Due to the scale of chronic kidney disease (CKD) [1], management of patients is delivered from a broad range of settings. Research into CKD is often focused towards interventions relevant to the later stages of disease seen in secondary care and can fail to acknowledge the large quantities of clinical input delivered in a community setting. Furthermore, while medical students are still taught a hierarchy of ‘conservative, medical, then surgical treatments’, guidelines for the management of CKD have focused on patient identification and pharmacological treatments [2] with scant data on public health interventions that may help ameliorate the growing problem of this condition at a ‘pre-health-care’ level.

In this issue, Strippoli et al. [3] address the received wisdom that drinking increasing amounts of fluid each day is associated with health benefits. This long-standing belief, repeated even in current governmental advice [4], is believed to originate from an opinion statement, made in the absence of robust epidemiological data, by the 1945 US Food and Nutrition Board of the National Research Council [5] recommending a daily fluid intake of 2.5 L. Using information on estimated daily fluid intake obtained as part of the Blue Mountains Eye Study (1992–1994), the authors considered the effect of increased fluid intake (importantly estimated from both fluids and prepared food as stated in the 1945 guidance) in relation to mortality and loss of estimated glomerular filtration rate (eGFR). In a population of 3858 patients with a median follow-up period of 13.1 years, greater volumes of fluid intake were not associated with reduced risk for death when fluid consumption was considered as a continuous variable (hazard ratio for death 0.99 [95% confidence interval (95% CI) 0.98–1.01] per 250 mL increase in total daily fluid intake), nor when upper and lower quartiles of fluid intake were compared. A similar result was seen in the 1479 patients with multiple measurements of renal function. Here, a non-significant increase in eGFR was associated with increasing daily fluid intake [0.06 mL/min/1.73 m² for every 250 mL increase in daily fluid take (95% CI −0.03 to 0.14)].

Although the existing literature surrounding this topic is conflicting [6, 7], the findings of this study fall in the majority camp and are aligned with prevailing nephrological opinion that increased fluid intake will not prevent the development of CKD. As many well-articulated views have been voiced in relation to the divergent findings in this area [8, 9], we highlight issues raised by this paper in relation to the utilization of existing data and the international need to address population health issues related to CKD.

As the number of large-scale observational studies increases, so does the need to maximize the value of the recorded data. Careful analyses of datasets such as the Framingham cohort [10] and NHANES I–III [11] have helped to answer clinical questions that were not formed or considered at the time of study initiation. This has allowed the value of these data to be maximized and has been due in part to the shared ‘open source’ nature of the information recorded, and in part to the well-considered study designs and evolution of the clinical information captured. Because of the perceived challenges of performing randomized, controlled trials in the CKD population, a number of observational studies addressing this topic have been established in recent years [12, 13]. These studies have had great value in generating hypotheses about factors related to progression and outcome in CKD but are associated with significant costs. The Chronic Renal Insufficiency Cohort was recently awarded an NIH grant of almost $8 million to enable continued follow-up [14]. Strippoli et al. are to be applauded for having identified the potential to add to our knowledge regarding fluid intake by using a pre-existing and, therefore, cost-effective resource. However, as the authors note, their analyses and conclusions are limited by what data were ‘not’ available; most notably information pertaining specifically to water consumption. Given the vintage of their data, this limitation clearly could not be addressed. However, it would be prudent for the nephrology community to consider defining population-level questions where simple standardized
extensions to data capture and the addition of rational patient surveys in existing studies could, at scale and pace, cumulative-ly begin to answer questions that could not be practically con-sidered in an independent study. This model of structured data collection could be further extended to patient level data as permanent records move from paper to electronic charts. In the USA, the Patient Protection and Affordable Care Act [15] has the potential to move reimbursement towards the value of care provided rather than paying mainly for diagnostic and therapeutic procedures. This may broaden and unify patient data collection between centres and could lead to answers to previously unimaginable population-level questions being within reach. Although suggesting a standardized national or international approach may seem naive and optimistic, inspiration should be taken from initiatives such as automated eGFR reporting. This initiative rapidly improved rates of identification of CKD [16], especially in countries with publicly funded health systems, and showed that unified changes in care are possible. More speculative future gains can be envisaged where it becomes possible to capture pre-illness data with systems to measure, for example, salt and fluid intake or physical activity. Although present access to such data remains limited, the growing ubiquity of smartphones and research into their role in improving health care [17] may offer a glimpse of the future. Applications specifically designed to log sleep, exercise, food and fluid intake, with minimal user input, already exist [18]. Development of such information capture at population level would offer the possibility of better understanding risk factor development and evolution.

Before capture of data can be meaningfully unified, research questions must first be defined. Although many papers have considered the effects of fluid intake on various outcomes, these studies have predominantly been cross-sectional analyses and, as noted in this issue, longitudinal behaviours are likely to play an important confounding role. As such, it is difficult to state with absolute confidence that the question of fluid intake in relation to health has been fully addressed, leaving a ready opportunity for further study. In the general population, the evidence for health benefits related to increased levels of physical activity is well established [19]. An increased mortality risk associated with reduced levels of physical function in CKD has been observed in several populations [20, 21]. However, the evidence base regarding the effect of other lifestyle interventions in this patient group is limited [22, 23]. Considering questions such as this, and other topics including cognitive functioning, socio-economic factors and access to primary care may provide the first step towards developing cost-effective public health interventions targeted towards CKD. In addition, issues of information governance and public acceptance must be considered. Even in the context of integrated care records, patient groups voice valid concerns regarding governance and access [24]. Measures such as the National Health Service Care Record Guarantee [25] are an important step towards offering the necessary securities but, ultimately, the onus will be on the medical community to effectively communicate the organizational, public and personal interests and mitigate fears of a ‘big brother’ approach to health.

In the current era where ‘big data’ are constantly alluded to and lauded, the question of structure and utility cannot be overlooked. The medical community is at a point of sea change in relation to the type and quantity of data that are readily available, and there is the chance for nephrology to lead the way in using this raw information to improve patient and population health. The long-term nature of kidney care has led to well-established links between renal physicians, primary care and other specialties such as cardiology and diabet-es. This offers the opportunity for renal research to utilize data from a range of sources, and also to help orchestrate inter-disciplinary links and guide design of data capture. Without careful thought and planning about how we intend to use this resource, big data will be nothing more than a big mess.

CONFLICT OF INTEREST STATEMENT

None declared.


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The K-factor in chronic kidney disease: biomarkers of calcification inhibition and beyond

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There is a huge body of unambiguous evidence that cardiovascular calcification represents one of the most stringent mortality risk factors in patients suffering from chronic kidney disease (CKD). The more advanced the stage of CKD, the more frequently and the more severe such calcifications develop. With regard to pathophysiology, it is evident that numerous factors are involved in this process of hydroxyapatite deposition into the vessel wall, including calcium and phosphate overload, calciprotein particles, apoptosis, osteochondrogenic trans-differentiation of the vascular smooth muscle cells (VSMCs), lack of calcification inhibitors etc. [1, 2]. One of the key calcification inhibitors is vitamin K-dependent matrix Gla protein (MGP), a 14 kDa protein exclusively expressed in chondrocytes and VSMCs [3]. MGP function appears to be sub-optimal in CKD patients and MGP may thus appear to be an appealing and promising target for vasculo-protective intervention [4]. The current pilot trial by Caluwé et al. [5] lends support to a straightforward therapeutic approach into this direction.

Several investigations tackled progression of cardiovascular calcification in the past. Substantiated calcification data in end-stage renal disease was produced by trials targeting hyperphosphataemia and hyperparathyroidism as well as studies investigating the effects of renal transplantation. The most frequently studied intervention was the comparison between calcium-containing versus calcium-free phosphate binders. While most studies in this area demonstrated superiority of calcium-free binders in this context, some did not, and especially two recent trials performed in patients in CKD stages 3b–4 raised questions about the effects of phosphate binding in such earlier stages of CKD and emphasized some safety concerns about the use and dosage of calcium-containing binders in CKD patients not on dialysis [6, 7]. However, we now have a meta-analysis of all available randomized, controlled trials (RCTs) in this context...