge burden of CKD and other NCDs. Notably, in 2016, the WHO formulated an action plan for the prevention and control of NCDs in the WHO European region[226]. Although improvements to lifestyle might seem fairly simple, convincing the general population to make these changes is a complex matter. Reallocation of resources currently allocated to treatment towards prevention and education initiatives and policies might be required[227], such as by decreasing reimbursement of expensive therapies or withdrawal of reimbursement of drugs without evidence-based benefit.

Although the benefits of screening for CKD might extend to the prevention of cardiovascular disease as well as loss of kidney function, the cost-analyses and clinical data on which effectiveness calculations were based are debatable. Currently, no evidence exists to support CKD screening in the general population[175], and screening patients with diabetes or hypertension is the preferred approach for practical, societal, and economic reasons.

To date, most studies on preventive drugs for CKD have focused on expensive novel medications, whereas cheap existing drugs have been neglected despite their clear socioeconomic benefit. Regulatory and scientific communities should redefine their interests and focus on low-budget medication.

Many stakeholders will be required to guide society towards a healthy lifestyle to prevent the development of NCDs, including CKD and ESRD. National and regional governments will be required to take a leading role in a regulatory capacity and through enlightened public policy and health campaigns aimed at behavioural change. At the international level, the aim should be towards harmonizing strategies between countries. Current disparities offer opportunities for improvement if countries are willing to learn from each other. However, NCD prevention and control should not be restricted to interventions by authorities and regulatory bodies, but also requires concerted efforts from the nutritional and pharmaceutical industries, the retail sector, the medical community, consumers, and patients — all helping to move society towards a healthier lifestyle.

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Author contributions

All authors contributed to researching data for the article, discussing the article's content, and revising or editing the manuscript before submission. R.V. wrote the first draft of the article, and then coordinated subsequent versions with input from the other authors.

Competing interests statement

R.V. has received speakers' and consultancy honoraria and travel support from Nikisho, Nipro, Fresenius Medical Care, Bayer and Astra-Zeneca. L.A. has received speakers' and consultancy honoraria from Sanofi, Bayer, Novartis and Astra-Zeneca. E.B. has received speakers' honoraria from Fresenius Medical Care and Baxter Health Care. R.G. is member of steering committees of randomized controlled trials (co)sponsored by Bayer, Genzyme-Sanofi, Ipsen and Otsuka, and has received research grants from these companies as well as from Abbvie, Baxter and the Dutch Kidney Foundation. R.O. has consulted for Astellas, Fresenius Medical Care, TEVA and Pfizer and his unit has received research grants from Astellas, TEVA, Pfizer, Amgen and Novartis. M.J.P. has received grant funding from Sigma Tau, GSK, Boehringer Ingelheim, Pfizer, MundiPharma, GMASOL, Ingress Health, Bayer, Bristol-Myers Squibb, AbbVie, MSD, Sanofi and Astra, and received honoraria from Vertex, Pfizer, Quintiles, Mapi, Astellas, Novartis, OptumInsight, Swedish Orphan, Innoval, Jansen, Sanofi, Intercept, Pharmerit, GSK and MSD, and has stocks in Ingress Health. W.V.B. has received honoraria from Fresenius Medical Care, Gambro and Baxter Healthcare, and is a member of the steering committee of clinical studies sponsored by Fresenius Medical Care and Baxter Healthcare. J.J.G.-Z., N.L., R.L.M, M.T. and C.Z declare no competing interests.

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