RESEARCH ARTICLE

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Modification of cardiovascular disease risk by health behaviour change following type 2 diabetes diagnosis

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Abstract

Aims: Among adults with type 2 diabetes (T2D), unhealthy behaviours are associated with increased risk of cardiovascular disease (CVD) events. To date, little research has considered whether healthy changes in behaviours following T2D diagnosis reduce CVD risk.

Methods: A cohort of 867 adults with screen-detected T2D, participating in the Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION)-Cambridge trial, were followed for 10 years for incidence of CVD events. Diet, alcohol consumption, moderate/vigorous physical activity and smoking were assessed by questionnaire at the time of T2D screening and 1 year later. We estimated associations between health behaviours and CVD using Cox regression. We assessed modification of the associations by behaviour change in the year following T2D diagnosis.

Results: Smoking [hazard ratio (HR): 1.73 (95% CI: 1.04, 2.87)] and high fat intake [HR: 1.70 (95% CI: 1.02, 2.85)] were associated with a higher hazard of CVD, while high plasma vitamin C [HR: 0.44 (95% CI: 0.22, 0.87)] and high fibre intake [HR: 0.60 (95% CI: 0.36, 0.99)] were associated with a lower hazard of CVD. Reduction in fat intake following T2D diagnosis modified associations with CVD. In particular, among those with the highest fat intake, decreasing intake attenuated the association with CVD [HR: 0.75 (95% CI: 0.36, 1.56)].

Conclusion: Following T2D diagnosis, decreasing fat intake was associated with lower long-term CVD risk. This evidence may raise concerns about low-carbohydrate, high-fat diets to achieve weight loss following T2D diagnosis. Further research considering the sources of fat is needed to inform dietary recommendations.

Trial registration: This trial is registered as ISRCTN86769081. Retrospectively registered on 15 December 2006.

KEYWORDS

alcohol drinking, cardiovascular diseases, diabetes mellitus, type 2, diet, exercise, health behaviour, smoking

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1 | INTRODUCTION

Health behaviours contribute to the development and progression of type 2 diabetes (T2D), including the risk of cardiovascular disease (CVD) complications.[1-3] Moderate levels of physical activity, a nutritionally balanced diet and smoking cessation are recommended for the management of T2D.[4] Studies have suggested that healthy changes in these behaviours after T2D diagnosis may reduce CVD risk.[5-8] However, these studies have not explored whether the association between changes in diet or physical activity and CVD outcomes varies according to baseline levels of these behaviours.

Previously, The Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION)-Cambridge trial found that participants who increased their physical activity following T2D diagnosis had a lower 5-year risk of CVD events compared to participants who did not.[7] Baseline differences in physical activity among participants who increased activity levels, compared to those who did not, may have contributed to the observed association, but this was not explored. To date, little research has investigated whether associations between physical activity levels and CVD are modified by changes in physical activity following T2D diagnosis.

Dietary behaviours, such as higher fibre intake, have been associated with lower risk factors for CVD in people with T2D.[9] Additionally, changes in these behaviours following T2D diagnosis, such as increasing fruit and vegetable intake, have been associated with reduced CVD risk factors.[5] Separately, ADDITION-Cambridge previously found that reducing alcohol consumption in the year following T2D diagnosis lowered 5-year and 10-year incidence of CVD events.[7,8] However, whether the effect of dietary behaviours and alcohol consumption on CVD risk is modified by behaviour changes following T2D diagnosis remains to be established.

T2D diagnosis may be a 'teachable moment' when those diagnosed become aware of the benefits of adopting healthier behaviours. Participants in the ADDITION-Cambridge cohort were newly diagnosed with screen-detected T2D at time of enrolment and were therefore at an early stage of disease progression. Behaviour changes may affect people differently depending on their behaviours at the time of T2D diagnosis. We aimed to identify whether changes in behaviours impacted the association between behaviours prior to T2D diagnosis and long-term CVD risk. Our objectives were to evaluate the associations between health behaviours at diagnosis and the 10-year incidence of CVD, and to assess whether behaviour changes made within the first year following diagnosis modified these associations.

Novelty statement:

What is already known on this subject?
- Diet and physical activity are risk factors for type 2 diabetes (T2D) and cardiovascular disease (CVD).
- Little research has assessed whether changes in these behaviours following T2D diagnosis modify CVD risk.

What has this study found?
- High fat intake was associated with higher 10-year hazard of CVD. However, reducing fat intake in the year after T2D diagnosis attenuated this risk.

What are the clinical implications of the study?
- Among those with newly diagnosed T2D, reducing fat intake may lower long-term risk of CVD. This suggests caution is warranted regarding the increasing use of low carbohydrate diets to treat CVD, as such diets typically result in increases in fat intake.

2 | METHODS

2.1 | Population

ADDITION-Cambridge is a population-based screening programme for T2D, followed by a cluster-randomized intervention trial to evaluate the effectiveness of intensive multifactorial treatment compared to routine care in reducing CVD risk in those with screen-detected T2D.[10,11] Screening invitations were sent to 33,539 individuals who met eligibility criteria: aged 40–69 years, at high risk of undiagnosed diabetes and registered at a participating general practice (GP) within Eastern England (n = 49).[10] High risk was determined by a validated risk tool using routinely collected information from participants' medical records.[12] Of those invited, 73.5% attended the first stage of screening.[13] Diabetes was diagnosed according to World Health Organization criteria (1999).[14] This identified a cohort of 867 individuals with screen-detected T2D, all of whom consented to participate in the treatment study and were enrolled between 2002 and 2006. Participants at practices randomized to routine care (n = 23) received diabetes care according to National Health Service guidelines.[10] Participants at practices randomized to intensive treatment (n = 26) received more frequent consultations and educational material packs on healthy behaviours, while physicians were encouraged to follow a protocol that featured earlier use of medication to achieve more intensive treatment targets.[10] Results suggested that the intervention did not significantly improve CVD outcomes.[11] Thus, data

from the two arms were pooled for the present study: an observational secondary analysis of the ADDITION-Cambridge cohort. Ethical approval was obtained from relevant Multi-Centre Research Ethics Committees.[10]

2.2 | Measurements

Smoking, alcohol consumption, physical activity, fibre, total energy and fat intake, were ascertained by self-report, while plasma vitamin C was measured using a fluorometric assay.[10] All behaviours were measured at baseline (T2D diagnosis) and 1 year later. Physical activity was assessed by the validated European Prospective Investigation into Cancer (EPIC)-Norfolk Physical Activity Questionnaire[10] and was defined as moderate/vigorous physical activity (MVPA) in the past year. Fibre, total energy and fat intakes over the past year were estimated by the validated EPIC-Norfolk food frequency questionnaire.[10] Smoking status (never, former, current), alcohol consumption (units/week), MVPA (minutes/week), plasma vitamin C (μmol/l), fibre intake (g/day), total energy intake (Kcal/day) and percentage of total energy intake from fat (%) are targets of healthy behaviour recommendations for those with T2D. Body mass index (BMI) was derived from measures at baseline using a fixed rigid stadiometer and SECA scales. Socio-demographic information (age, sex, age left full-time education, occupational social class) and prescribed medication use were also self-reported at baseline.

2.3 | CVD outcomes

CVD outcomes were assessed from date of T2D diagnosis to 31 December 2014 and were defined as a composite of first cardiovascular event during the study period, including cardiovascular mortality, non-fatal myocardial infarction, non-fatal stroke, non-traumatic amputation and revascularization.[10] National registers, hospital and GP records were used to ascertain incidence of non-fatal CVD events, while Office of National Statistics mortality data was used to ascertain incidence of deaths.[7,10] All events were independently adjudicated. Outcomes were ascertained for 99.9% of participants.[13]

2.4 | Statistical analysis

2.4.1 | Health behaviours and CVD incidence

Continuous values of plasma vitamin C, fibre intake, total energy intake, percentage of total energy from fat and MVPA were categorized in quartiles. Supplemental analyses considered percentage of energy from saturated fat and mono- and poly-unsaturated fats. For alcohol consumption, categories of abstainer (0 units/week), light–moderate (1–14 units/week) and heavy (>14 units/week) were used. Referent groups were quartile one for all health behaviours except total energy intake (which used quartile three), smoking (never) and alcohol consumption (1–14 units/week). Hazard ratios (HRs) for the association between each health behaviour at baseline and 10-year CVD incidence were estimated by Cox proportional hazards regression. Participants were at risk for an incident CVD event from date of T2D diagnosis. Follow-up time was censored at the earlier of first CVD event, non-CVD death, or 31 December 2014. The Schoenfeld residuals test and log-log survival curves indicated no violations of the proportional hazards assumption.

All models were adjusted for age (continuous), sex (men/women), occupational social class (managerial/professional, intermediate, routine/manual), age left full-time education (<16 years, 16–18 years, >18 years), baseline BMI (continuous), baseline anti-hypertensive medication use (yes/no), baseline lipid-lowering medication use (yes/no), treatment group (intervention/routine care) and baseline smoking status where smoking was not the primary exposure (current, never/former). Confounders were selected a priori and were variables previously established to be associated with the exposure and outcome. We did not adjust for glucose-lowering medication use because only four participants reported use at baseline. Robust standard errors accounted for clustering by GP.

We performed a complete case analysis. Individuals were excluded from an analysis if they were missing behaviour or covariate information. Separately, we performed a sensitivity analysis excluding 99 participants who reported having a history of CVD prior to enrolment.

2.4.2 | Behaviour change and CVD incidence

To assess whether behaviour changes made in the year following T2D diagnosis modified the baseline associations, we modelled an interaction term between the behaviour at baseline and behaviour change between baseline and 1 year. Behaviour change was defined as the value at baseline subtracted from the value at 1 year. In these models, the risk period for CVD events began at the 1-year follow-up visit. Modification by change in smoking status was not investigated as too few participants changed their smoking status ($n = 21$). The *testparm* command was used to assess the presence of statistically significant interaction simultaneously across the categories of each health behaviour. A Wald test *p*-value <0.05 suggested that change in behaviour modified the baseline association with CVD. We then assessed if the presence of modification differed depending on baseline

exposure category. HRs for the association between a one standard deviation (SD) increase and decrease in each health behaviour with CVD were calculated from the linear combination of estimates generated from the models. These HRs were then compared to the HRs unadjusted for interaction terms to examine whether behaviour change modified the baseline association between the behaviour and CVD risk.

3 | RESULTS

Of the 867 study participants, median age at diagnosis was 62.7 years and 61% were men (Table 1). Mean baseline BMI was 33 kg/m^2. There were 126 CVD events during the study period: 31 CVD deaths, 21 myocardial infarctions, 33 strokes, 40 revascularizations and one amputation. Mean follow-up time was 9.6 years from T2D diagnosis. Seven hundred and fifty-eight (87%) participants attended for 1-year measurements.

Compared to never smokers, former and current smokers had a higher hazard of CVD, with HRs of 1.61 (95% CI: 1.07, 2.42) and 1.73 (95% CI: 1.04, 2.87) respectively (Table 2). Those in the highest quartile of fat intake had a higher hazard of CVD compared to participants with the lowest intake [HR: 1.70 (95% CI: 1.02, 2.85)]. Compared to those with the lowest levels of plasma vitamin C, those with the highest levels had a 56% lower hazard of CVD (95% CI: 0.22, 0.87). Those with the highest fibre intake had a lower hazard of CVD compared to those with the lowest intake [HR: 0.60 (95% CI: 0.36, 0.99)]. Results were robust to the inclusion of participants with a CVD history prior to diagnosis (Table S1).

The association between percentage of energy from fat and CVD was modified by changes in fat intake in the year following T2D diagnosis (p-value for interaction term: 0.04). Among those in the highest quartile of fat intake at baseline, a one SD (6.48%) increase in energy from fat was associated with a higher hazard of CVD [HR: 4.20 (95% CI: 1.48, 11.89)], while a 6.48% decrease was not associated with CVD [HR: 0.75 (95% CI: 0.36, 1.56)] (Table 3). A 6.48% decrease among those in the second and third quartiles of fat intake, although not statistically significant, showed a lower hazard of CVD, [HR: 0.76 (95% CI: 0.30, 1.94)] and [HR: 0.50 (95% CI: 0.21, 1.17)] respectively. Analyses separating percentage of energy from saturated and unsaturated fat showed no statistically significant associations with CVD (Table S2). Modification of these associations by 1-year changes in saturated or unsaturated fat intake was not statistically significant. However, increases in saturated fat intake among individuals with high baseline saturated fat intake appeared to correspond with an increase 10-year hazard of CVD. Among individuals who reduced their saturated fat intake, there was no elevated risk of CVD (Table S3).

The Wald test *p*-value for overall interaction was >0.05 for other behaviours (Table 3). However, the magnitudes of the stratified HRs for plasma vitamin C and MVPA, while not statistically significant, suggest the potential for modification by behaviour change. For plasma vitamin C, a one SD (22.85 μmol/L) decrease showed a higher hazard of CVD among those in the third highest quartile of intake [HR: 1.70 (95% CI: 0.68, 4.29)]. For MVPA, a one SD (860.31 min/week) decrease was associated with a higher hazard of CVD among those in the second, third and fourth quartiles [HR: 3.86 (95% CI: 0.68, 21.72)], [HR: 3.18 (95% CI: 1.16, 8.78)] and [HR: 1.59 (95% CI: 0.73, 3.43)] respectively. For alcohol consumption, fibre intake and total energy intake, the results provided no indication of modification by behaviour change.

4 | DISCUSSION

Among the 867 adults with screen-detected T2D enrolled in ADDITION-Cambridge, current or former smoking and a high percentage of energy from fat were associated with a higher hazard of 10-year CVD incidence, while higher levels of plasma vitamin C and fibre intake were associated with a lower hazard of CVD incidence. The association between percentage of energy from fat and CVD risk was modified by changes in fat intake in the year following T2D diagnosis, where a 6.48% decrease attenuated the association with CVD. We did not detect statistically significant modification of the associations between other behaviours and CVD.

To date, little research has assessed the impact of within-individual changes in health behaviours following T2D diagnosis on CVD events. We found that, while high fat intake was associated with elevated CVD risk, there was no elevated risk of CVD among those who had decreased their fat intake in the year after T2D diagnosis. Saturated fat showed similar but non-statistically significant associations with CVD, while unsaturated fat intake was not associated with CVD risk. This may suggest that the observed association between fat intake and CVD may be primarily driven by changes in saturated fat as opposed to unsaturated fat intake. However, future research focused on dietary sources of fat intake would be better suited to address this question. This result is supported by a recent meta-analysis which showed that reductions in saturated fat lowered risk of CVD events[15] and one study has reported this among individuals with T2D.[16] These findings are particularly relevant given the recent popularity of low-carbohydrate diets for T2D treatment. The effects of low-carbohydrate diets on CVD risk remain unclear,[17,18] however several studies have found that low-carbohydrate diets, particularly those coupled with high animal fat intake, are associated with higher all-cause mortality rates.[19-21] Our research supports that a diet leading to higher fat intake may increase long-term CVD risk, which raises concerns

TABLE 1 Characteristics of study participants at baseline by cardiovascular disease (CVD) status at 10-year follow-up. Data are presented as n (%) unless stated otherwise. ADDITION-Cambridge 2002–2014 (n = 867)

Variable	Category/Unit	n (%)	CVD event (n = 126)	No CVD event (n = 741)
Socio-demographic				
Age[b]	Years	867 (100)	65 (59, 69)	62 (56, 67)
		867 (100)		
Sex	Men	530 (61)	94 (18)	436 (82)
	Women	337 (39)	32 (9.5)	305 (91)
Occupational social class		847 (98)		
	Managerial/ Professional	278 (33)	38 (14)	240 (86)
	Intermediate	197 (23)	24 (12)	173 (88)
	Routine/ Manual	372 (44)	59 (16)	313 (84)
Age left full-time education		851 (98)		
	<16 years	418 (49)	64 (15)	354 (85)
	16–18 years	335 (39)	45 (13)	290 (87)
	>18 years	98 (12)	14 (14)	84 (86)
Clinical				
Body mass index[a]	kg/m^2	862 (100)	33.1 (6.4)	33.5 (5.6)
Glucose-lowering medication		865 (100)		
	Yes	4 (0.5)	1 (25)	3 (75)
Anti-hypertensive medication		865 (100)		
	Yes	499 (58)	85 (17)	414 (83)
Lipid-lowering medication		865 (100)		
	Yes	209 (24)	52 (25)	157 (75)
Treatment group		867 (100)		
	Intervention	452 (52)	62 (14)	390 (86)
	Routine care	415 (48)	64 (15)	351 (85)
Health behaviours measured at baseline				
Smoking status		866 (100)		
	Current	157 (18)	25 (16)	132 (84)
Alcohol consumption[b]	units/week	853 (98)	3 (0, 9)	3 (0, 10)
MVPA[b]	minutes/week	864 (100)	577.9 (197.5, 1072.3)	541.4 (213.4, 1195.6)
Plasma vitamin C[a]	μmol/l	779 (90)	48.4 (23.6)	53.0 (22.5)
Fibre intake[a]	g/day	855 (99)	15.9 (7.5)	17.0 (6.7)
Total energy: Men[a]	Kcal/day	523 (99)	2110.5 (717.8)	2038.5 (735.9)
Total energy: Women[a]	Kcal/day	330 (98)	1825.4 (1057.4)	1842.5 (607.2)
Percentage of energy from fat[a]	%	855 (99)	33.8 (6.7)	32.8 (6.1)

Abbreviation: MVPA, Moderate/Vigorous Physical Activity.

[a]Data are presented as mean (SD) for normally distributed variables.

[b]Data are presented as median (25th, 75th percentile) for non-normally distributed variables.

regarding low-carbohydrate high-fat approaches. However, further research considering the sources of fat is needed to inform dietary recommendations.

Prior research has shown that increased MVPA following T2D diagnosis lowers CVD risk.[7] We did not identify any impacts of increases in physical activity on the observed associations with CVD, perhaps due to the small average increases in activity (27.76 min/week), and the low power of the effect modification analyses. For this reason, the lack of evidence from this study on the effect of increases in MVPA on CVD should not undermine the established benefits of physical activity on CVD risk. Furthermore, we did not detect an

TABLE 2 Hazard ratios for 10-year cardiovascular disease (CVD) incidence associated with each health behaviour at baseline. ADDITION-Cambridge 2002–2014 (n = 867)

Health behaviour category	n CVD cases/n total	Hazard ratio (95% CI) for CVD[a]
Smoking status		
Never	27/291	1
Former	69/388	1.61 (1.07, 2.42)
Current	23/148	1.73 (1.04, 2.87)
Alcohol (units/week)		
1–14	66/425	1
0	34/241	1.04 (0.60, 1.78)
>14	18/150	0.77 (0.46, 1.28)
MVPA (minutes/week)		
Q1 (0–210.5)	30/199	1
Q2 (545.0)	23/212	0.80 (0.47, 1.39)
Q3 (1178.9)	39/209	1.32 (0.77, 2.27)
Q4 (6902.7)	27/205	0.80 (0.49, 1.33)
Plasma vitamin C (μmol/L)		
Q1 (2.9–36.7)	35/189	1
Q2 (53.6)	23/187	0.67 (0.42, 1.09)
Q3 (67.2)	31/184	0.93 (0.55, 1.59)
Q4 (129.3)	16/185	0.44 (0.22, 0.87)
Fibre intake (g/day)		
Q1 (3.0–12.1)	43/204	1
Q2 (15.7)	24/206	0.54 (0.34, 0.86)
Q3 (19.3)	25/207	0.56 (0.30, 1.02)
Q4 (48.0)	25/200	0.60 (0.36, 0.99)
Total energy (Kcal/day)[b]		
Q1 (M: 558.6–1580.8) (W: 519.4–1420.8)	32/202	1.16 (0.69, 1.96)
Q2 (M: 1932.6) (W: 1744.7)	26/205	1.03 (0.60, 1.77)
Q3 (M: 2406.3)[c] (W: 2147.1)	27/205	1
Q4 (M: 5153.4) (W: 4713.4)	31/203	1.45 (0.89, 2.34)
Percentage of energy from fat (%)		
Q1 (12.6–29.1)	26/202	1
Q2 (33.1)	32/210	1.35 (0.77, 2.36)
Q3 (37.2)	22/206	0.95 (0.53, 1.70)
Q4 (56.3)	37/199	1.70 (1.02, 2.85)

Abbreviations: MVPA, Moderate/Vigorous Physical Activity, Q1/2/3/4, Quartile 1/2/3/4.

[a]Adjusted for age, sex, age left full-time education, occupational social class, baseline body mass index, baseline anti-hypertensive medication use, baseline lipid-lowering medication use, treatment group and baseline smoking status where smoking was not the primary exposure variable. All models accounted for clustering by general practice.

[b]Quartile cut points given for men ('M') and women ('W') separately.

[c]Referent group for total energy intake is Q3.

association between changes in plasma vitamin C and CVD, although this has been demonstrated previously.[5,16] The null association in our study may also be due to the small average changes in plasma vitamin C levels (1.99 μmol/L) as well as the low power of the stratified effect modification analyses.

A recent ADDITION-Cambridge analysis found reducing alcohol consumption by >2 units/week was associated with lower 10-year hazard of CVD.[8] However, our results did not find changes in alcohol consumption following T2D diagnosis to modify the association between baseline alcohol consumption and CVD. One key distinction is that in this analysis we did not count abstainers among those who reduced their alcohol intake. The average change among moderate drinkers was insubstantial, which may have limited our ability to detect modification, further impacted by the low power of the stratified analyses. Additionally, changes in fibre intake and total energy intake were not found to modify the baseline associations with CVD. This may be because the average changes in fibre intake and total energy intake, aside from the group with the highest total energy intake at baseline, were small.

A key limitation of this study is the low number of events, which may have impacted our ability to detect associations. Stratified models assessing modification by behaviour change compromise statistical power, limiting our ability to detect effect modification. Results for alcohol consumption, fibre intake and total energy intake suggest an absence of interaction on the multiplicative scale, however, we did not assess interaction on the additive scale. Additionally, results are sensitive to how behaviour change has been defined. A one SD change may constitute quite a large behaviour change (e.g. increasing fibre intake by 11 g/day equates to eating three pears), and the average behaviour changes among the cohort were generally small. Behaviour change was measured 1 year after diagnosis and may not have been maintained long term. It is possible that changes in behaviours may take longer than 10 years to generate differences in CVD risk. Despite the small number of events and small changes in behaviours, it is evident that increases in fat intake may be harmful. We cannot exclude the possibility that changes in other behaviours may be beneficial or harmful in circumstances where larger changes are achieved and where changes are maintained for longer periods of time.

Another limitation is the exposure assessment. Except for plasma vitamin C, behaviours were ascertained by self-report, which may result in exposure misclassification and would consequently attenuate the observed associations. Social desirability bias may have influenced reporting of health behaviours,[22] including alcohol consumption and smoking. Additionally, weight-dependent bias may have resulted in those with higher BMI under-reporting dietary intakes. Furthermore, we tested for effect modification by six variables, and while we did not correct for multiple testing,

TABLE 3 Hazard ratios for 10-year cardiovascular disease (CVD) incidence associated with a one standard deviation (SD) increase and decrease in the health behaviour in the year following diabetes diagnosis. ADDITION-Cambridge 2002–2014 (n = 857[*])

Health behaviour category	n CVD cases / n total	Wald test p-value[**]	Mean (SD) behaviour change	Hazard ratio (95% CI) for a 1 SD increase[a]	Hazard ratio (95% CI) for a 1 SD decrease[a]
Alcohol (units/ week)		1.00	−0.90 (6.34)		
1–14	59/379		−0.02 (4.65)	1	1
0	20/186		0.23 (0.73)	0.71 (0.01, 46.44)	n/a
>14	14/126		−5.31 (11.79)	0.73 (0.44, 1.21)	0.74 (0.34, 1.60)
MVPA (minutes/ week)		0.23	27.76 (860.31)		
Q1 (0–210.5)	19/163		204.26 (432.85)	1	1
Q2 (545.0)	17/181		245.63 (456.58)	0.42 (0.14, 1.28)	3.86 (0.68, 21.72)
Q3 (1178.9)	34/187		166.57 (710.32)	1.18 (0.54, 2.62)	3.18 (1.16, 8.78)
Q4 (6902.7)	24/179		−446.08 (1247.66)	0.96 (0.47, 1.94)	1.59 (0.73, 3.43)
Plasma vitamin C (μmol/L)		0.14	1.99 (22.85)		
Q1 (2.9–36.7)	24/155		13.97 (18.40)	1	1
Q2 (53.6)	18/150		4.96 (20.90)	0.78 (0.39, 1.58)	0.60 (0.21, 1.71)
Q3 (67.2)	27/155		−0.29 (21.04)	0.68 (0.30, 1.55)	1.70 (0.68, 4.29)
Q4 (129.3)	11/152		−10.52 (23.97)	0.28 (0.07, 1.06)	0.53 (0.19, 1.46)
Fibre intake (g/ day)		0.96	1.77 (10.79)		
Q1 (3.0–12.1)	31/161		3.56 (5.29)	1	1
Q2 (15.7)	19/173		2.76 (5.41)	0.57 (0.14, 2.27)	0.50 (0.07, 3.42)
Q3 (19.3)	22/189		3.45 (17.26)	0.67 (0.28, 1.59)	0.57 (0.17, 1.97)
Q4 (48.0)	21/177		−1.91 (8.40)	0.78 (0.28, 2.16)	0.50 (0.16, 1.59)
Total energy (Kcal/day)[b]		0.88	−259.16 (658.35)		
Q1 (M: 558.6– 1580.8) (F: 519.4– 1420.8)	25/164		101.80 (466.47)	0.94 (0.41, 2.19)	1.53 (0.65, 3.62)
Q2 (M: 1932.6) (F: 1744.7)	20/176		−39.85 (520.80)	1.00 (0.51, 1.97)	1.08 (0.48, 2.44)
Q3 (M: 2406.3)[c] (F: 2147.1)	19/179		−303.84 (500.18)	1	1
Q4 (M: 5153.4) (F: 4713.4)	28/179		−726.74 (710.17)	1.89 (0.78, 4.56)	2.17 (1.18, 4.01)
Percentage of energy from fat (%)		0.04	−1.83 (6.48)		
Q1 (12.6–29.1)	23/178		2.69 (6.36)	1	1

(Continues)

TABLE 3 (Continued)

Health behaviour category	n CVD cases / n total	Wald test p-value[**]	Mean (SD) behaviour change	Hazard ratio (95% CI) for a 1 SD increase[a]	Hazard ratio (95% CI) for a 1 SD decrease[a]
Q2 (33.1)	27/181		−1.66 (5.40)	1.67 (0.59, 4.72)	0.76 (0.30, 1.94)
Q3 (37.2)	16/176		−3.49 (5.23)	0.97 (0.33, 2.86)	0.50 (0.21, 1.17)
Q4 (56.3)	27/165		−5.24 (6.22)	4.20 (1.48, 11.89)	0.75 (0.36, 1.56)

Abbreviations: MVPA, Moderate/Vigorous Physical Activity, Q1/2/3/4, Quartile 1/2/3/4.

[a]Hazard ratios calculated from the linear combination of estimates generated from proportional hazards regression models for the association between each health behaviour and CVD.

[b]Quartile cut points given for men ('M') and women ('W') separately.

[c]Referent group for total energy intake is Q3.

*10 participants were excluded since they experienced a CVD event or non-CVD death in the first year of follow-up.; **p-value for the test of no interaction between the health behaviour at baseline and behaviour change, across all categories of the health behaviour.

we interpreted results with caution considering the magnitude and precision of the estimates, in light of the large number of tests run. Participants were invited to the screening programme based on a diabetes risk score which selected individuals with higher BMI. It is possible that the cohort may be more (or less) responsive to changes in diet than individuals with lower BMI. Finally, the majority of participants had overweight/obesity at the time of T2D diagnosis and were white. Thus, results from this study may not be generalizable to other groups. It is possible that the observed associations between dietary fat and CVD risk may vary among subgroups with different diabetes characteristics or cardiovascular risk factors, and future research with the appropriate data should explore this question.

ADDITION-Cambridge had a high attendance at screening and all eligible individuals identified with T2D consented to enrol. Since T2D was screen detected and behaviour measurements were repeated the year after diagnosis, this study was able to assess behaviour change early in T2D progression. This ability, along with the population-based nature of the study, are particular strengths compared to other research on health behaviours among adults with T2D. Other strengths are the objective assessment of plasma vitamin C, a marker of fruit and vegetable intake, and the independent adjudication of CVD events.

This study emphasizes the importance of healthy vitamin C, fibre and fat intake, and the prevention of smoking in reducing CVD risk among those with T2D. Additionally, these results support recommending those newly diagnosed with T2D to reduce their fat intake, as this may lower their hazard of CVD incidence and mitigate effects of a high-fat diet on long-term CVD risk. This evidence may raise concern regarding low-carbohydrate diets in diabetes treatment, as these diets typically lead to increases in fat intake. Future research incorporating data on the sources of fat intake are needed to inform dietary recommendations. Few studies have assessed long-term health impacts of changes in behaviours following T2D diagnosis and further research is needed to support

these results. Future studies using objective behaviour measurements and with longer follow-up will help to better our understanding of the role of behaviour changes following T2D diagnosis in the prevention of CVD.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Informed consent was obtained from all individual participants included in the study. Ethical approval was obtained from local research ethics committees (Cambridge, ref:01/063; Huntingdonshire ref:00/609; Peterborough and Fenland, ref:P01/95; West Essex, ref:1511–0103; North and Mid Essex, ref:MH395 MREC02/5/54; West Suffolk, ref:03/002; Hertfordshire and Bedfordshire, ref:EC03623; and the Eastern Multi-Centre Research Ethics Committee, ref:02/5/54).

coordination (Gwen Brierley, Richard Salisbury) and data collection (Kit Coutts).

DATA AVAILABILITY STATEMENT

The dataset used in the current study is available from the corresponding author on reasonable request.

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REFERENCES

1. Uusitupa M. Lifestyles matter in the prevention of type 2 diabetes. *Diabetes Care*. 2002;25(9):1650–1651.
2. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344(18):1343–1350.
3. Liu G, Li Y, Hu Y, et al. Influence of lifestyle on incident cardiovascular disease and mortality in patients with diabetes mellitus. *J Am Coll Cardiol*. 2018;71(25):2867–2876.
4. American Diabetes Association. 4. Lifestyle Management. *Diabetes Care*. 2017;40(Supplement 1):S33–S43.
5. Lamb MJE, Griffin SJ, Sharp SJ, Cooper AJM. Fruit and vegetable intake and cardiovascular risk factors in people with newly diagnosed type 2 diabetes. *Eur J Clin Nutr*. 2017;71(1):115–121.
6. Pan A, Wang Y, Talaei M, Hu FB. Relation of smoking with total mortality and cardiovascular events among patients with diabetes mellitus. *Circulation*. 2015;132(19):1795–1804.
7. Long GH, Cooper AJM, Wareham NJ, Griffin SJ, Simmons RK. Healthy behavior change and cardiovascular outcomes in newly diagnosed type 2 diabetic patients: a cohort analysis of the ADDITION-cambridge study. *Diabetes Care*. 2014;37:1712–1720.
8. Strelitz J, Ahern AL, Long GH, Boothby CE, Wareham NJ, Griffin SJ. Changes in behaviors after diagnosis of type 2 diabetes and 10-year incidence of cardiovascular disease and mortality. *Cardiovasc Diabetol*. 2019;18(1):98.
9. Fujii H, Iwase M, Ohkuma T, et al. Impact of dietary fiber intake on glycemic control, cardiovascular risk factors and chronic kidney disease in Japanese patients with type 2 diabetes mellitus: the Fukuoka Diabetes Registry. *Nutr J*. 2013;12:159.
10. Echouffo-Tcheugui JB, Simmons RK, Williams KM, et al. The ADDITION-Cambridge trial protocol: a cluster – randomised controlled trial of screening for type 2 diabetes and intensive treatment for screen-detected patients. *BMC Public Health*. 2009;9(1):136.
11. Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomised trial. *Lancet*. 2011;378(9786):156–167.
12. Griffin SJ, Little PS, Hales CN, Kinmonth AL, Wareham NJ. Diabetes risk score: towards earlier detection of Type 2 diabetes in general practice. *Diabetes Metab Res Rev*. 2000;16(3):164–171.
13. Waugh NR, Shyangdan D, Taylor-Phillips S, Suri G, Hall B. Screening for type 2 diabetes: a short report for the national screening committee. *Health Technol Assess*. 2013;17(35):1–90.
14. Alberti KG, Definition ZPZ. diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. *Diabet Med*. 1998;15(7):539–553.
15. Hooper L, Martin N, Jimoh OF, Kirk C, Foster E, Abdelhamid AS. Reduction in saturated fat intake for cardiovascular disease. *Cochrane Database Syst Rev*. 2020;8:CD011737.
16. Tanasescu M, Cho E, Manson JE, Hu FB. Dietary fat and cholesterol and the risk of cardiovascular disease among women with type 2 diabetes. *Am J Clin Nutr*. 2004;79(6):999–1005.
17. Gao JW, Hao QY, Zhang HF, et al. Low-carbohydrate diet score and coronary artery calcium progression: results from the CARDIA study. *Arterioscler Thromb Vasc Biol*. 2021;41(1):491–500.
18. Hu T, Jacobs DR, Bazzano LA, Bertoni AG, Steffen LM. Low-carbohydrate diets and prevalence, incidence and progression of coronary artery calcium in the Multi-Ethnic Study of Atherosclerosis (MESA). *Br J Nutr*. 2019;1–8.
19. Mazidi M, Katsiki N, Mikhailidis DP, Sattar N, Banach M. Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies. *Eur Hear J*. 2019;40(34):2870–2879.
20. Seidelmann SB, Claggett B, Cheng S, et al. Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. *The Lancet Public Health*. 2018;3(9):e419—e428.
21. Li S, Flint A, Pai JK, et al. Low carbohydrate diet from plant or animal sources and mortality among myocardial infarction survivors. *J Am Hear Assoc*. 2014;3(5):e001169.
22. Crutzen R, Göritz AS. Social desirability and self-reported health risk behaviors in web-based research: three longitudinal studies. *BMC Public Health*. 2010;10:720.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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