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Editorial

The Global Promise of Healthy Lifestyle and Social Connections for Better Health in People With Diabetes

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In this issue, Dunkler et al[1] report novel estimates of how lifestyle behaviors and social connections influence the risk for chronic kidney disease (CKD) and all-cause mortality in people with type 2 diabetes. The authors followed nearly 7,000 patients with diabetes from ONTARGET (Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial) in North America, South America, Europe, Asia, and Australia. After an average follow-up of 5.5 years, those with healthier diets, more frequent physical activity, healthier weight, no tobacco use, and larger social networks had significantly lower onset of CKD and risk for death. Combining these 5 factors, 13% of the new cases of CKD and 38% of deaths were estimated to be preventable with adherence to healthier levels of each factor. Improvement in any one of these 5 factors was estimated to reduce CKD incidence by 5% and mortality by 16%.

Previous studies have evaluated the potential combined impact of adherence to basic lifestyle behaviors in relation to incident cardiovascular disease, heart failure, and diabetes in generally healthy populations.[2-5] The present findings build upon and extend this evidence by studying a large, multinational (40-country) sample of patients with diabetes and assessing not only mortality, but also the onset of CKD, a major complication of diabetes.[6] In most nations, diabetes is the leading cause of end-stage renal disease, creating tremendous health and economic burdens. Modifiable predictors of CKD among patients with diabetes include higher blood glucose level and blood pressure, each heavily influenced by lifestyle.

Quantifying the potential benefits of adherence to specific behaviors informs priorities for prevention strategies at the individual and population level. Crucially, none of the lifestyle targets evaluated by Dunkler et al were extreme or unattainable. For example, benefits of physical activity corresponded to increasing physical activity from one to a few days per week or from several days to all. The "optimal" dietary pattern was also not extreme: in this population of patients with diabetes, 34% were already achieving the target diet.

Importantly, this investigation appropriately focused on overall diet patterns, including specific foods, rather than only isolated nutrient targets such as fat or saturated fat. People who follow healthier food–based diet patterns have much lower risk for cardiometabolic diseases, with causality of these cohort observations confirmed by randomized clinical trials of physiologic risk factors and disease endpoints.[7-10] Among different dietary components evaluated in ONTARGET, fruits and vegetables had the largest benefits: an additional 2 servings per week of fruits or vegetables were estimated to result in 3% to 4% fewer deaths. These findings support the importance of healthier food choices among patients with diabetes globally. Notably, the attributable impact of nonoptimal body weight, arguably one of the hardest lifestyle factors to modify, was very low after accounting for dietary habits, alcohol use, physical activity, and social connections, each of which can be more rapidly and readily improved.

Considerable prior evidence indicates that people with greater self-perceived social support and social interaction have better lifestyle behaviors and health outcomes.[11] Although the directionality and causality of these associations require further investigation, it seems very plausible that greater social support facilitates happier healthier lives. From clinical experience, patients with less support often have more trouble with medication adherence, lifestyle change, and fundamental life tasks such as those related to housing, shopping, and transportation. The self-reported measure assessed by Dunkler et al, really more a measure of sociability, friendship, and human interaction rather than networks per se, supports these prior concepts. Importantly, beyond the general support provided by human connections, objectively measured social networks are also linked to negative health behaviors due to apparent transmission of unhealthy habits across several degrees of connection.[12] This suggests that people should not simply aim to have many friends, but also choose their friends wisely.

Because ONTARGET enrolled participants from 40 nations, the findings support the relevance of healthy lifestyle and social connections for patients with diabetes from around the world. Similar results have been observed among individuals with prevalent cardiovascular disease recruited from multiple

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Box 1. Evidence-Based Strategies to Support and Facilitate Lifestyle Change

Individual Level[a]
- Set specific, proximal, shared goals
- Establish self-monitoring
- Establish regular follow-up (eg, in-person, telephone, electronic)
- Provide regular feedback
- Increase self-efficacy
- Leverage family and peer support

Health Systems Level
- Update provider licensing and certification examinations to include substantial focus on lifestyle and behavior
- Mandate detailed standardized fields on diet, activity, and smoking in all electronic health records
- Create electronic systems for patient scheduling, tracking, and patient and provider feedback
- Modify quality benchmarks and reimbursement guidelines to incentivize behavior change efforts
- Use integrated multidisciplinary clinical teams to optimize lifestyle change

Community Level
- Sustained focused media and education campaigns
- School programs (eg, procurement standards, school garden programs, multicomponent interventions on diet and physical activity)
- Comprehensive worksite wellness (including education, incentives, peer support, environmental and policy changes)
- Taxes (eg, tobacco, sugary beverages, other unhealthy foods)
- Subsidies (eg, fruits, vegetables, nuts, fish)
- Quality standards and restrictions (eg, trans fat content, sodium content, standards on marketing of tobacco and foods/beverages to children)
- Environmental planning to encourage healthier lifestyles (eg, locations, intersections, and qualities of homes, schools, workplaces, recreational spaces, food outlets)

[a]Including both the clinical setting and using novel mobile, personal sensor, and other technology approaches outside the clinic.
Source: Mozaffarian.[10]

countries, for whom adherence to basic guidance on diet, exercise, and smoking was associated with a substantially lower risk for recurrent cardiovascular events.[13]

Some limitations warrant discussion. Due to its observational design, residual confounding from other participant characteristics may partly account for some of the benefits attributed to these various lifestyle factors. Conversely, each of these lifestyle factors was measured with some error, which would cause underestimation of its true impact. Moreover, a long-term randomized trial with blinded, placebo-controlled, factorial intervention on each of these factors would neither be feasibly nor ethically practical. Taking into account these contrasting issues, the present findings can be considered reasonable estimates of the overall benefits of healthier lifestyles and social connections in patients with diabetes.

Strangely, the authors only evaluated a potential J-shaped relation for sodium, and used a remarkably broad reference intake of 3,000 to 6,000 mg/d. Estimated habitual sodium intake was also derived from a single morning urine sample, rather than from a 24-hour collection or multiple 24-hour collections. The unique biases of sodium assessment in observational studies, whether by urine collection or dietary questionnaire, are well established.[14] These include incomplete 24-hour urine collections (not applicable here given the use of a single sample), potential for systematic (nonrandom) over- or underestimation of 24-hour excretion when using equation-based estimates from single samples, reverse causation (patients at higher clinical risk, eg, those with hypertension, actively lowering their sodium), and confounding by total caloric intake and physical activity (given the strong correlation between sodium intake and total caloric intake). These limitations together could explain the J-shaped association between estimated sodium intake and clinical end points in the present work and other prior studies.[15] For instance, in this study, only 10.6% of patients had sodium intakes $< 3{,}000$ mg/d, and only 1%, $<1{,}500$ mg/d. Careful adjustment for reverse causation, lower physical activity, and other illness causing lower caloric intake would be essential to ensure that any observed higher risk in these small numbers of patients is not due to bias. In comparison, during extended surveillance in a large sodium reduction trial with robustly measured sodium excretion from multiple 24-hour urine collections, patients with sodium intakes $< 2{,}300$ mg/d experienced 32% fewer cardiovascular events compared with those consuming 3,600 to 4,800 mg/d, with evidence for linearly decreasing risk across the full range of sodium intake.[16]

The assumptions underlying population-attributable fractions warrant discussion. The population-attributable fraction, used by Dunkler and colleagues