



# Nutrition and Type 2 Diabetes: Computational Optimization Modeling to Expand the Evidence Base for South Asians

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The burden of diabetes continues unabated, with global estimates of 537 million people with diabetes in 2021, projected to increase to 783 million by 2045, with more than 90% of cases being type 2 diabetes (T2D) (1). This burden is not distributed equally. South Asians, people originating from the Indian subcontinent, whether living in South Asia or elsewhere as immigrants or their descendants, have substantially higher prevalence of T2D than Europeans, and evidence for their high T2D incidence has also emerged more recently (2,3). There is an urgent need for tackling modifiable risk factors to stem the tide. Dietary modification is a critical part of the strategies to combat this public health challenge for the management of T2D and its potential remission as well as for its primary prevention (4–6). Many dietary factors have been identified that elevate or mitigate the risk of T2D, spanning overall dietary patterns and foods and the nutrients they contain, both macronutrients, i.e., carbohydrates, fat, or protein, and micronutrients, such as vitamins and minerals (6,7). The vast majority of the evidence base has been generated by research conducted in European-origin populations (6,7), so what dietary strategies should be recommended for South Asians?

In this issue of *Diabetes Care*, Anjana et al. (8) researched one important aspect of diet: macronutrient composition.

Specifically, they investigated optimal macronutrient distributions for the remission and prevention of T2D using data from the Indian Council for Medical Research–India Diabetes (ICMR-INDIAB) national study. They applied a data-driven programming approach with optimization modeling to simulate manipulation of proportions of dietary macronutrients to achieve target goals for glycated hemoglobin (HbA<sub>1c</sub>) level as a marker of glyce-mic control. Their analyses generated different optimal macronutrient combinations for each of four outcomes: remission of newly diagnosed T2D, with 49–54% carbohydrate, 19–20% protein, and 21–26% fat; remission of prediabetes to normoglycemia, with 50–56% carbohydrate, 18–20% protein, and 21–27% fat; prevention of progression from prediabetes to T2D, with 54–57% carbohydrate, 16–20% protein, and 20–24% fat; and prevention of progression from normoglycemia to T2D, with 56–60% carbohydrate, 14–17% protein, and 20–24% fat. Based on these results, the authors recommended reductions in carbohydrate calories and an increase in protein calories for both the remission and prevention of T2D (8).

Several strengths of this research are commendable, including a nationally representative sample of men and women as well as rural and urban residents, a nationally relevant and validated dietary assessment instrument, and robust

analyses that accounted for a comprehensive set of potential confounding factors.

However, the interpretation of the current results is constrained by three main limitations. First, regarding study design, the ICMR-INDIAB is a cross-sectional study with the inability to examine temporality of associations; only a one-sixth sample (16%) of the original study was included, with 18,090 of 113,043 participants, with an unknown degree of bias. Overweight was defined as BMI of 23 to <25 kg/m<sup>2</sup>, the impact of which is unquantified in relation to the World Health Organization recommended cut points of BMI of 23 to <27.5 kg/m<sup>2</sup> for overweight and ≥27.5 kg/m<sup>2</sup> for obesity in Asian populations (9). U.K. national guidance also recommends these criteria for U.K.-based South Asians (10). Different Indian states and territories provided data over different time periods within 2010–2020, with unknown impacts. With India's large size and substantial regional variation in cultures and cuisines, it would be of interest to conduct analyses accounting for region. Second, although the authors appropriately acknowledged the challenges of dietary assessment, it would nonetheless be important to examine the impact of isocaloric macronutrient substitutions. Their focus on quantity ignores that health effects vary by macronutrient quality, food sources of macronutrients, and the wider dietary quality (6,11) (Fig. 1). Third, despite the authors'

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description of the methodology to identify ranges of macronutrient intakes to move the HbA<sub>1c</sub> closer to the target value, a degree of computational ambiguity and black-box remains. Modeling assumptions are unclear, such as, but not limited to, the use of a reduction factor for variabilities in dietary intake, different scenarios not being tested dynamically, and the generalizability of current linear HbA<sub>1c</sub> models to other data sets remaining untested.

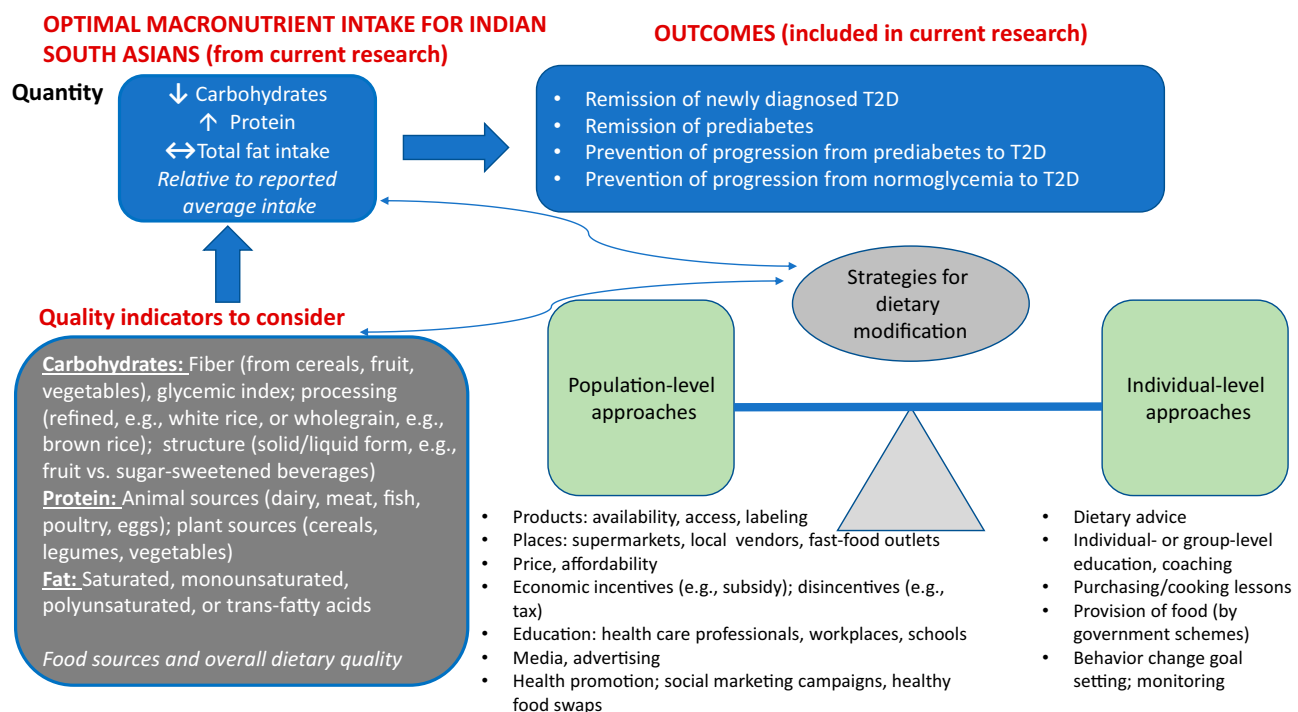
Nevertheless, the current findings are novel, helping to fill an important knowledge gap for evidence on macronutrients in South Asians. By examining each of the macronutrients concurrently, this research highlighted the relevance of lower carbohydrate consumption but also that of higher protein consumption, confirming previous hypotheses on the role of carbohydrates (12–14) and protein (3,12,14,15) for T2D in South Asians. Another novel finding is the stratification of macronutrient composition by different glycemic categories, with nuanced findings that optimal macronutrient proportions vary by glycemic state and person characteristics, including sex, obesity status, rural or urban residence, and physical activity levels.

How achievable are the macronutrient goals this study advocates? The data-

driven macronutrient recommendations for carbohydrates and fat are narrower than, but within, the Indian national acceptable macronutrient distribution range (AMDR) for adults (carbohydrates, 45–65%; fat, 15–35%) (16). However, the computed optimal protein intake (14–20%) considerably exceeded the AMDR upper limit, an AMDR of 5–15%. The suggested macronutrient recommendations are ambitious in terms of the reported intake among the ICMR-INDIAB study population: average carbohydrate intake was higher, at 60.5–62% of total energy across glycemic categories, while protein intake was considerably lower than optimal, at 11.8–12.1% of energy. The authors' contention that shifting diets to meet these optimal intakes would be easily feasible is arguable. Consider protein consumption, typically low in South Asian diets (17). In fact, South Asia has the lowest protein intake across world regions (13), and India has the lowest consumption of protein-source foods across South Asia, meeting on average only 53% of the protein food requirement (18). Fat intake in South Asians is lower than that in European populations (13), but carbohydrate intake in South Asians is among the world's highest (12–14). Cereals, contributing to high carbohydrate consumption in South Asia,

also account for the largest source (~60%) of protein in South Asian diets, predisposing to low-quality protein consumption (17). Despite national Indian nutrition recommendations promoting increasing protein intake from legumes and milk, these intake levels remain low, each accounting for ~11% of protein intake, owing to issues of production, availability, access, cost, and affordability as well as challenges in subsidies and food distribution schemes (19). A range of joint policy interventions will be needed to shift population diets, with action required from national and state governments. Nutrition education of health professionals and individual behavior change will also be necessary (Fig. 1).

While these big factors are at play, research must continue to build the necessary evidence base for optimal dietary recommendations so health care and public health professionals can integrate them into health care and preventive efforts. The study from Anjana et al. (8) contributes meaningfully to that evidence base and should provide a stimulus for further research using prospective studies and randomized intervention trials. Current gaps in understanding, such as the observed differences in the proportion of those reaching remission from



**Figure 1**—Macronutrient intake recommendations for the remission or prevention of T2D in Indian South Asians considering not only quantity but also the quality and food sources of macronutrients. Strategies for dietary modification include both population-level and individual-level approaches.

T2D and from prediabetes and the role of macronutrient quality and food sources, should specifically be addressed.

Implications of the current study in the wider context bear scrutiny. A recommendation to reduce the high carbohydrate consumption in South Asian diets is consistent with wider evidence of benefits of lower carbohydrate diets for the remission and management of T2D. However, clinical trial evidence indicates that diets lower in carbohydrates are effective for glycemic control in the short term (3–6 months) but are not sustained in the long term (20,21). Such time horizons remain untested in the current study. The findings should also be placed in the context of there not being an effective one-size-fits-all dietary strategy. Energy-deficit (low-calorie) diets are effective for the remission of T2D at 2 years of follow-up in Europeans (22), and evidence of remission is also emerging in India (23). For the primary prevention of T2D among those with prediabetes, the Indian Diabetes Prevention Program provided evidence for the efficacy of a combination of reduction in calories, refined carbohydrates, and fats together with an increase in fiber intake and physical activity (24). Similarly, a combination of lifestyle health behavioral interventions has been effective in South Asians in and outside India (25).

Future research will help to unravel a menu of effective dietary strategies for South Asians. Meanwhile, the immediate contribution of the current study is the use of computational tools to advance the understanding that lowering carbohydrate intake and raising protein intake hold potential for reducing the high burden of T2D in South Asians.

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