older people with chronic kidney disease and low-grade acidosis (BiCARB) Study Group.[543] It contributed 33 of 152 versus 33 of 148 kidney failure outcomes to the meta-analysis in its bicarbonate versus placebo arms, respectively (HR: 0.97; 95% CI: 0.64–1.49). Importantly, the BiCARB trial, which studied people with CKD G3–G4 aged ≥60 years and sodium bicarbonate concentration <22 mmol/l, also found no evidence of benefit on nonkidney outcomes to support oral sodium bicarbonate supplementation (the primary outcome was based on the Short Physical Performance Battery at 12 months, and secondary outcomes included generic and disease-specific QoL assessments, anthropometry, kidney function, walk distance, BP, and bone and vascular health markers). Allocation to oral sodium bicarbonate was associated with higher costs and lower European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L) assessed QoL over 1 year.[543]

Licensed non-alkali oral interventions may be an alternative to oral sodium bicarbonate to treat metabolic acidosis but have not been shown to have particular advantages.[544,545] Although placebo-controlled trials have found no good evidence that correcting sodium bicarbonate levels has important effects on clinical outcomes, the Work Group concluded that the intervention is clearly effective at increasing serum bicarbonate concentration and is a suitable treatment to avoid more severe acidosis with potential for clinical implications. The Work Group suggests that a serum bicarbonate of <18 mmol/l in adults is desirable to avoid, but large RCTs are required to determine a precise threshold whereby the treatment of low serum bicarbonate levels leads to improvements in clinical outcome. As correction of bicarbonate to the normal range has not been demonstrated to reduce the risk of kidney failure, lower thresholds to initiate therapy than 18 mmol/l could be considered (see Research Recommendations).

Dietary approaches. Dietary modifications that limit the consumption of acid-rich foods and/or increase the intake of alkaline-rich foods reduce the net endogenous acid production and can serve as an additional strategy to control metabolic acidosis in people with CKD.[546,547] Such diets are generally low in animal protein or have a higher consumption of plant-based foods over animal-based foods (i.e., plant-dominant diets such as Mediterranean or vegetarian diets). Four small RCTs of alkaline-rich plant-based diets in adults with CKD demonstrate a comparable benefit to oral sodium bicarbonate in controlling metabolic acidosis.[548–551]

Special considerations

Pediatric considerations. As in adults, children with CKD often have metabolic acidosis. In the CKiD and the Cardiovascular Comorbidity in Children with Chronic Kidney Disease Study (4C) studies, 38%–60% of children had a serum bicarbonate of <22 mmol/l, varying by CKD category. Low bicarbonate was associated with increased risk of disease progression.[395,552] It should also be noted that for younger children, the normal range for sodium bicarbonate is as low as 17 mmol/l. In children, metabolic acidosis is also likely to cause growth retardation. Data from the observational CKiD study revealed that prepubertal children with acidosis who were treated with alkali had improved growth.[553] In children with normal GFR but renal tubular acidosis, prolonged acidosis can also result in poor growth. The KDOQI guideline on bone metabolism for children with CKD recommends the prevention of acidosis in children to optimize growth.[554] There have not been any trials examining the effect of bicarbonate supplementation on CKD progression or growth in children.

3.11 Hyperkalemia in CKD

Definition and prevalence. Potassium is key to cell membrane electrophysiology, with abnormalities predisposing to abnormal cardiac conduction and arrhythmias. The kidneys play a key role in potassium homeostasis with decreased GFR generally associated with increased potassium concentration (Table 24; Figure 29[555]). The definition of hyperkalemia is based on the distribution of potassium values in the general population. Hyperkalemia is uncommon when the eGFR is >60 ml/min per 1.73 m^2 and increases with lower GFR.

Adults with CKD G3, A1 in the general and high-risk population cohorts, contributing to the CKD-PC, had an adjusted prevalence of hyperkalemia (defined as a serum potassium >5.0 mmol/l) of 8.8% and 4.5% in those with and without diabetes, respectively, increasing to 34.4% and 23.7% by CKD G5, A3 (Figure 30).[541] Note that there is variability in the prevalence of hyperkalemia, and it is not inevitable at lower

Table 24 | Variation of laboratory values in a large population database[a] by age group, sex, and eGFR; potassium, mmol/l, mean (SD), and n = 4,278,600

			GFR category (ml/min per 1.73 m^2)							
Measure, mean (SD)	Age (yr)	Sex	105+	90–104	75–89	60–74	45–59	30–44	15–29	0–14
Serum potassium	≥65	Female	4.1 (0.5)	4.2 (1.3)	4.2 (0.5)	4.3 (0.5)	4.3 (1.3)	4.4 (0.5)	4.5 (1.0)	4.5 (2.0)
		Male	4.2 (0.5)	4.3 (0.6)	4.3 (1.1)	4.4 (0.6)	4.4 (0.7)	4.5 (1.1)	4.6 (0.6)	4.6 (1.6)
	<65	Female	4.1 (0.7)	4.2 (1.3)	4.3 (17.0)	4.2 (1.0)	4.3 (0.5)	4.3 (0.6)	4.4 (0.6)	4.5 (1.1)
		Male	4.2 (0.4)	4.3 (0.5)	4.3 (0.6)	4.3 (0.4)	4.4 (0.5)	4.5 (0.6)	4.5 (0.7)	4.6 (0.7)

eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate.
[a]Data from the Optum Labs Data Warehouse, a longitudinal, real-world data asset with deidentified administrative claims and electronic health record data. The database contains longitudinal health information on enrollees and patients, representing the diversity of geographical regions across the United States.