

# Risk Behavior Patterns and Outcomes of CKD—Potential for Individualizing Behavioral Interventions



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Chronic kidney disease (CKD) is a growing public health problem worldwide associated with increased risk of cardiovascular disease (CVD), end-stage renal disease (ESRD), and premature deaths.<sup>1</sup> The Global Burden of Disease Study 2015 estimated that worldwide deaths due to CKD increased by 31.7% in 10 years, from 938,000 in 2005 to 1.2 million deaths in 2015.<sup>1</sup> Population aging and increasing prevalence of diabetes and hypertension contributed mainly to the increased burden of CKD.<sup>2</sup> CKD shares many risk factors with CVD, and CKD itself is a major risk factor for CVD. Current CKD guidelines recommend lifestyle modifications such as regular physical activity, abstinence from smoking, achieving a healthy weight, and adopting a healthy diet

comprising low-fat and higher consumption of whole grains, fruits and vegetables for prevention of onset or progression of CKD based on studies conducted in general populations.<sup>3</sup> Although CKD shares many of the traditional cardiovascular risk factors, associations of these risk factors and effectiveness of modifying these risk factors on outcomes in CKD patients have not been similar to those of the general population. Of particular interest, although obesity is an established risk factor for adverse cardiovascular events in the general population, being overweight or obese has been shown to be protective against adverse outcomes, in particular in individuals with advanced stages of CKD.<sup>4</sup> In the context of CKD, a nonlinear relationship exists between body mass index (BMI) and CKD, such that individuals at both extremes are vulnerable to adverse outcomes; in other words, the underweight and the morbidly obese may be at-risk populations. Impact of dietary changes in CKD populations has been inconsistent.<sup>5,6</sup> In a

meta-analysis of cohort studies including 15,285 adults with CKD, adopting a healthy dietary pattern was associated with reduced mortality risk, but no significant associations were observed with ESRD or with CVD.<sup>5</sup> A recent Cochrane review evaluating the effectiveness of dietary interventions in 1639 persons with CKD concluded that the benefit of dietary interventions on mortality, cardiovascular events, and ESRD in people with CKD is uncertain.<sup>6</sup> Nevertheless, some behavioral interventions have been shown to be effective in specific subgroup populations. For example, weight loss has been shown to be beneficial in those with diabetic kidney disease.<sup>7</sup> In a previous study based on the Chronic Renal Insufficiency Cohort (CRIC), Ricardo *et al.* observed a significant interaction between age and physical activity in CKD patients, in that ideal physical activity was protective against atherosclerotic outcomes in adults aged <65 years; however, it increased the risk in older adults aged ≥65 years, suggesting that the extent of vascular disease in older adults may be too advanced to be modified by physical activity.<sup>8</sup> Risk behaviors commonly co-occur. Identifying individuals engaged in 2 or more risk behaviors concurrently based on combination of risk behaviors or higher-order interactions will allow for the identification of high-risk subgroups for whom interventions may be beneficial and may provide useful information to decision makers. To this end, in this issue, Schrauben *et al.* examined the associations of patterns of health behavior engagement with outcomes including CKD progression, atherosclerotic outcomes, and deaths in a large cohort of men and women (n = 5499) with

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mild-to-moderate CKD who participated in the CRIC study in the United States.<sup>9</sup> Combinations of health behavior patterns were identified based on recommended health behaviors using a latent class analysis (LCA), a novel subgroup approach for identifying latent profiles or classes of individuals sharing similar characteristics without considering outcomes. Recommended health behaviors were guided by previous guidelines, and included body mass index (BMI 20–25 kg/m<sup>2</sup>), healthy diet score, and recommended levels of physical activity, blood pressure (systolic ≤140 and diastolic ≤90 mm Hg), and HbA1c levels (≤7%). Interactions by age and diabetes in the association between behavior patterns and outcomes were evaluated by stratifying the population by age group (<65 years vs. ≥65 years) and presence or absence of diabetes.

Schrauben *et al.* identified 3 similar patterns of health behavior in both individuals aged <65 years as well as those ≥65 years: 1 healthy (high levels of engagement in recommended health behaviors), and 2 less healthy (i) more-obese and sedentary (low levels of recommended BMI and physical activity) and (ii) less-obese and smoker (high levels of smoking but recommended BMI). The prevalence of healthy pattern was higher among adults aged <65 years (55.7%) compared to older adults (42.3%). Among the 2 unhealthy patterns, the more-obese and sedentary pattern was the predominant type (40%–50%) in both age groups, whereas <10% adopted the less-obese and smoker pattern. In the younger age group, the authors found the unhealthy patterns to be associated with increased risk of deaths in the diabetic adults and cardiovascular events in nondiabetic adults.

Among older adults, the less healthy patterns were associated with deaths in nondiabetic adults. Among individual behaviors, although current smoking and high blood pressure were significantly associated with outcomes in both age groups, BMI and diet were differentially associated, in that unhealthy BMI range in the younger age group and unhealthy diet in the older age group with diabetes were protectively associated with CKD progression.

It must be pointed out that the low event rate observed in certain subcategories considerably limits making meaningful inferences; for example, in adults <65 years of age, only 5 deaths were observed among the group comprising less-obese/smoker/nondiabetic (<3 years). It is possible that the lack of association observed in this group could be due to a sample size issue. Also, smoking behavior defined in this study did not capture information such as pack-years, brand of product and pattern of smoking, and so forth, and the broad classification of ever and current smoking may have misclassified the exposure. Second, obesity pattern based on visceral adiposity or body composition is important in terms of conferring risk for adverse outcomes. Body composition is also a concern among elderly individuals. Specifically, aging-related sarcopenic-obesity is associated with global functional decline and its impact on CKD progression is probably worthy of further elucidation. Another point to note is that weight gain may be associated with CKD progression. Therefore, single point estimate of BMI may not be sufficient for risk stratification. Instead, one may need to take into account interval weight gain, in particular among those with diabetes. In corollary, weight management among individuals with diabetes reduces the risk of CKD.

Taken together, the present article may have underappreciated the importance of obesity. Third, follow-up of one-third of the participants recruited from Phase III, which included older patients (aged 45–79 years, vs. 21–74 years in Phase I) was shorter, with <3 years. Fourth, severity of CKD or change in renal function or change in smoking behavior in the recent past or during follow-up were not considered. Fifth, participants included in this study were not entirely representative of the CKD population, as those with an estimated glomerular filtration rate 60 to 70 ml/min per 1.73 m<sup>2</sup> were also included at baseline.

The impact of age- and diabetes-specific behavioral engagement pattern and individual behaviors with outcomes in CKD patients provided by Schrauben *et al.* suggest the potential for tailoring behavioral recommendations specific to subgroups with varying patterns of risk behaviors. For example, blood pressure control could be prioritized for both age groups, whereas increasing physical activity could be an intervention target for persons with diabetes, irrespective of age. Behavioral interventions based on more homogeneous subgroups or risk clusters would be more effective than adopting a “one size fits all” approach in chronic disease management. However, replication in other CKD populations would be needed to confirm whether the identified behavior patterns could improve individualized risk assessment and decision making for use in the larger CKD populations.

## DISCLOSURE

All the authors declared no competing interests.

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