Macronutrient Recommendations for Remission and Prevention of Diabetes in Asian Indians Based on a Data-Driven Optimization Model: The ICMR-INDIAB National Study

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OBJECTIVE

To derive macronutrient recommendations for remission and prevention of type 2 diabetes (T2D) in Asian Indians using a data-driven optimization approach.

RESEARCH DESIGN AND METHODS

Dietary, behavioral, and demographic assessments were performed on 18,090 adults participating in the nationally representative, population-based Indian Council of Medical Research–India Diabetes (ICMR-INDIAB) study. Fasting and 2-h postglucose challenge capillary blood glucose and glycosylated hemoglobin (HbA_{1c}) were estimated. With HbA_{1c} as the outcome, a linear regression model was first obtained for various glycemic categories: newly diagnosed diabetes (NDD), prediabetes (PD), and normal glucose tolerance (NGT). Macronutrient recommendations were formulated as a constrained quadratic programming problem (QPP) to compute optimal macronutrient compositions that would reduce the sum of the difference between the estimated HbA_{1c} from the linear regression model and the targets for remission (6.4% for NDD and 5.6% for PD) and prevention of progression in T2D in PD and NGT groups.

RESULTS

Four macronutrient recommendations (%E- Energy) emerged for *1*) diabetes remission in NDD: carbohydrate, 49–54%; protein, 19–20%; and fat, 21–26%; *2*) PD remission to NGT: carbohydrate, 50–56%; protein,18–20%; fat, 21–27%; *3* and *4*) prevention of progression to T2D in PD and NGT: carbohydrate, 54–57% and 56–60%; protein, 16–20% and 14–17%, respectively; and fat 20–24% for PD and NGT.

CONCLUSIONS

We recommend reduction in carbohydrates (%E) and an increase in protein (%E) for both T2D remission and for prevention of progression to T2D in PD and NGT groups. Our results underline the need for new dietary guidelines that recommend appropriate changes in macronutrient composition for reducing the burden due to diabetes in South Asia.

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Correcting unhealthy dietary habits has emerged as a valuable tool not only to prevent the development and progression of type 2 diabetes (T2D) (1) but also to induce "remission" of T2D to normoglycemia in at least a subset of individuals (2). Imbalance in macronutrient intake has been linked to insulin resistance and chronic disease risk (3). However, there is still a lot of uncertainty and controversy on the ideal diet composition for T2D remission/prevention (4). Considering these challenges, mathematical optimization techniques have been used to compute macronutrient distribution range to reduce T2D risk (5). Nevertheless, the role of optimization tools for recommending macronutrient compositions to reduce diabetes risk in larger populations is unexplored. The quadratic programming problem (QPP) has been explored to provide individual nutrient recommendations closer to their current consumption (6).

The QPP is an optimization technique with a convex objective (e.g., minimizing the square of the error between measured and computed glycosylated hemoglobin [HbA_{1c}]) subject to constraints over a convex set (see Supplementary Fig. 2.1 for details). A convex set is a set in which all the points on any straight line connect 2 points contained in the set. The convex problems can be solved in polynomial time, and the solution obtained is global (i.e., the optimal solution obtained for the decision vectors is unique). Examples of convex optimization problems are linear programming, and quadratic programming, among others. In particular, minimizing linear and quadratic objectives with linear constraints are optimization problems widely used in least squares.

National surveys in India (7,8) have attempted to document the dietary intakes of the population but are inadequate to inform macronutrient modeling because they are not representative of the entire nation or are limited to household food purchases or measure diet diversity in women and children. They also do not provide dietary recommendations for prevention and management of chronic diseases. Existing recommendations have focused on single macronutrients (9); therefore, there is a need for guidelines on comprehensive macronutrient distribution. The present analysis of data from the Indian Council for Medical Research-India Diabetes (ICMR-INDIAB) national study aims to provide optimal macronutrient recommendations for remission and prevention of T2D using optimization models in Asian Indian adults according to age, sex, BMI, and physical activity levels of the population.

RESEARCH DESIGN AND METHODS

Study Population and Sampling

The ICMR-INDIAB study is a cross-sectional, population-based survey of adults aged ≥20 years. The methodological details of the study have been published elsewhere (10,11). In brief, the study sampled 113,043 (33,537 urban, 79,506 rural) residents of 30 states/Union Territories of India, using a stratified multistage sampling design (details in Supplementary Material 1.1–1.3).

For the current study, every fifth individual who participated in the main study was included (n = 22,735). Of these, dietary data were available for 20,860 individuals with a response rate of 91.8%. Individuals with self-reported T2D (n = 1,404), outliers for energy intake (n = 1,340 with $<$500 and $>$4,200 kcal), and those with very low HbA_{1c} ($<$4%; n = 26) were excluded from further analysis. The final dietary data included 18,090 individuals, with 49% men and 27% urban, which is representative of the demography of the nation (Supplementary Fig. 1.1).

The study was approved by the Institutional Ethics Committee (Madras Diabetes Research Foundation, Chennai, Tamil Nadu, India), and written informed consent was obtained from all study participants. The study was registered with the Clinical Trials Registry of India (CTRI/2019/03/018095).

Exposure Assessment

A structured questionnaire was used to obtain data on demographic and behavioral aspects. Anthropometric, clinical, and biochemical assessments were performed using standardized protocols (Supplementary Material 1.4.1–1.4.2) (10). Biochemical analyses, including fasting and 2-h postglucose load blood glucose measurements, were performed in individuals without self-reported T2D. The assessment of HbA_{1c} was performed according to standard protocol in every fifth participant (Supplementary Material 1.4.3).

Physical Activity Assessment

The interviewer-administered Madras Diabetes Research Foundation Physical Activity Questionnaire (M-PAQ), validated in both urban and rural settings (12), was used to capture frequency and duration of regular, obligatory, and discretionary activities in all domains (occupation, general activity [including sleep, personal care, and domestic chores] transport, and leisure activities).

Dietary Assessment

Detailed dietary assessment was performed using the interviewer-administered, validated Madras Diabetes Research Foundation Food Frequency Questionnaire (M-FFQ) (13). This captures both urban and rural food choices of India with standard portion sizes (small/medium/large) and portion tools (cup/tsp/tbsp). Individuals were asked to report the usual frequency that best represented their dietary habits over the past 1 year. A visual atlas of Indian foods with real food images was used to help individuals estimate the precise portion size and tool. The individual's average daily dietary intake (total calories and macronutrients)

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was calculated using the in-house EpiNu version 2.0 software. The M-FFQ showed good reproducibility assessed by intraclass coefficients for macronutrients. Briefly, the intraclass coefficient for carbohydrate ranged from 0.69 to 0.76, protein from 0.61 to 0.67, and total fat from 0.63 to 0.69 for both rural and urban India (13). Energy-adjusted (residual method) macronutrients were further used in the analysis to correct measurement errors associated with total energy intake (14).

Definitions

- Newly diagnosed diabetes (NDD) was defined as HbA_{1c} ≥6.5% and/or fasting blood glucose ≥7 mmol/L (≥126 mg/dL) or 2-h postglucose load (capillary) blood glucose ≥12.2 mmol/L (≥220 mg/dL) (12).
- Prediabetes (PD) was defined as HbA_{1c} 5.7%–6.4% or if fasting glucose was ≥100–125 (≥5.6–6.9 mmol/L) and/or if 2-h postload glucose (capillary) value was ≥160 and <220 mg/dL (≥8.9 to <12.2 mmol/L) (15).
- Normal glucose tolerance (NGT) was defined as HbA_{1c} ≤5.6%, fasting blood glucose <5.6 mmol/L (<100 mg/dL), and 2-h postglucose load (capillary) <8.9 mmol/L (<160 mg/dL) (15).
- Physically active: Moderate and vigorous physical activity levels (PAL) were combined for the "active" category based on PAL cutoffs for moderate (1.70–1.99) and vigorous (2.0–2.4) activities (16).
- Physically inactive was defined as sedentary PAL of 1.40–1.69 (16).
- Overweight was defined as a BMI ≥23 kg/m^2 but <25 kg/m^2 for both sexes for South Asians (based on the World Health Organization Asia Pacific Guidelines) (17).
- Diabetes remission was defined as the return of HbA_{1c} to <6.5% without medications in an individual with diabetes (18).
- Target HbA_{1c} was set to 6.4% and 5.6% for remission of NDD and PD respectively.

Statistical Analysis

Statistical analyses were performed using SAS 9.0 statistical package (SAS Institute, Cary, NC). Continuous variables are presented as median and interquartile range (being not normally distributed), and categorical variables are presented as *n* (%). Significance was tested using the Kruskal-Wallis test and χ^2 test for continuous and categorical variables, respectively. A *P* value <0.05 was considered significant. The following variables were determined as a priori potentially affecting HbA_{1c}: age, sex, BMI, family history of T2D, systolic and diastolic blood pressure, PAL, fasting and 2-h postglucose load blood glucose, the main cereal staple (rice/wheat/millet), type of diet (vegetarian/nonvegetarian, etc.), total energy, and macronutrients (g and %E)—carbohydrate, dietary fiber, protein, total fat, and fatty acids.

Optimization-Driven Recommendations for Macronutrients

For proposing data-driven macronutrient recommendations for different glycemic categories, a linear regression model capturing the influences of covariates on HbA_{1c}% was developed using an optimization routine (Supplementary Tables 2.1–2.2 and Figs. 2.2–2.4). The model provided coefficients that captured the influence of each factor on the HbA_{1c}% outcomes. This was a linear regression model solved using the conventional least squares method with specific modifications (see Supplementary Material 2.1 and 2.2 for more details). In the HbA_{1c}% equation, the nondietary covariates were fixed, and dietary covariates (the macronutrients) were taken as optimization variables. Consequently, the HbA_{1c} estimated by the linear regression was:

$$HbA1c_{est} = A \times X + B \times Z \qquad (1)$$

Where *X* models the vector of nondietary covariates, such as age, sex, and activity levels, etc, and selected dietary factors (other than macronutrients), as mentioned in the *Statistical Analysis* section. The coefficient *A* was computed by a linear regression model. Besides, *Z* models the macronutrients and *B* their linear regression coefficients. The $HbA1c_{est}$ can therefore be expressed as a linear combination of nondietary and dietary factors. To recommend optimal macronutrients, the optimization problem aimed to reduce the sum of the difference between $HbA1c_{est}$ and the target that was fixed depending on the glycemic category. The target HbA_{1c} was set to 6.4% and 5.6% to define remission of NDD and PD respectively.

$$Min(HbA1c_{est} - Target)^2 \qquad (2)$$

A quadratic objective term was used as both positive and negative deviations were penalized alike. The error was minimized by computing the optimal macronutrient composition in the expression $HbA1c_{est} = A \times X + B \times Z$. In addition, the macronutrient compositions had a range determined from the data, and their total consumption could not exceed 100%. This aspect was modeled using the constraints:

$$Z_{min} \leq Z \leq Z_{max} \text{ and } \Sigma Z = 100 \qquad (3)$$

By solving the constrained optimization problem with the quadratic objective in Eq. 2 and constraints in Eq. 1 and Eq. 3, macronutrient recommendations could be obtained. Nevertheless, usually a range of recommendations is preferred in studies pertaining to larger populations considering the variabilities in dietary intake. Therefore, a reduction factor "*r*" (capturing the percentage reduction) was introduced to model the reduction factor on the sum of the $HbA1c_{est}$ for each of the glycemic categories. This constraint was given by

$$HbA1c_{est} \leq r^* \Sigma(HbA1c_{est}) \qquad (4)$$

In addition, the constraints for the $HbA1c_{est}$ were given by

$$HbA1c_{est}^{min} \leq HbA1c_{est} \leq HbA1c_{est}^{max} \qquad (5)$$

where $HbA1c_{est}^{min}$ and $HbA1c_{est}^{max}$ model the minimum and maximum HbA_{1c} levels for a particular glycemic category.

Note: In this analysis, the HbA_{1c}% is used as the outcome variable based on which the analysis considered NDD and PD diagnosed by a designated HbA_{1c} cutoff.

A similar approach was used for both remission and prevention of progression to diabetes. This led to four different categories of recommendations, they are:

1. NDD remission
2. PD remission
3. Prevention of progression to NDD in PD
4. Prevention of progression to NDD in NGT

A flowchart indicating the methodology and workflow with details is provided in Supplementary Fig. 2.5.

The QPP was solved in MATLAB 2020a version using the quadprog routine.

Data and Resource Availability

Data are available on reasonable request.

RESULTS

Table 1 summarizes the demographic and nutritional profile of the 18,090 individuals stratified by three glycemic categories: NDD (n = 1,594), PD (n = 7,336), and NGT (n = 9,160). Those with NGT were younger and had significantly lower BMI, systolic and diastolic blood pressure, fasting and postprandial glucose levels, and HbA_{1c} compared with PD and NDD (all values $P < 0.0001$). Inactivity levels were high in all three glycemic categories, with the highest in NDD. The total calorie intake was significantly different between groups (P = 0.01). Individuals with NGT had the highest consumption of carbohydrates and protein (g/day and %E) and the highest glycemic index and glycemic load. However, total fat, saturated fat, and mono- and polyunsaturated fat (%E) were higher in NDD and PD.

The nutrition profile of all three glycemic categories stratified by place of residence (urban/rural), sex, physical activity, age, and BMI are provided in Supplementary Tables 3.1–3.5. Supplementary Table 3.1 provides the nutrition profile stratified by place of residence. Total calorie and fat intake were significantly higher in urban compared with rural areas across glycemic categories, while carbohydrate, glycemic index, and glycemic load were higher in rural areas, and there were

Table 1—Demographic and nutritional profile of Asian Indians stratified by glycemic status (N = 18,090) from 27 states and 3 Union Territories

Description	Adults with NDD n = 1,594	Adults with PD n = 7,336	Adults with NGT n = 9,160	P value	Overall population N = 18,090
Age (years)	48 (22)	44 (21)	36 (19)	**<0.0001**	40 (22)
Men, n (%)†	774 (49)	3503 (48)	4,521 (49)	0.12	8,798 (49)
Urban, n (%)†	551 (35)	2,075 (28)	2,254 (25)	**<0.0001**	4,880 (27)
Rural, n (%)†	1,043 (65)	5,261 (72)	6,906 (75)	**<0.0001**	13,210 (73)
BMI (kg/m^2)	24 (7)	23 (6)	21 (5)	**<0.0001**	22 (6)
Blood pressure					
Systolic (mmHg)	132 (23)	127 (21)	124 (20)	**<0.0001**	126 (21)
Diastolic (mmHg)	83 (14)	82 (13)	80 (14)	**<0.0001**	81 (13)
Fasting blood glucose (mg/dL)	128 (45)	105 (11)	88 (11)	**<0.0001**	95 (18)
2-h postprandial blood glucose (mg/dL)	155 (106)	124 (31)	110 (23)	**<0.0001**	117 (31)
HbA_{1c} (%)	6.6 (1.4)	5.5 (0.7)	5.1 (0.4)	**<0.0001**	5.3 (0.6)
Family history of diabetes, n (%)	194 (12)	697 (10)	679 (7)	**<0.0001**	1,574 (9)
Smoking (yes), n (%)†	222 (14)	1,060 (14)	1,458 (16)	**0.01**	2,740 (15)
Alcohol (yes), n (%)†	216 (14)	987 (14)	1,376 (15)	**0.01**	2,579 (14)
Physically active, n (%)†	477 (30)	2,462 (34)	3,287 (36)	**<0.0001**	6,226 (34)
Physically inactive, n (%)†	1,117 (70)	4,874 (66)	5,873 (64)	**<0.0001**	11,864 (66)
Total energy (kcal)	2,062 (1,009)	2,069 (982)	2,043 (1,018)	**0.01**	2,054 (1,005)
Carbohydrates (g)	324 (39)	324 (42)	326 (45)	0.12	325 (43)
Carbohydrates (%E)	61.4 (7·9)	61.4 (8·3)	61.7 (9.3)	**<0.0001**	61.6 (8.7)
Glycemic load	164 (48)	166 (50)	169 (54)	**<0.0001**	168 (52)
Glycemic index (%)	61 (10)	61 (10)	63 (10)	**<0.0001**	62 (10)
Total dietary fiber (g)	37 (12)	37 (12)	37 (13)	0.86	37 (12)
Total dietary fiber (%E)	3.5 (1.2)	3.5 (1.2)	3.4 (1.3)	0.84	3.5 (1.2)
Protein (g)	63 (10)	63 (11)	64 (11)	**0.0002**	63 (11)
Protein (%E)	11.8 (2.0)	11.8 (2.1)	12.0 (2.4)	**<0.0001**	11.9 (2.2)
Total fat (g)	60 (16)	60 (17)	59 (18)	**<0.0001**	59 (17)
Total fat (%E)	25.2 (7.0)	25.1 (7.8)	24.6 (8.2)	**<0.0001**	24.8 (8.0)
Total saturated fatty acid (g)	22 (22–23)	21 (21–22)	21 (20–21)	**<0.0001**	21 (21–21)
Total saturated fatty acid (%E)	9.3 (9.1–9.6)	9.0 (8.9–9.1)	8.6 (8.5–8.6)	**<0.0001**	8.8 (8.7–8.9)
Total monounsaturated fatty acid (g)	15 (14–15)	15 (15–15)	14 (14–14)	**<0.0001**	14 (14–14)

Data are presented as median (interquartile range), unless indicated otherwise. Bold P values are statistically significant. SI conversion factor: To convert fasting blood glucose and postprandial blood glucose to mmol/L multiply by 0.0555. P value <0.05 considered as significant with Kruskal-Wallis test for continuous variable. †P value <0.05 considered as significant with χ^2 test for categorical variables.

no significant differences in protein and fiber intake (g/day and %E). Supplementary Table 3.2 shows the nutritional profile stratified by sex. While total calorie intake was higher in men in all categories, carbohydrate intake (g/day and %E) did not significantly differ by sex. In the PD and NGT categories, men reported higher protein, while women had higher fat intake. Supplementary Table 3.3 depicts the nutritional profile stratified by physical activity levels. Those who were physically active consumed more calories and carbohydrates across glycemic categories, whereas fat intake was significantly higher among inactive individuals. Absolute protein intake (g/day) did not differ by physical activity levels in NDD and PD. The nutritional status stratified by age is given in Supplementary Table 3.4. No significant differences in intakes of macronutrients were observed between the two age categories (≥60 years vs. <60 years). However, total calorie intake was significantly lower in older individuals compared with younger individuals. Supplementary Table 3.5 shows the nutritional profile stratified by BMI. Overweight and obese individuals consumed more fat and less carbohydrates across glycemic categories.

The macronutrient recommendations computed through the optimization approach for remission and prevention of progression to T2D in the three glycemic categories with various stratifications are given in Tables 2–4. Four recommendations emerged, with two recommendations for remission in NDD and PD (Tables 2 and 3) and two for prevention of progression to T2D in PD and NGT (Table 4). Overall, the recommendation for the NDD category was suggested by the optimization algorithm for reducing mean HbA_{1c} by 15–20% (denoted by “r” in the optimization routine). This reduction in HbA_{1c} translates to remission in 66–78% of individuals with NDD. The optimal macronutrient ranges (%E) to achieve this remission in NDD were carbohydrates, 49–54; proteins,19–20; fat, 21–26; and dietary fiber, 5–6. The fat recommendation was lower for rural compared with urban counterparts (21–24 vs. 23–25%E, respectively). However, carbohydrate and dietary fiber recommendations for rural residents were 1% higher than for urban. The optimization results based on physical activity levels showed that for active individuals, the carbohydrate intake could be in the range of 52–55%E, whereas for inactive individuals, a lower range of 50–52% was recommended. Besides, women were recommended a 2% greater reduction in carbohydrates than men. Further, older individuals (≥60 years) were recommended 1%E lower carbohydrates and 1%E higher protein compared with younger individuals. Similarly, for overweight and obese, an additional 2% reduction in carbohydrates (49–52%E vs. 52–54%E) was recommended compared with individuals with normal BMI (Table 2).

Table 2—Optimized macronutrient recommendations for NDD remission (n = 1,000)

Stratification	Macronutrient percentage of energy (%E)	Individuals attaining remission (%)
Overall	Carbohydrates: 49–54 Proteins: 19–20 Fat: 21–26 Dietary fiber: 5–6	66–78
Urban	Carbohydrates: 52–53 Proteins: 18–20 Fat: 23–25 Dietary fiber: 4–5	79–87
Rural	Carbohydrates: 52–54 Proteins: 18–20 Fat: 21–24 Dietary fiber: 5–6	67–80
Inactive	Carbohydrates: 50–52 Proteins: 19–20 Fat: 22–25 Dietary fiber: 6	81–86
Active	Carbohydrates: 52–55 Proteins: 18–19 Fat: 23–25 Dietary fiber: 3–5	71–84
Men	Carbohydrates: 51–54 Proteins: 19–20 Fat: 21–25 Dietary fiber: 5–6	67–78
Women	Carbohydrates: 50–52 Proteins: 19–20 Fat: 22–25 Dietary fiber: 6	82–86
Age <60 years	Carbohydrates: 52–54 Proteins: 18–19 Fat: 21–25 Dietary fiber: 5–6	52–63
Age ≥60 years	Carbohydrates: 50–53 Proteins: 19–20 Fat: 21–25 Dietary fiber: 6	81–86
Overweight and obese	Carbohydrates: 49–52 Proteins: 19–20 Fat: 22–26 Dietary fiber: 6	66–80
Normal BMI	Carbohydrates: 52–54 Proteins: 18–20 Fat: 23–25 Dietary fiber: 4–5	86

Optimization was carried by QPP.

Remission of PD to NGT (Table 3) could be induced in 52–78% of individuals. Overall, the optimal macronutrient recommendations for this category were carbohydrates, 50–56%E; protein, 18–20%E; fat, 21–27%E; and dietary fiber, 3–5%E.

Table 3—Optimized macronutrient recommendations for PD remission (*n* = 3,094)

Stratification	Macronutrient percentage of energy (%E)	Individuals attaining remission (%)
Overall	Carbohydrates: 50–56 Proteins: 18–20 Fat: 21–27 Dietary fiber: 3–5	52–78
Urban	Carbohydrates: 52–54 Proteins: 16–20 Fat: 21–26 Dietary fiber: 3–5	52–78
Rural	Carbohydrates: 52–55 Proteins: 17–20 Fat: 21–26 Dietary Fiber: 4–5	52–78
Inactive	Carbohydrates:52–54 Proteins: 18–20 Fat: 21–24 Dietary fiber: 5–6	51
Active	Carbohydrates: 52–58 Proteins: 18–19 Fat: 20–26 Dietary fiber: 3–4	40–64
Men	Carbohydrates: 52–55 Proteins: 18–20 Fat: 20–24 Dietary fiber: 5–6	48–53
Women	Carbohydrates: 52–53 Proteins: 18–20 Fat: 22–24 Dietary fiber: 5–6	50–80
Age <60 years	Carbohydrates: 52–55 Proteins: 18–19 Fat: 20–25 Dietary fiber: 5–6	53–65
Age ≥60 years	Carbohydrates: 51–54 Proteins: 19–20 Fat: 21–24 Dietary fiber: 5–6	50
Overweight and obese	Carbohydrates: 50–53 Proteins: 19–20 Fat: 21–25 Dietary fiber: 6	35–76
Normal BMI	Carbohydrates: 52–54 Proteins: 18–20 Fat: 21–26 Dietary fiber: 4–5	51

Optimization was carried by QPP.

A 1%E higher carbohydrate intake was recommended for rural residents compared with their urban counterparts. Physically inactive individuals were recommended greater reduction (4%E) in carbohydrates as against active individuals, who could increase fat calories by 2%. Recommendations stratified by sex indicated a 2% increase in carbohydrate calories for men compared with women. On the other hand, older individuals were suggested a 1% decrease in each of carbohydrate and fat calories but a 1% increase in protein compared with younger individuals. Similarly, overweight/obese individuals were recommended to reduce carbohydrate and fat by 1% and increase fiber by 1% compared with those with normal BMI.

The third and fourth recommendations of macronutrient composition to aid in prevention of progression to T2D for individuals with PD and NGT are summarized in Table 4. The macronutrients (%E) that would prevent progression to T2D for PD were carbohydrates, 54–57; protein, 16–20; fat, 20–24; and dietary fiber, 3–6 for all stratifications (urban/rural, inactive/active, sex, age, overweight/normal BMI). Similarly, for NGT, the macronutrients (%E) were carbohydrates, 56–60; protein, 14–17; fat, 20–24; and dietary fiber, 3–6 for all stratifications.

CONCLUSIONS

Here we report key findings that emerged from modeling the proportions of dietary macronutrients in relation to the remission/prevention of progression to T2D in Asian Indians. We recommend reductions in carbohydrate calories and an increase in protein calories for both remission and prevention of T2D in all glycemic categories. Further, to prevent progression in PD and NGT categories, we have identified a minimum protein intake of 14–16%E. Physically inactive, obese, and older individuals, as well as those residing in urban locations, required greater reductions in carbohydrate (%E) intake.

The national Acceptable Macronutrient Distribution Range (AMDR) for adults derives 45–65% of its total dietary calories from carbohydrates, 5–15% from protein, and 15–35% from fat (19). Our findings suggest that a lower range of carbohydrate intake (49–56%E), a higher range of protein (14–20%E), and a narrower range of fat intake (21–27%E) would be optimal for remission/prevention of T2D. The nutrition profile of our study participants was similar to the recent “What India Eats” study, which reported higher carbohydrates and lower fat intake in rural compared with urban areas (20). However, compared with our findings, the earlier study reported higher protein intake in rural (69 g vs. 63 g) and lower intake in urban (55.4 g vs. 63–64 g) areas (20). Our optimization model-based macronutrient recommendations contrast with those derived from substitution models in Western studies (9), in that the latter suggest increasing carbohydrate calories to replace the fat calories by 2–3%. These differences are perhaps due to the inherently high carbohydrate

Table 4—Macronutrient recommended for prevention of progression to diabetes in PD and NGT

Stratifications	PD (*n*)	NGT (*n*)	Macronutrients. %E PD (*n* = 3,094)	Macronutrients. %E NGT (*n* = 9,160)
Overall	3,094	9,160	Carbohydrates: 54–57 Protein: 16–20 Fat: 20–24 Dietary fiber: 3–6	Carbohydrates: 56–60 Protein: 14–17 Fat: 20–24 Dietary fiber: 3–6
Urban	912	2,254		
Rural	2,182	6,906		
Inactive	2,086	5,873		
Active	1,008	3,287		
Men	1,576	4,521		
Women	1,518	4,639		
<60 years	2,384	8,174		
≥60 years	710	986		
Overweight/obese	1,601	3,059		
Normal BMI	1,493	6,101		

Optimization was carried by QPP.

and lower fat content in Indian versus Western diets, such that reducing carbohydrate calories would have a proportionately greater benefit in the former. We showed in an earlier publication that reducing carbohydrate intake to <65%E can reduce the risk of T2D by 70% (21,22). We now show that remission in T2D would require further reduction of carbohydrate intake to 49–54%E. We showed earlier that urban Asian Indian adults derive 61–64% of their total daily energy intake from carbohydrate (23). In general, low- and middle-income countries consume carbohydrate in the range of 60–70%E (24). Hence, the study findings can be extended to such high carbohydrate–consuming countries.

As our recommendations do not entail drastic changes from the usual carbohydrate intake of the population, we believe that they are eminently feasible, acceptable, and sustainable on a large scale, in contrast to the widely used keto diet, paleo diet, very low-calorie diet, and other "diabetes reversal" diets that require much more extreme reductions in carbohydrate and calorie intake (2,25).

We recommend a fat intake of 21–27%E for remission and prevention of T2D, which is essentially similar to earlier guidelines. However, further studies are required to elucidate the optimal distribution of different types of fat in the diet. Similarly, our dietary fiber recommendations agree with the national recommendations of 25–40 g/2,000 kcal/day (19). The Asian Indian diet has been traditionally considered deficient in quantity and quality of protein (26), and this has been postulated to predispose to T2D by reduction in lean body mass (27). Increasing protein intake should therefore be relevant for prevention/remission of diabetes via its potential effect on maintenance of skeletal muscle mass (28). National dietary recommendations for India now recommend alteration of the ratio of protein intake from dietary cereal-legume-milk from 11:1:3 to 3:1:2.5 (19), suggesting that an increase in dietary protein intake is feasible in India, using sources of protein that are easily available.

Inactive, older, and obese individuals in our study needed a greater reduction in carbohydrate with higher intake of protein. Also, individuals in rural areas (who are more likely to be engaged in physically active occupations) were found to require a lesser reduction of carbohydrate for improvement of glycemic status compared with their urban counterparts. These subtle differences can have significant implications in designing policy initiatives for reduction of diabetes risk in different subsections of the Asian Indian population.

The current study has several strengths. Firstly, the ICMR-INDIAB study has been performed on a nationally representative sample, and this substudy on diet has equal representation from each state/Union Territories in India and from both urban and rural areas.

Secondly, the macronutrients were all adjusted for total energy intake, whereby the measurement error of nutrient intake associated with total energy is minimized.

Thirdly, the optimization method used has firm mathematical background on optimality conditions, convergence, and feasibility that makes it easier to adopt, and the problem being convex, could be solved in reasonable time for even large data sets. For the first time, recommendations have been provided for different stratifications of glycemic categories in the population.

Further, the recommendations are based on modifications of current population-based consumption levels. They do not entail drastic changes in the usual diet patterns and should therefore be easier to comply with and are likely to be more sustainable. Moreover, the findings are generalizable to other low- and middle-income South Asian countries with high diabetes prevalence, as they have a similar dietary profile to India with very high carbohydrate intakes (24,29).

However, the study has some limitations. Even when collected using the best available measures, assessment of self-reported dietary intake is complicated by challenges such as complexity of many foods, inability to describe specific foods, natural day-to-day variability in intake, and limitations of food composition databases. The quality of macronutrients for recommendations (types of fats, carbohydrates, and proteins) is another important aspect of optimized diet that is not included in the current study due to lack of adequate details (fatty acids, glycemic index, glycemic load, and protein-quality score) for the reported processed and cooked foods. The method heavily relies on the HbA_{1c} model to be linear that worked for the data considered in our analysis, and generalization of the approach across data sets may be difficult. In the current study, modeling efforts could not be further tested dynamically to assess the change in dietary macronutrients to effect a change (i.e., reduction in the diabetes risk). The FFQ was collected only once due to the cross-sectional design of the study; hence, changes in diet and lifestyle that have occurred subsequently may have an influence on the data. It should also be noted that these recommendations are derived from the macronutrient calories reported by the population in each glycemic category and therefore do not represent personalized recommendations for diabetes remission or prevention but rather a single population-level recommendation in each category. Finally, the, associations should be confirmed in prospective studies (ideally through randomized, long-term intervention studies) both on remission as well as prevention of progression to T2D.

This report presents a population-based approach for remission and prevention of progression to T2D by reorganizing macronutrient compositions using a data-driven optimization approach. We recommend reduction in carbohydrate and an increase in protein intake for both remission in NDD and PD as well as for prevention of progression to diabetes in PD and NGT categories. As our analyses have been performed on data from the nationally representative ICMR-INDIAB study covering all states of India, our findings comprehensively capture the inherent diversities in the food habits and culture and our recommendations can be applied to the entire Indian population. These model-based recommendations highlight and suggest the need to develop guidelines for appropriate dietary macronutrient composition, which could be an important step to reduce T2D risk in India.

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Author Contributions. R.M.A. and V.M. conceived and designed the study and were involved in implementation of the study, training the team, designing quality assurance measures, interpretation of the data, and original drafting and revision of the report. R.M.A. and V.M. take full responsibility for the overall content of this work. S.S. conceived and performed formal analysis and writing the original draft. V.S. and R.U. were involved in the interpretation of the data and drafting of the report. S.R.J., B.S., N.T., P.K.J., A.G., S.B., S.C., and S.K. were responsible for the supervision of the study in their respective states and reviewing the report, provided scientific input for the study, were involved in the quality control, and helped to revise the report. A.K.D., S.V.M., T.K., and R.S.D. are members of ICMR-INDIAB Expert Group and helped to review the report. R.G. and V.S.M. coordinated investigations and contributed to writing the original draft. R.G. and G.G. helped in the field coordination of the study and methodology. K.A., P.T., and N.L. were responsible for data curation and statistical analyses. M.D. and R.P. were involved in the methodology and project administration, reviewing and editing report. A.V.K. and K.K. provided critical revision of the report. All authors contributed to revision of the report and approved the final submitted version. R.M.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Afshin A, Sur PJ, Fay KA, et al.; GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019;393:1958–1972
2. Lean MEJ, Leslie WS, Barnes AC, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet Diabetes Endocrinol 2019;7:344–355
3. Dehghan M, Mente A, Zhang X, et al.; Prospective Urban Rural Epidemiology (PURE) study investigators. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet 2017;390:2050–2062
4. Venn BJ. Macronutrients and human health for the 21st century. Nutrients 2020;12:2363
5. National Health and Medical Research Council Australia. Nutrient Reference Values for Australia and New Zealand. Macronutrient Balance. Page updated 4 February 2014. Accessed 23 July 2021. Available from: https://www.nrv.gov.au/chronic-disease/macronutrient-balance
6. van Dooren C. A review of the use of linear programming to optimize diets, nutritiously, economically and environmentally. Front Nutr 2018;5:48
7. National Sample Survey Office (NSSO). *Nutritional Intake in India, 2011-12.* India, National Sample Survey Office, 2014
8. National Family Health Survey (NFHS 4): 2015-2016. Mumbai, International Institute of Population Sciences (IIPS) and ICF; 2017
9. Faerch K, Lau C, Tetens I, et al. A statistical approach based on substitution of macronutrients provides additional information to models analyzing single dietary factors in relation to type 2 diabetes in Danish adults: the Inter99 study. J Nutr 2005;135:1177–1182
10. Anjana RM, Pradeepa R, Deepa M, et al. The Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study: methodological details. J Diabetes Sci Technol 2011;5:906–914
11. Anjana RM, Deepa M, Pradeepa R, et al.; ICMR–INDIAB Collaborative Study Group. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol 2017;5:585–596
12. Anjana RM, Sudha V, Lakshmipriya N, et al. Reliability and validity of a new physical activity questionnaire for India. Int J Behav Nutr Phys Act 2015;12:40
13. Sudha V, Anjana RM, Vijayalakshmi P, et al. Reproducibility and construct validity of a food frequency questionnaire for assessing dietary intake in rural and urban Asian Indian adults. Asia Pac J Clin Nutr 2020;29:192–204
14. Willett W. *Nutritional Epidemiology.* New York, Oxford University Press, 2013
15. American Diabetes Association. 2. Classification and diagnosis of diabetes: *Standards of Medical Care in Diabetes—2021*. Diabetes Care 2021;44(Suppl. 1): S15–S33
16. Human energy requirements. Report of a Joint FAO/WHO/UNU Expert Consultation; 2004. Accessed 23 July 2021. Available from: https://www.fao.org/3/y5686e/y5686e.pdf
17. World Health Organization. Regional Office for the Western Pacific. The Asia-Pacific perspective: redefining obesity and its treatment. Sydney: Health Communications Australia, 2000. Accessed 23 July 2021. Available from: https://apps.who.int/iris/handle/10665/206936
18. Riddle MC, Cefalu WT, Evans PH, et al. Consensus report: definition and interpretation of remission in type 2 diabetes. Diabetes Care 2021;44:2438–2444
19. ICMR Ministry of Health Family Welfare, NIN. *Nutrient Requirements for Indians: Recommended Dietary Allowances, Estimated Average Requirements – 2020*. New Delhi, Indian Council of Medical Research-National Institute of Nutrition, 2020
20. Hemalatha Laxmaiah A, Sriswan RM, Boiraju NK, Radhakrishnan KV. *What India Eats*. Hyderabad, Indian Council of Medical Research - National Institute of Nutrition, 2020
21. Anjana RM, Sudha V, Nair DH, et al. Diabetes in Asian Indians—how much is preventable? Ten-year follow-up of the Chennai Urban Rural Epidemiology Study (CURES-142). Diabetes Res Clin Pract 2015;109:253–261
22. Mohan V, Radhika G, Sathya RM, Tamil SR, Ganesan A, Sudha V. Dietary carbohydrates, glycaemic load, food groups and newly detected type 2 diabetes among urban Asian Indian population in Chennai, India (Chennai Urban

Rural Epidemiology Study 59). Br J Nutr 2009; 102:1498–1506
23. Radhika G, Sathya RM, Ganesan A, et al. Dietary profile of urban adult population in South India in the context of chronic disease epidemiology (CURES-68). Public Health Nutr 2011;14:591–598
24. Kang S, Kang M, Lim H. Global and regional patterns in noncommunicable diseases and dietary factors across national income levels. Nutrients 2021;13:3595
25. Shilpa J, Mohan V. Ketogenic diets: boon or bane? Indian J Med Res 2018;148:251–253
26. Swaminathan S, Vaz M, Kurpad AV. Protein intakes in India. Br J Nutr 2012;108(Suppl. 2):S50–S58
27. Wells JC, Pomeroy E, Walimbe SR, Popkin BM, Yajnik CS. The elevated susceptibility to diabetes in India: an evolutionary perspective. Front Public Health 2016;4:145
28. Kurpad AV, Vaz M. Protein and amino acid requirements in the elderly. Eur J Clin Nutr 2000;54(Suppl. 3):S131–S142
29. Gopalan HS, Misra A, Jayawardena R. Nutrition and diabetes in South Asia. Eur J Clin Nutr 2018;72:1267–1273