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ORIGINAL ARTICLE

Dietary changes in a diabetes prevention intervention among people with prediabetes: the Diabetes Community Lifestyle Improvement Program trial

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Abstract

Aims Diabetes prevention interventions have been less successful in Asian Indians compared to other populations, which may be due in part to dietary differences. The objective of this study was to determine the impact of a diabetes prevention intervention on diet and risk of diabetes in Asian Indians at high risk.

Methods Data were included from the Diabetes Community Lifestyle Improvement Program (D-CLIP), a randomized control trial to prevent diabetes in overweight/obese Asian Indian adults (20–65 years) with prediabetes. Respondents received standard treatment (control; $n=283$) or a 6-month intervention ($n=295$) that included education and support to reduce intakes of fat and total calories (kilocalories; kcal). Diet was ascertained using a food frequency questionnaire, and incident diabetes was determined from annual 2-h plasma glucose post-oral glucose tolerance test or biannual fasting plasma glucose.

Results There were 485 (control 240; intervention 245) respondents with complete diet data at baseline. At 6 months, the intervention was associated with decreased intake of total energy (− 185.6 kcal/day; 95% CI − 353.6, − 17.5 kcal/day) and refined cereals (− 7.2 g/1000 kcal; 95% CI − 12.7, − 1.7 g/1000 kcal), and increased intakes of fruits and vegetables (33.4 g/1000 kcal; 95% CI 16.0, 50.8 g/1000 kcal). The intervention group was half (HR 0.49; 95% CI 0.25, 0.94) as likely to develop diabetes at 1 year, and the hazard was significantly attenuated (12.2%; $P=0.015$) with adjustment for fruits and vegetable intake.

Conclusion The D-CLIP decreased the total energy intake and increased the intakes of fruits and vegetables, and reduced the 1-year incidence of diabetes by half.

Trial registration Clinicaltrails.gov # NCT01283308

Keywords Prediabetes · Diabetes mellitus, type 2 · Intervention study · Nutritional and metabolic diseases · Lifestyle risk reduction · Disease prevention · Secondary · Prevention

Background

The diabetes burden in India is great, with 73 million adults currently affected [1] and 77.2 million adults at risk with prediabetes [2]. The Diabetes Community Lifestyle Improvement Program (D-CLIP) was a randomized, controlled translational research study testing expert advice for diabetes prevention, proven lifestyle education curriculum (e.g., the US Diabetes Prevention Program [DPP] [3]) plus metformin when needed, among overweight Asian Indians (AIs) with prediabetes [4]. The D-CLIP intervention reduced diabetes incidence by 32% (95% CI 7–50) [5] in the intervention arm compared to controls; however, the study impact was much less than the 58% reduction of the original DPP [3].

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It is unclear if the reduced effects were due to the translational nature of D-CLIP or if AIs respond differently from other populations to programs like the DPP. Importantly, the DPP protocol was originally tailored to a population consuming an average of 34.1% of total energy from fat. Therefore, the dietary component of the DPP focused on decreasing, along with total energy intake, the percent of calories consumed from fat to < 30%. The dietary component of the translational studies of the DPP, including D-CLIP, focuses on achieving the same reduction in percent of calories consumed from fat to < 30%. This approach may be less suitable for AIs, who have been reported to have average fat intake comprising between 15.6% (rural) and 21.1% (urban) of total energy [6].

Intake of fat and other dietary difference could explain, in part, why translational studies of the DPP have been relatively less effective in AIs compared to other populations. However, few studies have investigated the impact of DPP-like interventions on dietary intake in general and specifically in AIs. Moreover, the impact of intervention-related dietary changes on diabetes risk in this population is unclear. The objective of the current study is to evaluate the impact of the D-CLIP intervention on the diets of overweight AIs with prediabetes and determine whether the resulting dietary changes were associated with decreased diabetes risk.

Methods

Briefly, D-CLIP was a randomized control trial (clinicaltrails.gov # NCT01283308) to prevent diabetes in South Asians at high risk of developing the disease. Subjects were recruited from community health assessments, clinic records, and direct referrals from study site clinicians in Chennai, India, from September 2009 to February 2012. Eligible participants were overweight or obese by body mass index (BMI) and/or waist circumference in accordance with the World Health Organization's guidelines for Asian populations (BMI of ≥ 23.0 kg/m^2 and/or a waist circumference ≥ 90 cm in males or ≥ 80 cm in females) [10], aged 20–65 years, and had prediabetes as indicated by impaired fasting glucose (IFT) and/or impaired glucose tolerance (IGT). IFT (5.6–6.9 mmol/L; 100–125 mg/dL) was determined from a fasting blood draw, whereas IGT (7.8–11.0 mmol/L; 140–199 mg/dL) was determined from 2-h plasma glucose concentration (2-h PG) following an oral glucose tolerance test (OGTT). All procedures and study materials were approved by the Emory University Institutional Review Board (IRB-00016503) and the Madras Diabetes Research Foundation Ethics Committee.

Respondents were randomized to receive standard treatment (control; $n = 283$) or a 6-month lifestyle intervention ($n = 295$). The standard treatment group met once each with a physician and dietician, attended two classes on healthy dietary changes, weight loss and exercise to reduce risk of diabetes, and received informational handouts related to prevention of diabetes through weight loss, heathy dietary changes and increased physical activity. Those in the intervention group received a structured educational curriculum delivered as weekly classes over 16 weeks (4 months), followed by 8 weeks of maintenance classes, for which respondents were encouraged to attend at least four classes. The curriculum was adapted from that of the DPP [12] and designed to reduce the incidence of diabetes through weight loss (≥ 7% weight loss), achieving at least 150 min of moderate activity weekly and reducing the intakes of fat (to < 30% of total energy) and total energy. The DPP curriculum materials were modified by the study team based on extensive clinical and intervention experience in this population, knowledge of the culture, and both published and unpublished findings on diet and physical activity behaviors and preferences of South Asian adults to be culturally appropriate for the target population and suitable for group-based instruction [4]. The methods of the D-CLIP study are described in further detail elsewhere [5, 13].

Herein, we describe the methods related to this secondary analysis. Interested adults aged 20–65 years living in Chennai, India, were screened to identify overweight or obese [body mass index (BMI) ≥ 23.0 kg/m^2 and/or waist circumference ≥ 90 cm in males or ≥ 80 cm in females] adults with prediabetes. Prediabetes included impaired fasting glucose [IFG, fasting plasma glucose (FPG) of 5.6–6.9 mmol/L; 100–125 mg/dL] and/or impaired glucose tolerance (IGT, 2-h post load glucose of 7.8–11.0 mmol/L; 140–199 mg/dL). Eligible participants were randomized to receive either standard of care control ($n = 283$) or a step-up diabetes prevention program ($n = 295$), which included 6 months of group-based, culturally tailored lifestyle education classes plus metformin for participants who remained at the highest risk of converting to diabetes at 4 months or later. The intervention classes followed a structured educational curriculum with 16-weekly active period classes, followed by 8 weeks of maintenance classes. The curriculum was adapted from the DPP [3] and designed to reduce diabetes incidence through weight loss (≥ 7% weight-loss), 150 min or more of moderate activity weekly, and reducing intakes of fat (to < 30% of total energy) and total calories. Metformin (500 mg/day twice daily) was given to the intervention group participants who presented with either IFG + IGT or IFG + HbA1c > 5.7% at month 4 or later. The Emory University Institutional Review Board (IRB-00016503) and the Madras Diabetes Research Foundation Ethics Committee approved the study procedures and materials.

Incident diabetes, the primary outcome, was ascertained from 2-h OGTT and FPG measurements. Starting at baseline, 2-h oral glucose tolerance tests (OGTT) were done

annually and FPG tests were done twice per year through the end of follow-up. In accordance with the American Diabetes Association (ADA) guidelines, incident diabetes was characterized as 2-h PG ≥ 200 mg/dL (11.1 mmol/dL) and/or FPG ≥ 126 mg/dL (7.0 mmol/L). No confirmatory or repeated test of diabetes status was performed in those with incident diabetes.

Dietary intake was measured at baseline, 6 months, and annually beginning in month 12, using a previously developed, semi-quantitative food frequency questionnaire (FFQ) designed to capture the usual intake during the preceding year. The 222-item FFQ was developed for use among adults in Southern India and was shown to have acceptable reproducibility and validity relative to dietary assessment using multiple 24-h dietary recall surveys [14]. Average daily intakes of 16 food/nutrient groups (listed below) were computed from reported frequencies and estimated typical serving sizes (in grams). Mean daily amounts consumed (in grams/day) were estimated for the following food/beverage groups: (1) alcohol; (2) refined cereals; (3) whole cereals; (4) oils and fats; (5) eggs; (6) fish; (7) legumes; (8) meat; (9) dairy; (10) millets; (11) nuts and seeds; (12) processed foods; (13) spices and condiments; (14) added sugars; (15) tubers; and (16) fruits and vegetables. To calculate macronutrients (grams of fat, carbohydrates, and protein) and total kilocalories (kcal), the resulting average intakes in grams were cross referenced with the EpiNu India® Database [14], which includes nutrient facts per 100 g for a comprehensive food composition table.

Socio-demographic characteristics including age, sex, family history of diabetes (first degree relative with diabetes) and education level and history of diabetes, prediabetes, and gestational diabetes were self-reported at baseline. Anthropometric measures were taken at baseline and every 6 months and included height, weight (in light clothing) and waist circumference (at the umbilicus). BMI was computed as weight in kilograms divided by height in meters squared (kg/m^2).

All analyses were conducted in Stata (version 14, StataCorp, College Station, Texas). Data were included for respondents with non-missing dietary data at baseline. In bivariate analyses, simple means and Student's *t* tests were used to compare differences in continuous variables by treatment group. Proportions and Pearson's Chi-square tests were used to evaluate differences in the distributions of categorical variables by treatment group. Variables found to significantly differ by treatment group were included in adjusted models.

Random-effects linear regression was used to model changes in intakes of 16 key food and beverage groups by treatment group over time, specifically focusing on between-group differences immediately following the 6-month intervention period. To account for within-subject dependence, standard errors were computed using the clustered sandwich variance estimator [15]. Each dietary variable of interest was modeled as a dependent variable in a series of discrete models. Study follow-up time was modeled using disjoint indicator variables corresponding to 6 and 12 months of follow-up time, and all dietary variables were modeled continuously as grams per 1000 kilocalories/day. To evaluate trends in dietary intake by treatment group over time, time was included as a continuous variable in separate models, and the *P* value corresponding to the coefficient was reported as *P* for trend. To evaluate time by treatment effects, terms for time (continuous), treatment group, and the interaction of time with treatment group were included in the model. A Wald test statistic was used to evaluate interaction, with $\alpha = 0.05$ as the threshold for statistical significance.

Cox proportional hazards models were used to determine the impact of between-group dietary changes on diabetes risk. Incident cases of diabetes were defined as having FPG ≥ 126 mg/dL (7.0 mmol/L) or 2hPG ≥ 200 mg/dL (11.1 mmol/L). Time to event was defined as the number of months from baseline to study visit at the time of diagnosis. Respondents who were lost to follow-up were censored. A crude hazard ratio comparing the diabetes risk among respondents in the intervention group to those in the control was estimated. To determine the contribution of dietary changes to the observed intervention effect, single nutrient-adjusted models were run to evaluate the change in hazard ratio upon controlling for intakes of fruits and vegetables, millets, refined cereals, spices and condiments, and whole grain cereals. Dietary variables were entered into the model as grams per 1000 calories, thereby controlling for total energy. Using the HR from the crude model as the reference value, change in the hazard ratio relative to the crude model was computed for each adjusted model, and ≥ 10% change in the hazard model *and* a significant ($P < 0.05$) likelihood ratio test were considered significant. Akaike information criteria (AIC) and Bayesian information criteria (BIC) were computed to allow for qualitative comparison of models. Hazards were computed for a year of follow-up, as there were too few incident cases ($n = 4$) of diabetes at 6 months of follow-up.

Results

Of the 578 respondents who underwent randomization (control 295; intervention 283), 28 were lost to follow-up (4.8%) and 65 (11.2%) were missing dietary data at baseline and were therefore not included in the analytic sample ($n = 245$ intervention arm, $n = 240$ control arm). Respondents who were lost to follow-up were not statistically different from those in the analytic sample with regard to any of the socio-demographic characteristics

Table 1 Selected socio-demographic and other characteristics of respondents from the Diabetes Community Lifestyle Improvement Program (D-CLIP) trial

	Control group	Intervention group	*P* value
N	240	245	
	Percent ± standard deviation		
Gender, %			
Female	97 (40.4%)	89 (37.1%)	0.354
Male	143 (59.6%)	156 (59.6%)	
Age, %			
20–35	50 (20.8%)	37 (15.1%)	0.242
36–50	132 (55.0%)	141 (57.6%)	
50+	58 (24.2%)	67 (27.3%)	
BMI category, %			
18.5–22.9 kg/m^2	14 (5.8%)	13 (5.3%)	0.949
23–27.4 kg/m^2	107 (44.6%)	112 (45.7%)	
≥ 27.5 kg/m^2	119 (49.6%)	120 (49.0%)	
High waist circumference, %			
No	18 (7.5%)	33 (13.5%)	0.032
Yes	222 (92.5%)	212 (86.5%)	
Type of prediabetes, %			
iIFG	71 (29.6%)	76 (31.0%)	0.808
iIGT	66 (27.5%)	71 (29.0%)	
IFG and IGT	103 (42.9%)	98 (40.0%)	
Income, INR			
Less than 10,000	58 (26.5%)	69 (30.9%)	0.163
10,000–15,000	45 (20.5%)	55 (24.7%)	
15,001–25,000	48 (21.9%)	32 (14.3%)	
More than 25,000	68 (31.1%)	67 (30.0%)	
Education, %			
< High school	23 (9.6%)	18 (7.3%)	0.657
High school	65 (27.2%)	76 (31.0%)	
Technical or undergraduate degree	87 (36.4%)	91 (37.1%)	
Postgraduate or above	64 (26.8%)	60 (24.5%)	
Family history of diabetes, %			
No	189 (78.8%)	187 (76.3%)	0.523
Yes	51 (21.3%)	58 (23.7%)	
History of prediabetes, %			
No	168 (70.0%)	174 (71.0%)	0.805
Yes	72 (30.0%)	71 (29.0%)	
Previously told (by a doctor) had diabetes, %			
No	219 (91.3%)	230 (94.3%)	0.201
Yes	21 (8.8%)	14 (5.7%)	
	Mean ± standard deviation		
Age, years	44.2 ± 9.6	45.1 ± 8.8	0.278
Weight, kg	74.4 ± 11.2	74.5 ± 11.4	0.975
BMI, kg/m^2	27.9 ± 3.6	27.8 ± 3.6	0.978
Waist circumference, cm	94.5 ± 8.6	94.6 ± 9.2	0.946
HOMA-IR	4.6 ± 16.9	6.4 ± 27.2	0.390
Fasting plasma glucose (mg/dL)	103.3 ± 9.1	102.8 ± 8.7	0.551
2-h plasma glucose (mg/dL)[a]	150.6 ± 25.4	147.6 ± 27.7	0.220

P value corresponds to a Student's *t* test for continuous variables, and a Pearson Chi-square test for categorical variables; $\alpha = 0.05$

BMI body mass index, *dL* deciliters, *HOMA-IR* homeostatic model of insulin assessment; *iIFG* isolated impaired fasting glucose, *iIGT* isolated impaired glucose tolerance, *INR* Indian rupees, *kg* kilograms, *m* meters, *mg* milligrams

[a]2-h plasma glucose concentration was measured following an oral glucose (75 g) tolerance test

Table 2 Baseline dietary characteristics of respondents from the Diabetes Community Lifestyle Improvement Program (D-CLIP) trial[*†]

	Control group	Intervention group	*P* value[*]
Alcohol	10.5 ± 57.1	8.7 ± 36.2	0.671
Refined cereals	304.4 ± 118.9	306.3 ± 118.4	0.863
Whole cereals	42.5 ± 35.3	40.4 ± 34.3	0.506
Oils and fats	47.2 ± 19.0	45.9 ± 19.2	0.459
Eggs	11.8 ± 16.8	10.2 ± 15.5	0.280
Fish	14.9 ± 20.1	16.5 ± 22.5	0.424
Legumes	79.5 ± 32.0	75.9 ± 31.9	0.218
Meat	19.8 ± 23.6	21.2 ± 26.6	0.548
Dairy	481.7 ± 256.8	462.8 ± 261.9	0.422
Millets	5.7 ± 20.2	4.5 ± 17.0	0.487
Nuts and seeds	39.1 ± 22.8	38.1 ± 26.0	0.655
Processed foods	0.3 ± 1.0	0.2 ± 0.7	0.289
Spices and condiments	33.2 ± 12.5	32.1 ± 13.1	0.320
Added salt	11.8 ± 4.9	11.4 ± 4.0	0.397
Added sugars	20.5 ± 14.7	20.6 ± 16.5	0.964
Tubers	28.4 ± 25.4	25.9 ± 22.6	0.243
Fruits and vegetables	547.7 ± 272.7	542.3 ± 259.2	0.823
Total energy (kilocalories/day)	2999.7 ± 839.6	2942.0 ± 889.9	0.463
Percent of calories from fat	27.9% ± 3.9%	27.5% ± 4.3%	0.251
Percent of calories from carbohydrates	60.7% ± 4.5%	61.1% ± 4.9%	0.301
Percent of calories from protein	11.5% ± 1.0%	11.5% ± 1.1%	0.904

Unless otherwise indicated, food and beverage intakes are expressed as grams per 1000 kilocalories per day

HOMA-IR homeostatic model of insulin assessment, *iIFG* isolated impaired fasting glucose, *iIGT* isolated impaired glucose tolerance, *kg* kilograms, *m* meters

*P value corresponds to a Student's t test for continuous variables and a Pearson Chi-square test for categorical variables; $\alpha = 0.05$

presented in Table 1. Table 2 shows the selected baseline dietary characteristics of the sample. Respondents consumed an average of 2971 kcal/day (SD 865 kcal/day) at baseline, 27.7% of which was from dietary fats and 60.9% from carbohydrates. A majority (56.3%) of respondents were of ages 36–50 years (mean 44.7; SD 9.2), with an average BMI of 27.8 kg/m^2 (SD 3.6 kg/m^2). There were no significant differences between study arms at baseline, except that the proportion of respondents with high waist circumference was marginally higher in the control group (92.5% vs. 86.5%; $P < 0.05$). Thus, sensitivity analyses were conducted in which models were further adjusted for prevalence of high waist circumference. The findings from these models were not appreciably different from those from the primary analyses.

At 6 months, 51 (10.5%) of respondents were lost to follow-up (intervention 27, 11.3%; control 24, 9.8%), and there were four incident cases of diabetes over 217 person-years of follow-up (18.4 cases/1000 person-years; 95% CI 6.9, 49.1 cases/1000 person-years). There was one case of incident diabetes in the intervention group (intervention 9.0 cases/1000 person-years; 95% CI 1.3, 64.2 cases/1000 person-years) and three cases in the control group (28.2 cases/1000 person-year; 95% CI 9.1, 87.3 cases/1000 person-years).

At 12 months, 61 (12.6%) respondents were lost to follow-up, of which 38 (15.8%) were from the control group and 23 (9.4%) from the intervention groups. There were 49 cases of diabetes over 437 person-years (112.1 cases/1000 person-years; 95% CI 84.7, 148.4 cases/1000 person-years). There were 17 incident cases of diabetes (75.2 cases/1000 person-years; 95% CI 46.8, 121.0 cases/1000 person-years) in the intervention group, and 32 incident cases of diabetes (151.7 cases/person-year; 95% CI 107.2, 214.5 cases/1000 person-years) in the control group. The incidence rate ratio (IRR), comparing 12-month incidence of diabetes in the intervention group to that of the control group, was 0.50 (95% CI 0.28, 0.89).

Table 3 shows the mean changes in intakes of selected nutrients and food groups in both study arms and difference of differences between groups at 6 and 12 months of follow-up. At 6 months, respondents in both the intervention and control groups saw decreases in total energy intake; however, intervention participants decreased their total energy intake by an additional 185.6 calories/day (95% CI − 353.6, − 17.5 calories/day) compared to control participants

Table 3 Change in dietary intake (by food/beverage group) over time among respondents in the D-CLIP trial

	Least-squares mean difference (95% CI)	
	Follow-up time, months	
	6	12
Total energy intake		
Intervention	−359.1 (−473.1, −245.0)	−209.3 (−328.0, −90.6)
Control	−173.5 (−297.0, −50.0)	−174.7 (−292.4, −56.9)
Difference of differences	−185.6 (−353.6, −17.5)	−34.7 (−201.9, 132.6)
P value, difference[†]	0.030	0.685
P value, group[‡]	0.456	0.002
P value, time	0.267	0.002
P value, group × time	0.073	< 0.001
Percent of energy from fat		
Intervention	0.2% (−0.4%, 0.9%)	0.7% (0.0%, 1.4%)
Control	0.0% (−0.7%, 0.7%)	0.2% (−0.5%, 0.8%)
Difference of differences	0.2% (−0.7%, 1.1%)	0.5% (−0.4%, 1.5%)
P value, difference[†]	0.635	0.259
P value, group[‡]	0.262	0.817
P value, time	0.238	0.772
P value, group × time	0.269	0.478
Percent of energy from carbohydrates		
Intervention	−0.3% (−1.0%, 0.4%)	−0.8% (−1.6%, −0.1%)
Control	−0.1% (−0.9%, 0.7%)	−0.5% (−1.3%, 0.2%)
Difference of differences	−0.2% (−1.2%, 0.9%)	−0.3% (−1.4%, 0.8%)
P value, difference[†]	0.736	0.627
P value, group[‡]	0.323	0.954
P value, time	0.326	0.233
P value, group × time	0.286	0.996
Percent of energy from protein		
Intervention	0.1% (−0.1%, 0.2%)	0.1% (−0.1%, 0.2%)
Control	0.0% (−0.1%, 0.2%)	0.1% (−0.1%, 0.3%)
Difference of differences	0.0% (−0.2%, 0.3%)	0.0% (−0.2%, 0.2%)
P value, difference[†]	0.717	0.905
P value, group[‡]	0.902	0.816
P value, time	0.977	0.239
P value, group × time	0.894	0.192
Alcohol		
Intervention	−0.1 (−1.4, 1.1)	0.2 (−0.9, 1.3)
Control	0.4 (−1.2, 2.1)	1.7 (−1.9, 5.3)
Difference of differences	−0.5 (−2.6, 1.6)	−1.5 (−5.3, 2.2)
P value, difference[†]	0.610	0.421
P value, group[‡]	0.933	0.335
P value, time	0.920	0.120
P value, group × time	0.636	0.531
Refined cereals		
Intervention	−7.0 (−10.8, −3.1)	−6.9 (−10.6, −3.2)
Control	0.2 (−3.8, 4.2)	−0.7 (−4.6, 3.2)
Difference of differences	−7.2 (−12.7, −1.7)	−6.2 (−11.6, −0.8)
P value, difference[†]	0.011	0.025
P value, group[‡]	0.246	0.828
P value, time	0.342	0.807
P value, group × time	0.759	0.368

Table 3 (continued)

	Least-squares mean difference (95% CI)	
	Follow-up time, months	
	6	12
Whole cereals		
Intervention	3.8 (1.9, 5.7)	3.8 (2.1, 5.4)
Control	2.2 (−0.1, 4.6)	1.7 (−0.2, 3.6)
Difference of differences	1.6 (−1.4, 4.6)	2.1 (−0.4, 4.6)
P value, difference†	0.299	0.101
P value, group‡	0.784	0.030
P value, time	0.836	0.034
P value, group × time	0.678	0.013
Oils and fats		
Intervention	0.2 (−0.4, 0.7)	0.3 (−0.2, 0.8)
Control	0.2 (−0.4, 0.8)	0.1 (−0.5, 0.6)
Difference of differences	0.0 (−0.8, 0.7)	0.2 (−0.5, 1.0)
P value, difference†	0.907	0.540
P value, group‡	0.582	0.670
P value, time	0.528	0.783
P value, group × time	0.636	0.801
Eggs		
Intervention	0.3 (−0.4, 0.9)	−0.1 (−0.6, 0.5)
Control	−0.1 (−0.8, 0.7)	0.5 (−0.6, 1.6)
Difference of differences	0.3 (−0.6, 1.3)	−0.6 (−1.8, 0.7)
P value, difference†	0.500	0.357
P value, group‡	0.369	0.692
P value, time	0.527	0.272
P value, group × time	0.470	0.582
Fish		
Intervention	−1.0 (−1.8, −0.1)	−1.0 (−1.8, −0.2)
Control	−0.7 (−1.6, 0.2)	−0.2 (−1.0, 0.7)
Difference of differences	−0.2 (−1.5, 1.0)	−0.8 (−2.0, 0.3)
P value, difference†	0.699	0.169
P value, group‡	0.402	0.119
P value, time	0.362	0.402
P value, group × time	0.401	0.583
Legumes		
Intervention	0.1 (−1.1, 1.3)	0.8 (−0.4, 2.0)
Control	0.7 (−0.4, 1.8)	0.5 (−0.9, 1.8)
Difference of differences	−0.5 (−2.2, 1.1)	0.4 (−1.4, 2.2)
P value, difference†	0.517	0.676
P value, group‡	0.428	0.312
P value, time	0.333	0.397
P value, group × time	0.413	0.677
Meat		
Intervention	−1.4 (−2.2, −0.5)	−1.0 (−2.0, −0.1)
Control	−0.4 (−1.2, 0.5)	−0.2 (−1.0, 0.6)
Difference of differences	−1.0 (−2.2, 0.2)	−0.8 (−2.1, 0.4)
P value, difference†	0.111	0.202
P value, group‡	0.462	0.202
P value, time	0.537	0.462
P value, group × time	0.676	0.833

Table 3 (continued)

	Least-squares mean difference (95% CI)	
	Follow-up time, months	
	6	12
Dairy		
Intervention	3.0 (−9.9, 15.9)	5.1 (−8.0, 18.1)
Control	−1.0 (−12.9, 11.0)	−0.1 (−13.3, 13.2)
Difference of differences	4.0 (−13.6, 21.6)	5.2 (−13.5, 23.8)
P value, difference[†]	0.658	0.587
P value, group[‡]	0.835	0.930
P value, time	0.846	0.950
P value, group × time	0.671	0.305
Millets		
Intervention	1.4 (0.2, 2.6)	0.7 (−0.3, 1.6)
Control	−0.4 (−1.1, 0.3)	0.0 (−1.3, 1.3)
Difference of differences	1.9 (0.5, 3.3)	0.7 (−0.9, 2.3)
P value, difference[†]	0.009	0.421
P value, group[‡]	0.477	0.464
P value, time	0.784	0.826
P value, group × time	0.979	0.314
Nuts and seeds		
Intervention	0.2 (−0.9, 1.3)	0.4 (−0.9, 1.6)
Control	0.5 (−0.7, 1.7)	1.0 (−0.2, 2.1)
Difference of differences	−0.3 (−2.0, 1.3)	−0.6 (−2.3, 1.1)
P value, difference[†]	0.707	0.493
P value, group[‡]	0.719	0.431
P value, time	0.749	0.119
P value, group × time	0.501	0.844
Processed foods		
Intervention	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)
Control	0.1 (0.0, 0.1)	0.0 (0.0, 0.1)
Difference of differences	−0.1 (−0.1, 0.0)	0.0 (0.0, 0.1)
P value, difference[†]	0.165	0.380
P value, group[‡]	0.442	0.073
P value, time	0.224	0.268
P value, group × time	0.274	0.075
Spices and condiments		
Intervention	0.7 (0.1, 1.2)	0.6 (0.1, 1.1)
Control	−0.1 (−0.6, 0.4)	0.1 (−0.5, 0.6)
Difference of differences	0.7 (0.0, 1.5)	0.6 (−0.2, 1.3)
P value, difference[†]	0.045	0.134
P value, group[‡]	0.358	0.525
P value, time	0.495	0.943
P value, group × time	0.977	0.554
Added salt		
Intervention	0.2 (0.1, 0.4)	0.2 (0.0, 0.3)
Control	0.2 (0.0, 0.4)	0.3 (0.1, 0.5)
Difference of differences	0.1 (−0.2, 0.3)	−0.1 (−0.4, 0.2)
P value, difference[†]	0.623	0.443
P value, group[‡]	0.800	0.075
P value, time	0.980	0.001
P value, group × time	0.908	0.011

Table 3 (continued)

	Least-squares mean difference (95% CI)	
	Follow-up time, months	
	6	12
Added sugars		
Intervention	−0.9 (−1.5, −0.3)	−0.8 (−1.5, −0.2)
Control	−0.1 (−1.0, 0.7)	−0.9 (−1.5, −0.3)
Difference of differences	−0.8 (−1.8, 0.3)	0.1 (−0.8, 1.0)
P value, difference[†]	0.153	0.786
P value, group[‡]	0.855	0.632
P value, time	0.893	0.015
P value, group × time	0.603	< 0.001
Tubers		
Intervention	−0.3 (−1.8, 1.1)	−0.4 (−1.3, 0.5)
Control	−0.5 (−1.9, 0.9)	−0.2 (−1.6, 1.1)
Difference of differences	0.2 (−1.8, 2.2)	−0.2 (−1.8, 1.4)
P value, difference[†]	0.845	0.840
P value, group[‡]	0.255	0.491
P value, time	0.252	0.618
P value, group × time	0.165	0.117
Fruits and vegetables		
Intervention	32.3 (18.1, 46.4)	11.4 (0.1, 22.7)
Control	−1.2 (−11.3, 9.0)	−1.6 (−11.3, 8.0)
Difference of differences	33.4 (16.0, 50.8)	13.0 (−1.8, 27.9)
P value, difference[†]	< 0.001	0.086
P value, group[‡]	0.674	0.707
P value, time	0.308	0.682
P value, group × time	0.066	0.940

Values are given as grams per 1000 kilocalories

[†]*P* value derives from a Wald test from an ordinary least squares regression model including disjoint indicator variables for treatment group, time, and time by treatment group. Test statistic corresponds to the coefficient comparing mean intake of the selected nutrients in the intervention group versus the control group at time t

[‡]*P* value derives from a Wald test from an ordinary least squares regression model including disjoint indicator variables for the treatment group, time as a continuous term, and continuous time by treatment group. Test statistic for group corresponds to the coefficient comparing treatment groups. Test statistic for time corresponds to coefficient for continuous time. Test statistic for group × time corresponds to coefficient representing the interaction of continuous time with treatment group

($P = 0.030$). Percent of calories consumed from fat, carbohydrates, or protein did not change significantly in either study arm at 6 months. Refined cereal intake decreased by an additional 7.2 g/1000 calories (95% CI − 12.7, − 1.7 g/1000 calories) among respondents in the intervention group (compared to those in the control group), whereas intakes of fruits and vegetables increased by an additional 33.4 g/1000 (95% CI 16.0, 50.8 g/1000 calories), along with intakes of millets (1.4 g/1000; 95% CI 02, 2.6 g/1000 calories) and spices and condiments (0.7 g/1000 calories; 95% CI 0.1, 1.2 g/1000 calories).

At 12 months, 6 months after the end of the lifestyle intervention classes, total energy intake was lower in both the intervention and control groups compared to baseline ($P < 0.05$), but the difference between groups was no longer statistically significant. At 12 months, the decrease in intake of refined cereals persisted in the intervention group (− 6.9 g/1000 calories; 95% CI − 10.6, − 3.2 g/1000 calories) statistically different from that of the control group ($P = 0.025$), but intake did not differ by treatment group for any other foods or macronutrient (including total energy) groups. There were significant time, group, and time by group effects for total energy intake, indicating that there were changes in both groups over time, but greater reduction in total energy intake with the intervention. Refined cereal intake remained significantly lower in the intervention group (− 6.9 g/1000 calories; 95% CI − 10.6, − 3.2 g/1000 calories). Whole cereal intake was significantly higher

(compared to baseline) in the intervention group (3.8 g/1000 calories; 95% CI 2.1, 5.4 g/1000 calories), and there were significant effects for group, time, and group by time. Intake of added sugars was lower at 12 months in the intervention group (−8 g/1000 calories; 95% CI −1.5, −0.2 g/1000 calories), and there were significant effects for time and time by group. Although the differences in differences in their intake at 12 were not statistically significant, there were significant group and group by time effects for intakes of whole cereals and added salt. The group effect for intake of whole cereals, which increased in the intervention group at 12 months compared to baseline intake (3.8 g/1000; 95% CI 2.1, 5.4), was also statistically significant ($P=0.013$).

Crude and nutrient-adjusted hazard ratios comparing the 1-year hazard of diabetes in the intervention group to that of the control group are presented in Table 4. In the crude model, intervention group respondents were half as likely (HR 0.49; 95% CI 0.25, 0.94) to develop diabetes in the first year of follow-up than those in the control group. In single nutrient-adjusted models, adjusting for intakes of fruits and vegetables (in grams/1000 calories) significantly attenuated the hazard ratio (12.2%, LRT *P* value 0.015) toward the null value. There were no significant changes in the hazard ratio when single nutrient-adjusted models were adjusted for intakes of millets, whole cereals, refined cereals, and spices and condiments (g/1000 calories). In multiple nutrient-adjusted models, controlling for intakes of fruits and vegetables, and spices and condiments, further attenuated the hazard ratio toward the null value (12.9%, LRT *P* value 0.008) (Table 4).

Conclusions

Findings from this study suggest that a lifestyle intervention including education and support to decrease intakes of fat and total calories in AIs at high diabetes risk significantly reduced total energy intake while increasing intakes of fruits and vegetables by the end of the intervention (month 6). Those in the intervention group were half as likely to develop diabetes as those in the control group at 1 year. As much as 12% of the risk reduction was attributable to changes in fruit and vegetable intake.

These findings are consistent with those from prior studies showing that combined fruit and vegetable intake was associated with decreased diabetes incidence [16], although not all studies have found a statistically significant relationship between combined intakes of fruits and vegetables and

Table 4 Crude and adjusted 1-year hazard ratios of diabetes by experimental condition among respondents in the D-CLIP study

	HR (95% CI)	Change in HR, %	AIC	BIC	Log likelihood	LRT chi-square	LRT *P* value
Crude hazard	0.490 (0.25, 0.94)	–	271.6	276.2	−134.80	0	0
Adjusted for energy intake	0.496 (0.26, 0.96)	1.2%	270.4	279.6	−133.21	3.19	0.074
Adjusted for intake of fruits and vegetables	0.550 (0.28, 1.07)	12.2%	267.7	277.0	−131.86	5.88	0.015
Adjusted for intake of millets	0.487 (0.25, 0.94)	−0.6%	272.7	282.0	−134.37	0.86	0.354
Adjusted for intake of refined cereals	0.483 (0.25, 0.93)	−1.4%	273.3	282.5	−134.65	0.32	0.572
Adjusted for intake of spices/condiments	0.479 (0.25, 0.92)	−2.2%	272.3	281.5	−134.13	1.34	0.247
Adjusted for intake of whole cereals	0.478 (0.25, 0.92)	−2.4%	271.9	281.1	−133.94	1.73	0.188
Adjusted for intake of fruits and vegetables and refined cereals	0.537 (0.28, 1.04)	9.6%	267.6	281.5	−130.81	7.99	0.018
Adjusted for intakes of fruits and vegetables and millets	0.548 (0.28, 1.06)	11.8%	269.1	282.9	−131.55	6.51	0.039
Adjusted for intakes of fruits and vegetables, and spices/condiments	0.553 (0.28, 1.08)	12.9%	265.8	279.7	−129.92	9.76	0.008
Adjusted for intakes of fruits and vegetables, spices/condiments and whole cereals	0.525 (0.27, 1.03)	7.1%	264.0	282.5	−128.02	13.56	0.004
Adjusted for intakes of fruits and vegetables, refined cereals millets, whole cereals, and spices and condiments	0.516 (0.26, 1.01)	5.3%	267.1	294.8	−127.56	14.49	0.013

AIC Akaike information criterion, *BIC* Bayesian information criterion, *D-CLIP* Diabetes Community Lifestyle Improvement Program, *HR* hazard ratio, *LRT* likelihood ratio test

For statistical significance, α_0 was set to 0.10

The analytic sample was restricted to those with complete data for the complete set of variables used in the models: 202 respondents in the control group, and 222 respondents in the intervention group. In sensitivity analyses, wherein models were carried out without exclusion, measures of model fit (AIC, BIC and log likelihood) were nearly identical to those resulting from our restricted analytic sample

diabetes risk [17–19]. Other studies reported individual protective effects for fruits (predominantly citrus) and leafy green vegetables [19], thereby suggesting that the relationship between intake and diabetes may vary according to sub-types of fruits and vegetables. Studies examining the relationship between diet and cardiovascular disease risk are consistent with this assertion; while both fruit and vegetable intakes are associated with decreased risk of coronary heart disease, consumption of green-leafy vegetable and fruits high in vitamin C are associated with the greatest risk reduction [20, 21]. Importantly, fruit and vegetable intake may be associated with other dietary changes associated with cardiometabolic health, such as decreased intake saturated fat and added sugar [22, 23] and increased intake of dietary fiber [24] and antioxidants [25].

Although the D-CLIP intervention was associated with changes in selected food and nutrient intakes, there was no significant effect on percent of calories from any macronutrient. This conflicts with the limited data on diet changes from similar intervention studies showing reductions in the percent of calories consumed from fat [26, 27]. However, respondents in these studies consumed higher average baseline amounts of fat (33.9–36.0% of total energy) than D-CLIP participants (27.7% of total energy). Further, given that D-CLIP participants were already consuming fat below 30% of the total energy at baseline, an intervention aiming to reduce total fat to less than 30% of total energy would be unlikely to result in reductions. Future studies should explore alternative dietary intervention strategies in this population.

D-CLIP respondents consumed 60.9% of total energy from carbohydrates. Carbohydrate intakes above 55% of total energy, even with a low-fat diet, are associated with insulin resistance, dyslipidemia [8, 28, 29], and diabetes [30]. The high intake of carbohydrates in D-CLIP participants could have increased diabetes risk, thereby diminishing the potential benefit of the intervention. Additionally, AIs may exhibit a 'high-risk' phenotype, increasing the likelihood of cardiometabolic dysfunction [31, 32]. Thus, the D-CLIP intervention reduced the 3-year incidence of diabetes by 30.0%, compared to the 58% reduction in risk observed in the DPP [3]. Similarly, the Indian Diabetes Prevention Programme saw a 28.5% reduction in the 3-year incidence of diabetes among respondents receiving a lifestyle intervention and metformin [33].

Diabetes incidence rates are markedly lower among predominantly white samples with prediabetes [3, 27]. In the DPP (54.7% White), the 3-year diabetes incidence in the control group was less than 30% [3]. Together, differences in diet and baseline risk among AIs could attenuate the benefit of diabetes prevention interventions such as D-CLIP.

This study has several limitations. This study used a semi-quantitative FFQ specifically developed for use in a South Indian population. Many of the 16 food groups used in this study do not have comparable analogs to those used in several recent reviews [16–19], making comparisons difficult. Another limitation is that although D-CLIP was sufficiently powered to detect meaningful between-group differences in the primary outcome, diabetes incidence, power to explore secondary outcomes may be limited. Still, we observed significant between-group differences in the intakes of several key foods shown previously to be related to diabetes risk. Moreover, the randomized controlled trial design allowed us to examine between-group differences in diet with minimal threat of confounding bias. Baseline comparison of study arms (Table 1) showed no differences in dietary intake, suggesting that the between-group differences in diet were attributable to the intervention.

Despite these limitations, this is one of the few studies examining diabetes incidence in AIs with prediabetes and, to our knowledge, the only such study reporting multiple, prospective measurements of diet over time. Our analyses included the measurement of diet at baseline, 6, and 12 months of follow-up, thereby allowing for the robust examination of dietary changes over time. Moreover, in our examination of incident diabetes using Cox models, diet was 'lagged' by one time point relative to ascertainment of the outcome of interest (incident diabetes). Accordingly, this study offers compelling evidence that respondents in the intervention arm not only made changes to their diet, but that these changes were responsible (in part) for reducing their diabetes risk.

Findings from the current study suggest that the D-CLIP intervention significantly reduced diabetes risk in overweight AI adults with prediabetes. There was no change in the percent of energy consumed from fat, but the intervention was associated with reduced caloric intake and increased intakes of fruits and vegetables, which accounted for 12% of the intervention effect. Increasing fruit and vegetable intakes in AIs with prediabetes may decrease diabetes risk, but reducing fat intake to < 30% of calories may not be appropriate for this population.

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site. LRS conducted the primary analysis. MBW, HR, KMVN, and VM designed the trial. MBW, HR, and RMA developed the lifestyle intervention curriculum. All authors contributed to the manuscript discussion, provided edits to the text, and reviewed and approved the manuscript. MVN and VM are co-primary investigators of the study and provided senior leadership and direction to the team. CNF 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.

Compliance with ethical standards

Conflict of interest No potential conflicts of interest relevant to this article were reported.

Ethical approval All procedures performed in studies involving human participants were approved by the Emory University Institutional Review Board (IRB-00016503) and the Madras Diabetes Research Foundation Ethics Committee and were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent All subjects provided informed consent.

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