



# The benefits of dietary fiber: the gastrointestinal tract and beyond

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Received: 9 October 2022 / Revised: 13 November 2022 / Accepted: 23 November 2022 / Published online: 6 December 2022  
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## Abstract

Dietary fiber is considered an essential constituent of a healthy child's diet. Diets of healthy children with adequate dietary fiber intake are characterized by a higher diet quality, a higher nutrient density, and a higher intake of vitamins and minerals in comparison to the diets of children with poor dietary fiber intake. Nevertheless, a substantial proportion of children do not meet the recommended dietary fiber intake. This is especially true in those children with kidney diseases, as traditional dietary recommendations in kidney diseases have predominantly focused on the quantities of energy and protein, and often restricting potassium and phosphate, while overlooking the quality and diversity of the diet. Emerging evidence suggests that dietary fiber and, by extension, a plant-based diet with its typically higher dietary fiber content are just as important for children with kidney diseases as for healthy children. Dietary fiber confers several health benefits such as prevention of constipation and fewer gastrointestinal symptoms, reduced inflammatory state, and decreased production of gut-derived uremic toxins. Recent studies have challenged the notion that a high dietary fiber intake confers an increased risk of hyperkalemia or nutritional deficits in children with kidney diseases. There is an urgent need of new studies and revised guidelines that address the dietary fiber intake in children with kidney diseases.

**Keywords** Fiber · Gut microbiome, Plant-based diets · Chronic kidney disease · Children · Pediatric Renal Nutrition Taskforce (PRNT)

## Introduction

Dietary fiber includes a heterogenous group of non-carbohydrate plant cell wall compounds (lignin, chitins, and waxes) and carbohydrate polymers that are neither digested nor absorbed by the human intestine (non-starch polysaccharides, resistant oligosaccharides, and resistant starch) [1]. Fiber is naturally present in whole grain foods, fruits, vegetables, tuberous roots, and legumes, while dietary fiber can also be chemically/physically extracted, enzymatically modified, or synthetically derived, and subsequently added to food [1]. Dietary fiber is considered an essential constituent of a healthy diet and has been associated with several health benefits. In healthy adults, a high dietary fiber intake has been associated with a significant reduction in all-cause mortality and major cardiovascular events, a beneficial lipid profile, a lower incidence of diverticular disease, and a lower risk of malignancies such as colorectal cancer [2–7]. Although similar data on the multisystem benefits of fiber in children is lacking, healthy children with higher intakes of dietary fiber are shown to have an improved diet quality,

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defined as a diversified, balanced, and healthy diet, which provides energy and all essential nutrients for growth and a healthy and active life [8, 9].

Recent data suggests that dietary fiber and plant-based diets have important benefits for patients with kidney diseases. In this review, we summarize the evidence on potential gastrointestinal (GI) and non-GI benefits and risks of dietary fiber in healthy children and children with kidney diseases. Given that the evidence for dietary fiber intake and its benefits in children with kidney diseases is limited, relevant meta-analyses and randomized controlled trials (RCTs) in adults with kidney diseases are also included (Fig. 1).

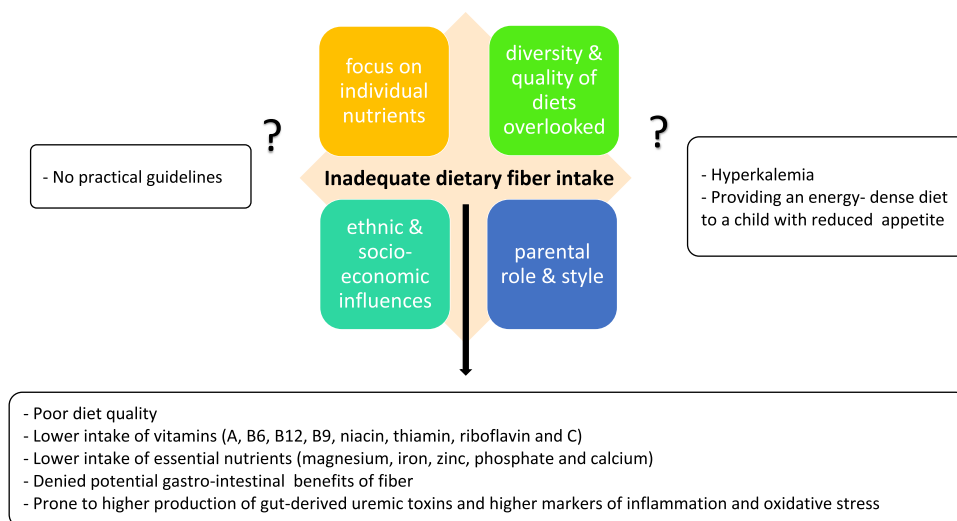
## Dietary fiber intake in healthy children and children with kidney diseases

Observational studies have demonstrated that a substantial proportion of children fail to meet the recommended dietary fiber intake [1, 9]. Irrespective of the definition of dietary fiber used, nutritional surveys have shown that dietary fiber intake is estimated to be less than half the recommended amount set by guidelines [8]. O’Neil et al. demonstrated an overall low consumption of whole grain, an important source of dietary fiber, in healthy children; a mean number of whole grain servings of 0.45, 0.59, and 0.63 were consumed in children aged 2–5, 6–12, and 13–18 years, respectively, which is far below the recommended intake range of 1.5 to 3.0 servings a day [9]. Moreover, the typical daily fruit intake in children is about half the recommended amount, and only 10% of Western populations achieve the recommended daily intake of fruit [9]. The reasons for a reduced consumption of dietary fiber in healthy children and adolescents are not clear, but might be related to poor availability and access to fiber-rich foods

as their caregivers often do not consume adequate dietary fiber either. Moreover, the caregivers’ dietary choices and their lifestyle, ethnic and socio-economic influences on one hand, and the child’s food preferences on the other hand are possible contributors of low dietary fiber intake [9].

A low dietary fiber intake is even more pronounced in children with kidney diseases including in those with chronic kidney disease (CKD), kidney transplant recipients, and children with tubulopathies. In a cohort of children with non-dialysis CKD stages 1–5, only 23% of children met the dietary fiber recommendations for healthy children. In advanced (pre-dialysis) CKD stages 4–5, the proportion of children who met the recommendations dropped to 9% [10]. These results were confirmed in a scoping review by Melhuish et al. [11], which concluded that dietary fiber intake in children with CKD was largely inadequate, and in those with a low dietary fiber intake, the diet quality was also poor with a low intake of fruits and vegetables. This low dietary fiber intake is likely a reflection of the traditional dietary recommendations in kidney diseases that have focused predominantly on the quantities of energy and individual nutrients such as protein, potassium, and phosphate, while current nutritional guidelines in kidney diseases have overlooked the intake of dietary fiber, fruits, and vegetables, as well as the quality and diversity of “kidney” diets [12]. In patients with kidney diseases, the dietary fiber recommendations for healthy children are particularly challenging to adhere to, due to the associated altered appetite inherent to the disease or its treatment, and the sometimes rigorous fluid restrictions in dialysis patients and the obligate urinary losses of fluid in children with tubulopathies that predisposes them to constipation. Moreover, the use of formulas and modular feeds in infants without fiber supplementation (as oligosaccharides), together with the possible restriction of potassium-rich

**Fig. 1** Dietary fiber intake in children with kidney disease, etiology, consequences and gaps



fruits, vegetables, and whole grains to avoid hyperkalemia, may also contribute to their limited intake of dietary fiber.

## Potential benefits of dietary fiber

### Gastrointestinal health and constipation

The benefits of dietary fiber in the maintenance of GI health and prevention of constipation are well established (Supplementary Table 1). Dietary fibers (i) increase the retention of water in the colon which results in softer stools, (ii) increase fecal bacterial mass and nitrogen excretion, (iii) maintain a healthy colonic microbiota ecosystem by promoting the growth of beneficial bacteria such as bifidobacterial and lactobacilli, and (iv) increase the production of short chain fatty acids (SCFAs) [1, 8, 13–18]. SCFAs, such as acetate, butyrate, and propionate, are released from saccharolytic bacteria when the dietary fiber is fermented and have anti-inflammatory and immunomodulatory effects, enhancing the integrity of the gut barrier.

Most data on the association between dietary fiber and GI health relates to constipation. In healthy children with constipation, single fiber supplements such as glucomannan, partially hydrolyzed guar gum, bran, and cocoa husk were found to increase stool frequency in comparison with placebo, while glucomannan also improved stool consistency, decreased abdominal pain, and reduced episodes of painful defecation (Supplementary Table 1) [19–22]. Studies using dietary fiber blends also demonstrated an improvement in constipation, an increase in daily bowel movements, and an improved stool consistency (Supplementary Table 1) [23–25].

Similarly, dietary recommendations that aim to increase dietary fiber intake may also prevent constipation, as demonstrated by Chao et al. [26] who showed a mean increase in daily bowel movements in the intervention group that underwent an education program [26]. Also, Maffei et al. [27] demonstrated improved bowel habits and a decrease in the requirement for disimpaction therapy in their cohort of children with constipation, and Paruzynski et al. [28] found a decrease in self-reported scores of straining and flatus by adding two servings of oatmeal. Of note, McClung et al. [29] pointed out that despite these dietary interventions, many children were unable to meet their recommended fiber intake.

There are, however, conflicting data with respect to dietary fiber intake and GI health and constipation. Horvath et al. [30] could not detect a benefit of glucomannan with respect to abdominal pain/cramps and stool consistency. Similarly, Brauchla et al. [31] found no change in the GI health questionnaires after introduction of two high-fiber snacks daily. Moreover, existing data remains inconclusive

in terms of the type, source, or amount of dietary fiber that will improve GI health in otherwise well children [32]. Moreover, the lack of a standard definition of GI health makes comparisons across studies difficult, and confounding factors in the etiology of childhood constipation such as dehydration and psychosomatic problems are often not considered [32]. Notwithstanding the limitations of the available literature and some controversial findings, the present evidence has resulted in high fiber foods and supplements recommended in many practical guidelines that tackle the prevention of constipation, irritable bowel syndrome, and diverticular disease [8, 32].

Similar beneficial effects of dietary fiber were observed in patients with kidney diseases (Supplementary Tables 2–3). While there are no published studies in children with kidney diseases, some observational studies and RCTs have reported beneficial effects of dietary fiber on constipation and GI symptoms in adults with CKD including those on dialysis [33–35]. Sutton et al. randomized 41 adult peritoneal dialysis (PD) patients on regular laxative use to high fiber supplement, high fiber diet, or placebo for 4 weeks; laxative dose decreased in both the high fiber supplement and high fiber diet groups (38% and 16% respectively), but these changes were not significant when compared to placebo [36]. Similarly, a crossover placebo-controlled randomized trial in 9 elderly patients on PD with constipation showed that supplementation with 20 g/day of fructo-oligosaccharides increased the frequency of defecation and improved their bowel habits [37].

### Uremic toxin production, inflammation, and oxidative stress

In addition to GI health, there are other benefits of an optimal dietary fiber intake. A high fiber intake has been linked to a lower production of gut-derived uremic toxins [12]. Gut-derived uremic toxins are organic metabolites produced by the gut microbiota which accumulate in patients with progressive decline in kidney function due to decreased renal excretion and/or increased generation of these metabolites [38]. The two most widely studied gut-derived uremic toxins are indoxylsulfate (IxS) and *p*-cresylsulfate (pCS), and their pro-inflammatory and pro-oxidative properties are well established in experimental studies [39]. By inducing the production of reactive oxygen species, these gut-derived metabolites activate the nuclear factor-kappa B pathway leading to oxidative stress and the production of pro-inflammatory cytokines [40, 41]. IxS and pCS are mainly produced by proteolytic bacteria. The proteolytic and saccharolytic fermentation characteristics of the microbiome are related to nutrient availability, i.e. the balance between respectively carbohydrate (such as fiber) and undigested protein. Therefore, a higher intake of dietary fibre shifts a dominantly

proteolytic microbial metabolism to a saccharolytic one, characterized by the incorporation of amino acids to bacterial growth and the use of dietary fiber as a source of energy, rather than being metabolised in precursors of uremic solutes [42]. Besides a decrease in gut-derived uremic toxin production, a high dietary fiber intake has been shown to decrease inflammation and oxidative stress by improving the integrity of the gut barrier through SCFA production with subsequent decrease in bacterial translocation [14].

**Uremic toxins** A single observational study has explored the potential benefits of dietary fiber intake with respect to uremic toxin production in pediatric CKD and found an inverse association between an increase in fiber consumption and serum concentrations of free IxS, free pCS, total and free indole acetic acid, total serum p-cresyl glucuronide, and free pCG levels (Supplementary Table 2) [10, 43].

In adults with CKD (Supplementary Table 3), the effect of fiber supplementation on uremic toxin levels has been investigated in some small short-term RCTs which have been summarized in two meta-analyses [44–52]. A meta-analysis of 7 RCTs with a total of 203 patients with CKD showed that a higher dietary fiber intake was associated with a significant reduction of pCS levels [50]. These results were confirmed by a more recent meta-analysis on 292 CKD patients (9 RCTs), which showed that dietary fiber supplementation can significantly reduce the plasma levels of IxS, pCS, blood urea nitrogen, and uric acid [47].

Although most of the trials included in these meta-analyses were characterized by small patient numbers (less than 50) and short-term follow-up, and some were of relatively low quality with conflicting results between studies, the adult literature concludes that higher dietary fiber intake is associated with reduced plasma levels of uremic toxins in adults with CKD [47, 50]. This is particularly relevant for patients with stage 5 chronic kidney disease, as many of these toxins are protein-bound solutes causing them to be difficult to remove with any dialysis modality [53, 54].

**Inflammation** Only two observational studies investigating the association between inflammation and dietary fiber intake have been performed in the healthy pediatric population (Supplementary Table 1) [55]. Navarro et al. [55] found that girls with the highest high-sensitive C-reactive protein (CRP) tertiles had the lowest intake of dietary fiber, suggesting a preventative role of dietary fiber intake with respect to systemic inflammation [55]. Similarly, Parikh et al. found that higher fiber consumption was associated with lower CRP levels [56].

Several RCTs in adults with kidney diseases have shown a similar beneficial effect of dietary fiber on markers of

inflammation [45, 48, 57, 58]. In fact, the anti-inflammatory effect of dietary fiber in adults with CKD seems to exceed the effect found in adults without CKD (Supplementary Table 3) [13, 14]. A recent meta-analysis investigated the effects of prebiotic, probiotic, and synbiotic adjuvant on inflammation and oxidative stress in adults on chronic hemodialysis (HD) and found that, even limiting the analysis to the trials concerning prebiotics only, a significant reduction of plasma interleukin-6 and a reduction, albeit not statistically significant, of CRP was found in patients, who received fiber supplementation [59].

**Oxidative stress** There are no pediatric studies that have examined the association of dietary fiber and antioxidant capacity. Xie et al. [60] randomized 124 HD adult patients with CKD to 10 g or 20 g per day of fiber versus placebo for 6 weeks, and they observed a significantly improved oxidative status and decreased systemic inflammatory state of hemodialysis patients [60]. In another RCT with 46 HD patients randomized to receive high amylose resistant starch or placebo for 8 weeks, a significant reduction of malondialdehyde in the supplemented group was observed, while the change in total antioxidant capacity did not reach statistical significance [57].

#### **Cardiovascular disease, risk factors, and all-cause mortality**

It is hypothesized that dietary fiber may protect against cardiovascular morbidity and mortality by attenuating risk factors such as metabolic syndrome, diabetes mellitus, hyperlipidemia, and obesity [1, 61–63]. This protection might be achieved through decreasing gut-derived uremic toxin production, decreasing inflammation and oxidative stress, and stimulating SCFA production and translocation into the blood that in turn results in an improved insulin sensitivity and a more alkaline environment. A meta-analysis of seventeen cohort studies published in 2013 by Threapleton et al. confirmed the association between low dietary fiber consumption and increased risk of cardiovascular disease in healthy adults [3]. Similarly, a meta-analysis of seven prospective cohort studies observed an 11% reduction in mortality risk for each 10 g/day increment of dietary fiber consumed [2].

**Survival** Despite the suggested association between dietary fiber intake and cardiovascular disease in the healthy adult population, there are no RCTs investigating this association in children or adults with kidney diseases. Also the effect of dietary fiber on mortality in adults with CKD has been investigated in observation studies only, the majority of which show a significant association between higher dietary fiber intake and an improved survival, but some have failed to find any benefits [13, 14, 64, 65]. A meta-analysis of seven

studies involving 15,285 participants showed that a healthy dietary pattern, higher in fruits and vegetables, fish, legumes, cereals, whole grains, and fiber and lower in red meat, salt, and refined sugars, is associated with lower mortality in people with kidney diseases [66]. Despite being based on sound data and supported by a strong rationale, the observational design of these studies makes it impossible to draw definitive conclusions about the effect of dietary fiber on survival in patients with CKD.

**Cardiovascular risk factors** In the healthy pediatric population, a prospective, randomized study showed that serum cholesterol concentration was inversely associated with dietary fiber intake [67]. Similarly, a 13-week cross-over RCT adding bran fiber to the individual's usual diet found a decrease in total and LDL cholesterol in the bran fiber arm [19]. In addition, several observational studies have assessed the relationship between dietary fiber intake and insulin sensitivity and adiposity. While some studies demonstrated a possible association between these risk factors and dietary fiber [31, 68–71], the results were not confirmed by others [72–74].

Surprisingly, the benefits of dietary fiber on key cardiovascular risk factors are largely unexplored in adults and children with kidney diseases, with few studies looking at the effects of fiber on lipid profile and glycemic control, and inconsistent findings reported [44, 49, 75]. One cross-sectional study performed in 45 pediatric kidney transplant recipients demonstrated an inverse relationship between dietary fiber intake and serum triglyceride concentration [76].

### Progression of kidney function

An intriguing hypothesis is that an optimal intake of dietary fiber may protect against CKD progression. The latter has been addressed in two trials in adults with diabetes: dietary fiber supplementation (10 g of a soluble fiber supplement added to the subject's usual diet) did not have any beneficial effects on changes in estimated glomerular filtration rate or microalbuminuria [77, 78]. A vegetarian diet rich in fiber was associated with a reduction in albuminuria in adults with types 1 and 2 diabetes, perhaps as a consequence of better glycemic control. In another meta-analysis based on 14 trials on 143 patients with CKD, Chiavaroli et al. [79] demonstrated that dietary fiber supplementation significantly reduced serum urea and creatinine levels compared with placebo. Further studies are needed to better explore the possible nephroprotective role of fiber in CKD, particularly in non-diabetic patients and children.

### Advantages of a plant-based diet

As plants are the sole natural source of dietary fiber, increasing dietary fiber intake is effectively achieved by recommending diets. Carrero et al. [12] defined plant-based diets as those that emphasize the consumption of plant foods (fruits, vegetables, nuts, seeds, oils, whole grains, and legumes) which may or may not include small or moderate amounts of meat, fish, seafood, eggs, and dairy. The advantage of prescribing a plant-based diet is that the individual may benefit from several other benefits associated with dietary fiber alone. For example, some plant foods have a high content of monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs). Especially relevant for kidney patients, plants contain high amounts of anions that mitigate metabolic acidosis and are characterized by a lower bioavailability of phosphate compared with phosphate derived from animal food sources. The latter may contribute to better serum phosphate levels [12]. Also, plant-based diets are rich sources of beneficial phytochemicals, vitamins, antioxidants, and minerals [12]. Several studies performed in healthy children have confirmed this finding. O'Neil et al. found that increasing the consumption of whole grain foods was associated with improved diet quality and nutrient intake in children and adolescents [9]. In all groups, the health energy index and the intakes of energy, fiber, PUFAs, vitamins B1, B2, B6, B9, A, and E, magnesium, phosphate, and iron were significantly higher, and the intakes of protein, total fat, saturated fatty acids, MUFAs, and cholesterol levels were lower in those consuming three or more servings of whole grain foods per day [9]. A striking finding in this study is the lower intake of added sugars, potassium, and sodium in children on the high fiber intake [9]. Similar results were reported by Nicklas et al. who demonstrated that a high fiber intake was associated with a greater likelihood of an adequate intake of several vitamins (A, B1–2–3–6–9–12, and C) and essential nutrients (magnesium, iron, zinc, phosphate, and calcium) [80].

The benefits of a plant-based diet in adult CKD patients have been explored. An RCT with 108 macroalbuminuric non-diabetic CKD patients showed that treatment with alkaline-producing fruits and vegetables was associated with a similar correction of metabolic acidosis compared with sodium bicarbonate medication along with with better blood pressure and lower low-density lipoprotein concentrations [81, 82].

### Potential risk of hyperkalemia with a high dietary fiber intake

The traditional view is that higher fiber intake in patients with CKD could be associated with a greater risk of hyperkalemia due to the higher intake of potassium-rich fruits,



vegetables, and whole grains. Although well-designed trials are lacking, the available evidence does not seem to support this concern. Some cross-sectional studies have failed to demonstrate a correlation between dietary potassium intake and serum potassium concentrations. In particular, a secondary analysis of a cohort of 224 adults receiving HD showed that dietary potassium explained less than 2% of the variability in serum potassium concentrations [83]. In a longitudinal observation study, El Amouri et al. [84] found that in pediatric patients with CKD stages 1 to 5, neither dietary potassium nor dietary fiber intake was associated with serum potassium concentrations in a model adjusted for eGFR, treatment with renin–angiotensin–aldosterone system blockers, serum bicarbonate concentration, and body surface area [84]. Of note, this study highlighted that the contribution of fruits and vegetables was only 16–34% of the total dietary potassium intake, while meat products contained nearly as much or more potassium than many fruits and vegetables, especially when potassium additives are used in processed foods [84]. The bio-availability of potassium in processed foods is much higher (about 90–100%) compared to its bioavailability in fruit and vegetables (about 60%) since plant cells are not easily digested and a significant proportion of ingested potassium is excreted in the feces [85]. Given the use of potassium-containing additives in processed foods is increasing worldwide, children who consume a significant proportion of processed “ready-to-eat” foods are more likely to have a higher potassium intake than those who consume predominantly fresh foods [86].

In addition to the low bioavailability of potassium from plant-based foods, studies in adults suggest that increasing fruit and vegetables reduces potassium absorption in the GI tract by delivery of fructose and alkali and increasing intestinal motility [87]; the high alkaline content of fruits and vegetables might reduce serum potassium by mitigating metabolic acidosis [12, 86]. Several observational studies in adult CKD and dialysis populations could not detect an increased risk of hyperkalemia when using plant-based diets or diets rich in fruits and vegetables. In a multinational cohort study on 8078 adults receiving HD, Saglimbene et al. [81] showed that serum potassium did not differ with lower, medium, and higher consumption of fruits and vegetables [81]. In a recent observational single-center trial on 150 HD patients, Gonzalez-Ortiz found that a higher plant-based diet score was not associated with serum potassium concentrations [88]. However, there are no studies that have examined the potential risk of hyperkalemia in children with kidney diseases who are on predominantly plant-based diets; therefore, plant-based diets for children with CKD should be used with caution, especially for those on dialysis with minimal diuresis. For a detailed approach to the management of hyperkalemia in children, we refer the reader to a recent

guideline on the management of hyperkalemia in kidney diseases by The Pediatric Renal Nutrition Taskforce [86].

### **Is there a risk of malnutrition for children following a plant-based diet?**

Some authors have raised concerns that plant-based diets might adversely affect the nutritional status of children and adolescents, as too much emphasis on high fiber foods could decrease energy intake [80]. Nevertheless, no study in the healthy pediatric population could confirm these concerns. For instance, Nicklas et al. demonstrated that a high fiber diet combined with a decreased fat intake meeting current nutritional recommendations does not adversely affect energy or nutrient intake, and in fact, an increase in nutrient density and a greater likelihood of an adequate intake of several key nutrients was found [80].

Studies in adult CKD patients confirm that a vegetarian diet is not associated with a worse nutritional status: in an RCT comparing a soya-based vegetarian low protein diet and an animal-based low protein diet, nutritional status (assessed by body mass index, mid-arm muscle circumference, lean body mass, and percent body fat) was not different between the two groups and the vegetarian diet was associated with a higher energy intake [89].

### **Conclusion and knowledge gaps**

Growing evidence suggests that an adequate dietary fiber intake confers several health benefits, without a significant risk of nutritional deficits or hyperkalemia. An adequate fiber intake can lead to not only an improvement in GI motility, but also to wider benefits such as decreased production of gut-derived uremic toxins and a reduced inflammatory state. Even more important, higher fiber diets tend to have a better diet quality by their increased nutrient density and by their greater likelihood of an adequate intake of key nutrients, which is especially important for children with kidney diseases, even those children on low potassium diets. Despite significant advances in our knowledge, evidence on the health benefits of dietary fiber intake in kidney patients—especially the pediatric population—remains poor, and well-designed randomized trials are urgently needed. Although the benefits of dietary fiber are well established, none of the current nutritional guidelines for patients with kidney diseases discusses the practical aspects of how an increased dietary fiber intake can be incorporated into the child’s diet nor the potential risk of hyperkalemia associated with plant-based diets in those with advanced CKD [12]. As most patients with kidney diseases consume amounts of dietary fiber that are well below recommendations for the general population, RCTs in “real-life” clinical settings

to come to clinical practice recommendations on dietary fiber intake for children and adults with kidney diseases are required to address these knowledge gaps.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s00467-022-05837-2>.

**Author contribution** Conceptualization: SE, FB, RS, MW, VS; formal analysis and investigation: SE, FB; writing—original draft preparation: SE, WS, JNA; writing—review and editing: SE, FB, RS, MW, VS, VWJ, DA, PN, RTJ; resources: SE, FB, RS; supervision: RS, VWJ

**Data availability** Not applicable

**Code availability** Not applicable

## Declarations

**Ethics approval** Not applicable

**Consent to participate** Not applicable

**Consent for publication** Not applicable

**Conflict of interest** The authors declare no competing interests.

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