



Dietary changes and associations with metabolic improvements in adults with Type 2 diabetes during a patient-centred dietary intervention: a secondary analysis

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-004953
Article Type:	Research
Date Submitted by the Author:	28-Jan-2014
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Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Nutrition and metabolism
Keywords:	Type 2 diabetes, Dietary analysis, Dietary change

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3 **Dietary changes and associations with metabolic improvements in**
4 **adults with Type 2 diabetes during a patient-centred dietary**
5 **intervention: a secondary analysis**
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35
36 Running title: Dietary change in adults with Type 2 diabetes
37

38 *Keywords: Type 2 diabetes, dietary analysis, dietary change*
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43
44 Bath Research Ethics Committee (05/Q2001/5)
45

46 Word count
47

48 Abstract: 299
49

50 Main text: 3758
51

52
53 Number of tables: 3
54
55
56
57
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3 1 Abstract
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5 2 *Objectives:* Examine dietary changes reported during a non-prescriptive dietary intervention
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7 3 and explore whether these changes had a role in observed improvements in HbA1c, weight,
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9 4 lipids and blood pressure.

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11 5 *Design:* Secondary analysis of data from the Early ACTivity in Diabetes randomised
12
13 6 controlled trial.

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15 7 *Participants* 262 patients with newly diagnosed Type 2 diabetes randomised to the dietary
16
17 8 intervention.

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19 9 *Outcomes and analysis:* Changes in energy intake, macronutrients, fibre and alcohol and in
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21 10 weight, waist circumference, lipids, HbA1c and blood pressure at baseline and 6 months.
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23 11 Multivariate models were used to examine associations between dietary changes and
24
25 12 metabolic variables.

26
27 13 *Results:* Men reported reducing mean energy intake from 1903 ± 462 kcal to 1685 kcal \pm
28
29 14 439 kcal ($p < 0.001$), increasing carbohydrate intake from $42.4 \pm 6.6\%$ to $43.8 \pm 6.6\%$
30
31 15 ($p = 0.002$) and reducing alcohol intake from 18 ± 20 g to 11 ± 14 g ($p < 0.001$). Women reported
32
33 16 reducing mean energy intake from 1582 ± 379 kcal to 1409 ± 326 kcal ($p < 0.001$) with no
34
35 17 change to macronutrient distribution and no reduction in alcohol. Fibre intake was
36
37 18 maintained. In men ($n = 148$) weak and clinically insignificant associations were found
38
39 19 between increased carbohydrates and reduction in HbA1c ($\beta = -0.003$ [-0.006, -0.001];
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41 20 $p = 0.009$), increased fibre and reduction in total cholesterol ($\beta = -0.023$ [-0.044, -0.002];
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43 21 $p = 0.033$), decreased total fat and reduction in LDL-cholesterol ($\beta = 0.024$ [0.006, 0.001];
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45 22 $p = 0.011$), and decreased alcohol and reduction in diastolic blood pressure ($\beta = 0.276$ [0.055,
46
47 23 0.497]; $p = 0.015$). In women ($n = 75$) associations were found between a decrease in trans-fats
48
49 24 and reductions in waist circumference ($\beta = -0.029$ [0.006, 0.052]; $p = 0.015$), total cholesterol
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51 25 ($\beta = 0.399$ [0.028, 0.770]; $p = 0.036$) and LDL cholesterol ($\beta = 0.365$ [0.042, 0.668]; $p = 0.028$).

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53 26 *Conclusion:* Clinically significant metabolic improvements observed in a patient-centred
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55 27 dietary intervention are not explained by changes in percentage intake of macronutrients.
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57 28 However, a non-prescriptive approach may promote a reduction in total energy intake whilst
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59 29 maintaining fibre consumption.
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3 30 Article summary
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5 31 Strengths and limitations
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- 8 32 • Describes the dietary intake of people soon after diagnosis of Type 2 DM living in the
9 33 UK, the dietary changes made during a dietary intervention and examines associations
10 34 between dietary changes and changes in metabolic outcomes. This intervention was
11 35 based on the dietary advice that is given in routine clinical practice in the UK.
12 36
13 37 • Only 53% of the participants provided food diary data at the end of the trial and these
14 38 people showed greater improvements in metabolic outcomes than those who did not
15 39 return food diaries. It is probable that they were more motivated than a typical patient
16 40 group and this limits the generalizability of the findings.
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3 41 Introduction
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6 42 Dietary management is recognised as highly important in the treatment of Type 2 diabetes
7 43 (Type 2 DM). Based upon meta-analyses of exercise and diet studies, the American Diabetes
8 44 Association (ADA) and European Association for the Study of Diabetes (EASD) recommend
9 45 that lifestyle interventions should be initiated as the first step in treating new-onset Type 2
10 46 DM [1]. Over the last 3 years, The Look Ahead research group, the Lifestyle Over and Above
11 47 Drugs in Diabetes (LOADD) and Early Activity in Diabetes (Early ACTID) randomised
12 48 controlled trials (RCTs) have shown that dietary interventions which target weight reduction
13 49 are beneficial and improve glycaemic control [2-4]. These trials achieved reductions in
14 50 HbA1c comparable to reductions demonstrated in patients starting metformin or a gliptin as
15 51 monotherapies [5] and, although the Look Ahead trial showed no reduction in cardiovascular
16 52 events after 9.6 years, participants in the intervention arm were less likely to be treated with
17 53 insulin [6].
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20 54
21 55 The effect of specific dietary changes on metabolic outcomes is still, unclear and no single
22 56 'diet for diabetes' has been identified [7]. In recognition of this both the 2012 ADA and
23 57 EASD joint guidelines and 2011 Diabetes UK nutritional guidelines emphasise the
24 58 importance of an individualised, patient-centred approach to diet rather than a prescriptive
25 59 approach [1 8]. Few studies have looked at what changes are made in response to this type of
26 60 dietary advice and how these impact on metabolic control.
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29 61
30 62 The Early ACTID trial included a non-prescriptive, patient-centred dietary intervention. The
31 63 trial aimed to assess whether adding physical activity to a dietary intervention produced
32 64 greater benefit than diet alone or usual care in individuals newly diagnosed with Type 2 DM
33 65 [4]. Participants who received the lifestyle interventions had better HbA1c, lower body
34 66 weight, less insulin resistance, and were on less medication than the control group at 6 and 12
35 67 months.
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38 68 The aim of this paper is to describe baseline energy and macronutrient intakes and the
39 69 reported changes made by men and women newly diagnosed with Type 2 DM who were
40 70 enrolled into the dietary intervention in the Early ACTID study. The associations between
41 71 changes to energy, macronutrients and metabolic outcomes were explored to determine the
42 72 effect of dietary changes on the metabolic variables.
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73 There is evidence that men and women living in the UK have differing dietary patterns [9].
74 Men have been reported to drink more alcohol and consume more meat but less fruit and diet
75 soft drinks than women [10]. Based on this evidence, we hypothesised that men and women
76 with Type 2 DM would make different dietary changes in response to the dietary intervention
77 and so gender differences were also examined.

78 Subjects and methods

79 *Subjects*

80 This paper is a secondary analysis of data from the Early ACTID randomised controlled trial.
81 Early ACTID was a diet and physical activity trial involving patients living in the South West
82 of England who were recruited within 5 to 8 months of a diagnosis of Type 2 DM from
83 December 2005 to September 2008. Full trial procedures with the CONSORT diagram and
84 results are described elsewhere [4 11 12].

85 *Overview of the dietary intervention*

86 Patients in the diet alone and the diet and physical activity groups received the same dietary
87 intervention. For the first 6 months the intervention aimed to promote dietary change. At
88 randomisation patients attended a one-hour appointment with a study dietitian followed by 2
89 further visits of 30 minutes. These visits were supported by 6 additional visits with a research
90 nurse, where 15 minutes were used to discuss dietary matters for both groups, reinforcing
91 dietary goals, and 15 minutes to discuss physical activity or other matters pertinent to the
92 patient, depending upon intervention group. Maintenance was the primary goal of the second
93 6 months and consisted of 2 more 30 minute dietitian visits and 4 additional visits with the
94 research nurses.

95 The dietary intervention was based upon the 2003 Diabetes UK healthy eating guidelines [13]
96 and employed goal oriented motivational interviewing [14]. Patients were encouraged to
97 discuss their reasons for change, any ambivalence about change and to set their own dietary
98 goals and identify their own strategies for achieving these goals. Prescriptive daily
99 requirements for energy or macronutrients were not calculated unless requested by the patient
100 and prescriptive meal plans or food lists were not used. Instead patients received study
101 specific written dietary information at each visit (available here:
102 <http://jcrubristol.org.uk/EA/ACTID%20patients%20Handbook/Forms/AllItems.aspx>) and

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3 103 were encouraged to use this to evaluate their own eating habits. The materials included
4 104 information on maintaining a regular meal pattern and including starchy carbohydrates as a
5 105 part of each meal, reducing total, saturated and *trans* fat intake, limiting non-milk extrinsic
6 106 sugars, aiming for 5 portions a day of fruit and vegetables and gave guidance on portion
7 107 control. The benefit of aiming for a 5 to 10% weight loss by reducing overall energy intake
8 108 was discussed with everyone. Goals were reviewed at each appointment and successes,
9 109 difficulties and new strategies discussed. Patients were encouraged to self-monitor their
10 110 weight and diet.

111 *Measurements*

112 Measures were taken at baseline (prior to randomisation) and repeated 6 and 12 months later.
113 Baseline and 6 month data were used in the current analysis, since outcomes at 6 months
114 were defined as the primary endpoint of the study. Measurements used in this analysis were
115 weight, height (to calculate body mass index (BMI)), waist circumference, blood pressure,
116 HbA1c, fasting lipids and minutes of moderate to vigorous physical activity (MVPA)
117 measured using accelerometry and defined as activity expending greater than 3kcal/kg/hour .
118 As previously described, blood measurements and anthropometric measures were carried out
119 using standardised procedures [11]. Smoking habits and use of dietary supplements were
120 assessed by a research nurse. The UK Index of Multiple Deprivation (IMD) 2007 was
121 calculated from home postcode and used as an indicator of socio-economic position [15].

122 *Dietary assessment and analysis*

123 Patients in the intervention arms were asked to complete 4-day food diaries prior to each
124 dietitian appointment, recording all foods and drinks consumed during those 4 days. Portion
125 sizes were estimated using household measures and package weights and brands indicated
126 where appropriate. The diaries were discussed during the appointments and used to identify
127 potential areas for change, difficulties in making change, and for patients to observe change
128 in their diets over time. Patients were asked to return all the diaries at the final visit for
129 further analysis. Those who did not return diaries at the visit were reminded by telephone and
130 e-mail to post outstanding diaries to the research team after the visit.

131 Baseline and 6-month food diaries were coded by one coder and checked for accuracy and
132 agreement by a second coder, using the dietary coding programme Diet in Data Out (DIDO),

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3 133 developed at the Medical Research Council Human Nutrition Unit in Cambridge, UK [16].
4 134 Diaries were analysed with the nutrient analysis programme Bristol General Analysis of
5 135 Dietary Experiments (BRIGADE) [17]. The nutrient database is based on *McCance and*
6 136 *Widdowson's Composition of Foods, 5th edition* [18], updated with the supplements to that
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8 137 edition, new data from the 6th edition and manufacturers' data. Additional nutrient data from
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10 138 the INTERMAP nutrient database for the UK were also used [19]. If no portion size
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12 139 information was given, age-appropriate portion sizes were assigned [20]. The mean daily
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14 140 consumption of each nutrient was calculated for each participant.

17 141 *Statistical analysis*

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20 142 As the dietary intervention was designed to be identical for both intervention groups and
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22 143 there were no difference in outcomes between the diet and diet and physical activity groups,
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24 144 the data were analysed as a cohort. Patients in the usual care group were excluded from the
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26 145 analysis since they did not receive the dietary intervention and were not asked to complete a
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28 146 diary at 6 months. Descriptive statistics were used for patient characteristics and for intakes
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30 147 of macronutrients at baseline and 6 months. Variables were checked for normal distribution;
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32 148 non-normal variables were log transformed prior to analysis. For ease of interpretation,
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34 149 arithmetic means and back transformed variables are presented. Independent *t*-tests were used
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36 150 to explore differences in continuous variables between men and women at baseline and
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38 151 between those who did and did not return food diaries, and chi-squared tests were used to
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40 152 explore differences in dichotomous variables. Paired sample *t*-tests were used to describe
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42 153 differences in energy and macronutrient intake between baseline and 6 months. McNemar
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44 154 tests were used to explore differences in numbers of people meeting recommendations at
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46 155 baseline and 6 months. As alcohol variables could not be transformed, the Mann Whitney U
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48 156 and paired sample Wilcoxon signed rank test were used to describe differences. Cases with
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50 157 missing data were excluded listwise.

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52 158 Multivariate regression models were used to investigate associations between changes in
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54 159 energy and macronutrient intake and the metabolic variables at 6 months in those who
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56 160 provided valid physical activity data. Change in energy intake was explored using a standard
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58 161 multivariate model. Each macronutrient was explored independently using a multivariate
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60 162 nutrient density model to adjust for change in energy intake. Change in percentage energy
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164 from each macronutrient was calculated and entered into the model with change in total

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3 164 energy included as a covariate. Change in fibre intake was explored using a standard
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5 165 multivariate model and entered as an absolute intake (in grams) with change to total energy
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7 166 intake as a covariate [21]. Models were adjusted for age, BMI, time since diagnosis, minutes
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9 167 of moderate to vigorous physical activity (MVPA) and dichotomous yes/no variables for
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11 168 smoking status, relevant lipid lowering, blood pressure and diabetes medication and dietary
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13 169 supplement use.

14 170 Due to the number of different analyses that were conducted the results are interpreted in
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16 171 terms of strength of evidence of associations [22]. This is an exploratory analysis and as such
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18 172 has not been adjusted for multiple comparisons, consequently p values of <0.05 are
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20 173 interpreted as some evidence of association, $p < 0.01$ as increasing evidence and $p < 0.001$ as
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22 174 strong evidence.

23 175 Results

24 176 *Study participants*

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28 177 A total of 593 patients were recruited into the Early ACTID study, with 494 being assigned to
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30 178 one of the intervention groups. 396 (80%) patients were recorded as completing food diaries
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32 179 at both baseline and 6 months but only 262 (53%) patients returned them, and 223 of these
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34 180 had valid accelerometry data at both time points. At 6 months 491 (99%) patients assigned to
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36 181 one of the intervention arms remained in the study, with 434 (88%) attending all scheduled
37
38 182 visits up to that point and a further 37 (8%) attending all except one.

39 183 Mean age was 62.4 (9.0) years, 97% of patients were white, 83% were married or with a long
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41 184 term partner and 41% were in the lowest IMD quartile. 40% of participants were on oral
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43 185 hypoglycaemic medication, 65% on lipid lowering medication and 66% on blood pressure
44
45 186 medication. Only 6% of patients were current smokers at baseline. Men and women had
46
47 187 similar characteristics, although there was some evidence that men were more likely to be on
48
49 188 lipid lowering medication than women (69% vs. 56%, $p = 0.041$).

50 189 Compared to the patients who did not return food diaries, those who did were older (62 years
51
52 190 vs 57 years, $p < 0.001$), with a lower mean weight (88.2 kg vs 93.3 kg, $p = 0.001$), lower mean
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54 191 BMI (30.7 vs 32.5, $p = 0.001$) and lower mean waist circumference (105 cm vs 108 cm,
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56 192 $p = 0.025$), but there was no difference in glycaemic control, lipids and blood pressure.

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3 193 *Metabolic outcomes*
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5 194 Table 1 shows the metabolic outcomes at baseline and 6 months for those who returned food
6 diaries. There was no difference in glycaemic control or blood pressure between men and
7 195 women, but women had higher total (p<0.001), LDL (p<0.001) and HDL (p=0.015)
8 196 cholesterol levels.
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12 198 Weight, waist circumference and BMI improved at 6 months for both men and women
13 (p<0.001). Men and women improved their HbA1c (men: p=0.006; women: p<0.001). Men
14 199 improved their fasting blood glucose (p=0.006) and there is some evidence that women
15 200 increased their HDL cholesterol (p=0.033).
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19 202 At 6 months those who returned food diaries had lost more weight (2.4 kg vs 1.3 kg,
20 p=0.001), reduced waist circumference more (2.7 cm vs 1.3 cm, p=0.022) and reduced
21 203 HbA1c (0.18% (2 mmol/l) vs 0% (0 mmol/l), p=0.02).
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25 205 *Nutrient analysis*
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29 206 Table 2 shows the mean reported energy and nutrient intakes at baseline and 6 months and
30 207 their mean reported changes.
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33 208 At baseline participants reported generally good dietary habits. 61% of women and 59% of
34 209 men reported the recommended total fat intake (less than 35% of energy from total fat) and
35 210 55% of women and 66% of men reported a low to moderate carbohydrate intake (<45% of
36 211 energy). Men were more likely to drink alcohol and more likely to drink to excess than
37 212 women with 49% of women and 28% of men recording no alcohol during the 4 days and 8%
38 213 of women and 19% of men reporting more than 30g of alcohol per day (p=0.022).
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42 214 At 6 months mean daily reported energy intake was reduced by 187 kcal (p<0.001). Men
43 215 reduced their energy intake more than women (218 ± 332 vs. 123 ± 270 kcal/day, p=0.022).
44 216 This was achieved by small reductions in all macronutrients, whilst maintaining fibre intake.
45 217 The mean percentage energy from macronutrients was unchanged for women whilst men
46 218 reported a small mean increase of 1.4 ± 5.9% (p<0.001) of energy from carbohydrates. Men
47 219 reported reducing mean alcohol intake (p<0.001), with 40% reporting no alcohol during the 4
48 220 days and 15% reporting more than 30g per day. There was no reported mean change in
49 221 alcohol intake for women. Despite no mean change to energy from saturated fat, more men
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222 met recommendations at 6 months (35% men at baseline vs. 49% at 6 months reporting less
223 than 10% energy from saturated fat, $p=0.007$). There was no change in the number of women
224 meeting recommendations (40% baseline vs 44% at 6 months, $p=0.71$).

225 Table 3 shows the regression coefficients and confidence intervals for changes in energy and
226 macronutrients that show evidence for associations with specific metabolic variables. In men
227 a 1% reduction in energy from alcohol was associated with a 0.276 mmHg reduction in
228 diastolic blood pressure (95% CI= 0.055 to 0.497). In women a 1% reduction in energy from
229 trans-fat was associated with a decrease in cholesterol of 0.399 mmol/l (95% CI= 0.028 to
230 0.770). In men a 1% increase in energy from carbohydrate was associated with a decrease in
231 HbA1c of 0.003% (95% CI= -0.006 to -0.001). There were no associations between change
232 in energy intake and the metabolic variables.

233

234 Discussion

235 *Main findings*

236 The main findings from this analysis are that patients who were randomised to the
237 intervention arms in the Early ACTID study and returned food diaries reported a good diet at
238 baseline but still achieved small dietary changes. They reported a mean decrease in energy
239 intake of around 200 kcal per day, during the first 6 months. Men reported a reduced alcohol
240 intake that produced a greater reduction in energy and reported a small increase in the
241 percentage energy from carbohydrate. Women reported modest reductions to all
242 macronutrients but made no changes to alcohol, their energy reduction was less and the
243 macronutrient ratio of their diets did not change. Both sexes maintained fibre intake.
244 Although changes in percentage intake of macronutrients were associated with metabolic
245 outcomes, these effect sizes were too small to be of clinical significance. These results
246 suggest that current recommendations that dietary advice is personalised, flexible and focuses
247 on realistic, achievable, and sustainable reductions in intake may promote dietary change in
248 people with T2 DM.

249 *Comparison with other studies*

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3 250 The Early ACTID dietary intervention was a pragmatic, ‘real world’ intervention, in which
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5 251 participants discussed dietary advice with dietitians and nurses to decide on their own dietary
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7 252 changes. The approach contrasts with dietary studies where participants are asked to make
8
9 253 specific, prescribed changes to the macronutrient composition, by lowering carbohydrate and
10
11 254 increasing protein [23-25] or to lower the glycaemic index [26 27]. The LOADD trial [3]
12
13 255 based a successful dietary intervention in patients with poor glycaemic control on very
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15 256 similar recommendations to those used in the Early ACTID intervention, but total energy
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17 257 intake and macronutrient ratios for each participant were calculated and diets were prescribed
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19 258 according to these calculations. The Early ACTID intervention did not compare a prescriptive
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21 259 with a non-prescriptive approach so cannot be used to demonstrate that this is superior but
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23 260 reductions in weight, waist circumference and HbA1c were achieved that are comparable to
24
25 261 those achieved during these interventions. Withdrawal rates for prescriptive dietary
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27 262 interventions range from 10% to 30% and these higher withdrawal rates may suggest that in
28
29 263 routine clinical care a more flexible approach can be advantageous in promoting retention. Of
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31 264 those participants in Early ACTID who either did not attend all appointments or withdrew
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33 265 completely, only one person stated that they did not see the benefit of the trial. The majority
34
35 266 could not schedule all 9 dietitian and nurse visits because of other commitments, 5 cited other
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37 267 health issues, 3 moved too far away, 1 said they ‘did not want to diet,’ 1 wanted to take
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39 268 orlistat from baseline and 3 gave no reasons. What is common to intervention trials in
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41 269 diabetes is that patients receive individual support and attend multiple appointments with a
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43 270 dietitian or a health practitioner who is expert in promoting dietary change. It is important to
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45 271 emphasise that this model is not routinely replicated in primary care for patients with Type 2
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47 272 DM.

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49 273 The associations between specific dietary changes and metabolic outcomes have not, as far as
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51 274 we are aware, previously been examined in patients with Type 2 DM. Effect sizes were small
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53 275 and not clinically significant but they are consistent with existing nutritional data on the
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55 276 benefits of a reduction in trans fats on lipids and waist circumference [28], an increase in
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57 277 fibre on LDL cholesterol [29] and a reduction in alcohol and blood pressure [30]. It is of
58
59 278 interest that this analysis found that there was no benefit in carbohydrate reduction in men
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279 with good glycaemic control who are already consuming a low to moderate carbohydrate
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281 diet. It is not possible to determine whether there is an optimum macronutrient distribution
for T2 DM from this analysis, particularly in those with poor glycaemic control, but there is

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3 282 no unequivocal evidence that low carbohydrate diets produce better blood glucose control or
4 283 weight loss than higher carbohydrate diets [31]. A meta-analysis of low carbohydrate diets
5 284 versus low fat diets conducted in 2012 [32] concluded that there was evidence of a small but
6 285 beneficial effect on lipid profiles of a low (defined as <45% energy from carbohydrate) or
7 286 very low carbohydrate (<60g carbohydrate) diet but no difference in improvements to weight
8 287 or glycaemic control.

13 288 *Strengths and weaknesses*

16 289 To our knowledge this is the first study to describe the dietary intake of people soon after
17 290 diagnosis with Type 2 DM living in the UK, the dietary changes made during an intervention
18 291 based on patient-centred, non-prescriptive dietary advice and that examines associations
19 292 between dietary change and metabolic variables. The demographics of the Early ACTID
20 293 participants included in this analysis suggest that these findings are only representative of the
21 294 white population; however the sample is socio-economically diverse with 40% of participants
22 295 living in areas of high economic deprivation.

26 296 The study has important weaknesses. Only 53% of the participants returned baseline and 6
27 297 month food diaries at the end of the trial and these people had a lower BMI and waist
28 298 circumference at baseline and achieved greater metabolic improvements. The participants
29 299 who did not return diaries reported mislaying them which may indicate less motivation and
30 300 less engagement with the trial. Participants who did return diaries could have been more
31 301 motivated to make dietary changes than a typical patient population, and, given that their
32 302 diets were good at baseline, may already have made dietary changes prior to entry into the
33 303 Early ACTID study. The relative lack of dietary data limits our ability to generalise these
34 304 findings to broader patient groups.

37 305 The use of any self-reported measure of diet, including 4-day food diaries, is a recognised
38 306 limitation in dietary studies. Under-reporting of food intake and selective under-reporting or
39 307 under-eating of foods perceived to be 'bad' are commonly documented, especially in people
40 308 who are obese [33 34]. Methods exist to estimate under-reporting, using calculated basal
41 309 metabolic rate and estimates of physical activity [35 36] but these methods assume that an
42 310 individual's weight is stable and are consequently inappropriate for use during a weight loss
43 311 trial. It should be noted that other dietary interventions in patients with Type 2 DM have
44 312 reported similar energy intakes [23 26] and an energy reduction of around 200kcal/day is

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3 313 plausible assuming a dynamic model of energy balance [37] and given the modest weight
4 314 reduction observed. It is also important to note that this is a secondary analysis so cause and
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6 315 effect cannot be assumed.
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8
9 316 *Conclusion*

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11 317 The Early ACTID trial indicates that a flexible, non-prescriptive approach to dietary advice
12 318 based on standard healthy eating guidelines in Type 2 DM given soon after diagnosis may be
13 319 effective in promoting small dietary change, even in patients with good glycaemic control.
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15 320 This supports current clinical practice and guidelines. The current analysis suggests that
16 321 changes in percentage intake of macronutrients did not have any clinically significant effect
17 322 on metabolic outcomes during the trial but this needs confirmation in a larger cohort, with
18 323 less good glycaemic control. Further research is needed on whether dietary changes made
19 324 using a non-prescriptive approach are sustainable and beneficial in the longer term in a more
20 325 typical patient population.
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Acknowledgements

We would like to acknowledge the participants in the Early ACTID trial, members of the Early ACTID team and steering committee, Dr Pauline Emmett for advice on dietary analysis, Dr Rosemary Greenwood for advice on statistical analysis and Professor Debbie Sharp for assistance in manuscript preparation.

Funding

The Early ACTID trial was supported by Diabetes UK, the UK Department of Health and Western Comprehensive Local Research Network. Pilot dietary analysis was supported by the Above and Beyond Foundation. C.Y. England is supported by NIHR Clinical Doctoral Research Fellowship 10-017.

Authors' contributions

This work forms part of the PhD of CYE which is supervised by RCA, JLT and RJ. RCA led the Early ACTID study and advised on clinical application of this work. CYE participated in data collection, data entry and was responsible for data analysis with guidance from JLT and RJ. ARC was responsible for the design of the ACTID physical activity intervention and for processing and analysis of the physical activity data. The first draft of the manuscript was prepared by CYE with critical input and revisions by all other authors. All authors approved the final manuscript.

Conflicts of interests

The authors declare that they have no conflict of interest

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Table 1: Metabolic characteristics at baseline and 6 months

Metabolic characteristics	Baseline			6 months			Change (6 months - baseline)		
	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)
Weight, kg	88.2 (16.1)	83.1 (17.9)	90.7 (14.5) ^c	85.9 (16.3)	80.7 (17.7)	88.5 (15.0)	- 2.3 (3.3) ^z	- 2.5 (3.3) ^z	- 2.3 (3.3) ^z
Body mass index, kg/m ²	30.7 (5.3)	31.9 (6.9)	30.2 (4.7) ^a	29.9 (5.4)	30.9 (6.2)	29.4 (4.9)	- 0.8 (1.2) ^z	- 1 (1.0) ^z	- 0.8 (1.1) ^z
Waist circumference, cm	105 (12)	102 (13) ¹	107 (11) ^b	103 (12)	100 (13)	104 (12)	- 3 (4) ^z	- 3 (4) ^z	- 3 (4) ^z
HbA1c, % (mmol/l)	6.66 (0.94) (49.0 (10.3))	6.67 (0.91) (49.0 (9.9))	6.65 (0.95) (49.0 (10.4))	6.47 (0.89) (47.0 (9.7))	6.41 (0.63) (47.0 (6.9))	6.51 (0.99) ¹ (48.0 (10.8))	- 0.18 (0.72) ^z (- 2.0 (7.9))	- 0.27 (0.63) ^z (- 3.0 (6.9))	- 0.14 (0.75) ^x (- 1.5 (8.2))
Total cholesterol, mmol/l	4.33 (0.90)	4.66 (0.89) ¹	4.16 (0.86) ^{1c}	4.29 (0.93)	4.66 (0.98)	4.11 (0.84)	- 0.03 (0.69)	0.01 (0.79)	- 0.06 (0.63)
LDL-cholesterol, mmol/l	2.30 (0.78)	2.55 (0.81) ³	2.18 (0.74) ^{2c}	2.27 (0.81)	2.51 (0.88) ³	2.15 (0.75) ¹	- 0.03 (0.67)	- 0.03 (0.76)	- 0.03 (0.62)
HDL-cholesterol, mmol/l	1.29 (0.33)	1.37 (0.39) ¹	1.25 (0.29) ^{1a}	1.34 (0.37)	1.45 (0.47)	1.28 (0.30)	0.05 (0.27) ^y	0.09 (0.37) ^x	0.03 (0.21)
Systolic blood pressure, mmHg	134 (16)	133 (16)	134 (15)	134 (15)	135 (16)	134 (14)	1 (12)	2 (13)	0 (12)
Diastolic blood pressure, mmHg	79 (8)	78 (8)	79 (8)	78 (8)	78 (8)	78 (8)	0 (7)	0 (8)	0 (7)
Physical activity (n=223)	(n=223)	(n=75)	(n=148)	(n=223)	(n=75)	(n=148)	(n=223)	(n=75)	(n=148)
Minutes of moderate to vigorous physical activity / day (MVPA)	26 (21)	21 (18)	29 (22)	33 (25)	21 (19)	38 (26)	7 (21)	1 (12)	10 (24)

a = p<0.05; b = p<0.005; c = p<0.001 women vs. men at baseline

x = p<0.05; y = p<0.005; z = p<0.001 baseline vs. 6 month

Numerical superscripts indicate number of participants with missing data for the variable of interest.

Table 2: Nutrient intake at baseline and 6 months

Mean daily intake nutrients	Baseline			6 months			Change (6 months - baseline)		
	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)
Energy (kcal)	1796 (461)	1582 (379)	1903 (462) ^c	1610 (418)	1459 (326)	1685 (439) ^c	-187 (315) ^z	- 123 (270) ^z	- 218 (332) ^{az}
Protein (g)	80 (19)	73 (16)	83 (20) ^c	74 (19)	68 (13)	77 (20) ^c	- 6 (17) ^z	- 5 (15) ^y	- 6 (19) ^z
Total carbohydrates (g)	202 (55)	186 (48)	211 (57) ^b	186 (53)	170 (39)	194 (58) ^b	- 17 (41) ^z	- 15 (33) ^z	- 17 (45) ^z
Total sugar (g)	81 (32)	77 (28)	83 (34)	75 (31)	71 (23)	77 (34)	- 6 (26) ^z	- 6 (21) ^x	- 6 (28) ^y
Starch (g)	119 (36)	105 (30)	126 (37) ^c	109 (31)	97 (26)	115 (32) ^c	-10 (28) ^z	- 9 (24) ^y	- 11 (30) ^z
Non-starch polysaccharide (g)	17 (5)	16 (5)	17 (5)	16 (5)	15 (4)	17 (5) ^a	- 1 (5)	- 1 (4)	0 (5)
Total fat (g)	69 (22)	61 (20)	73 (220) ^c	61 (20)	56 (19)	64 (20) ^b	- 8 (18) ^z	- 5 (17) ^x	- 9 (18) ^z
Saturated fat (g)	23 (9)	21 (8)	24 (9) ^b	20 (9)	19 (9)	21 (9)	- 3 (8) ^z	- 2 (7) ^x	- 3 (8) ^z
Trans fat (g)	2.3 (1.1)	2.0 (1)	2.4 (1.1) ^b	2.1 (1.1)	1.9 (1.1)	2.2 (1.1) ^a	- 0.2 (1.1) ^y	- 0.1 (1.1)	- 0.3 (1.2) ^y
Monounsaturated fat (g)	24 (8)	21 (8)	26 (8) ^c	22 (8)	20 (7)	23 (8) ^b	- 2 (7) ^z	- 1 (8) ^x	- 3 (7) ^z
Polyunsaturated fat (g)	13 (6)	12 (6)	14 (6) ^a	12 (4)	11 (4)	13 (5) ^a	- 1 (5) ^z	-1 (6)	- 1 (5) ^y
Alcohol (g)	14 (18)	7 (11)	18 (20) ^a	10 (13)	7 (9)	11 (14) ^b	- 5 (14) ^z	0 (10)	- 7 (15) ^{cz}
% Energy from protein	18.3 (3.6)	19.0 (3.7)	18.0 (3.5) ^a	18.8 (3.5)	19.0 (3.3)	18.7 (3.6)	0.5 (3.7) ^z	0.0 (3.6)	0.7 (3.8) ^y
% Energy from total carbohydrates	43.2 (6.6)	44.8 (6.4)	42.4 (6.6) ^a	44.1 (6.5)	44.7 (6.2)	43.8 (6.6)	0.9 (6.0) ^z	- 0.1 (6.2)	1.4 (5.9) ^y
% Energy from total fat	33.5 (5.6)	33.4 (5.8)	33.6 (5.5)	33.3 (5.8)	33.3 (6.4)	33.3 (5.4)	-0.2 (5.9)	- 0.1 (6.3)	- 0.3 (5.7)
% Energy from saturated fat	11.2 (3.1)	11.4 (3.4)	11.2 (3.1)	11.0 (3.4)	11.1 (3.6)	10.9 (3.2)	- 0.3 (3.3)	- 0.3 (3.1)	- 0.3 (3.5)
% Energy from trans fat	1.1 (0.4)	1.1 (0.43)	1.1 (0.5)	1.1 (0.5)	1.1 (0.4)	1.1 (0.5)	0.0 (0.5)	0.0 (0.5)	0.0 (0.5)
% Energy from monounsaturated fat	11.7 (2.5)	11.5 (2.6)	11.9 (2.5)	11.9 (2.5)	11.7 (2.7)	12.0 (2.5)	- 0.2 (2.8)	0.2 (3.2)	0.1 (2.6)
% Energy from polyunsaturated fat	6.5 (2.2)	6.7 (2.4)	6.4 (2.1)	6.6 (1.9)	6.6 (1.9)	6.6 (1.9)	0.1 (2.4)	0.0 (2.6)	0.2 (2.3)
% Energy from total sugar	17.2 (5.7)	18.7 (5.5)	16.5 (5.6) ^b	17.7 (5.7)	18.8 (5.4)	17.2 (5.8) ^a	0.5 (5.0)	0.2 (5.2)	0.7 (4.9)
% Energy from alcohol	5.0 (6.1)	2.9 (4.3)	6.1 (6.6) ^c	3.9 (4.9)	3.0 (3.9)	4.3 (5.3) ^a	- 1.2 (4.7) ^z	0.2 (4.0)	- 1.8 (5.0) ^{cz}

a = p<0.05; b = p<0.005; c = p<0.001 women vs. men
y = p<0.005; z = p<0.001 baseline vs. 6 months

Table 3: Associations between macronutrients and metabolic outcomes in men (n=148) and women (n=75) who provided physical activity data.

Macronutrient		Metabolic outcomes	Regression coefficient, β (95% Confidence interval)	p value
Change to % energy from total carbohydrates	Men	HbA1c	-0.003 (-0.006, -0.001)	0.009
	All	Total cholesterol	-0.023 (-0.044, -0.002)	0.033
Change to fibre (nsp) intake (g)	Men	Total cholesterol	-0.025 (-0.047, -0.003)	0.023
	All	LDL cholesterol	0.018 (0.003, 0.032)	0.016
Change to % energy from total fat	Men	LDL cholesterol	0.024 (0.006, 0.042)	0.011
	All	Waist circumference	0.014 (0.003, 0.024)	0.011
Change to % energy from trans fat	Women	Waist circumference	0.029 (0.006, 0.052)	0.015
		Total cholesterol	0.399 (0.028, 0.770)	0.036
		LDL cholesterol	0.365 (0.042, 0.688)	0.028
Change to % energy from monounsaturated fats	All	LDL cholesterol	0.036 (0.006, 0.065)	0.018
	All	Diastolic blood pressure	0.217 (0.020, 0.414)	0.031
Change to % energy from alcohol	Men	Diastolic blood pressure	0.276 (0.055, 0.497)	0.015

All models are adjusted for change in energy intake, outcome at baseline, age, BMI, time since diagnosis, medication, dietary supplements, mean daily minutes of moderate to vigorous physical activity.

For each macronutrient listed a 1% (1g for fibre) increase is associated with the change in outcome listed

BMJ Open

Dietary changes and associations with metabolic improvements in adults with Type 2 diabetes during a patient-centred dietary intervention: an exploratory analysis

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-004953.R1
Article Type:	Research
Date Submitted by the Author:	13-May-2014
Complete List of Authors:	England, Clare; University of Bristol, Centre for Exercise, Nutrition and Health Sciences Thompson, Janice; The University of Birmingham, School of Sport & Exercise Sciences Jago, Russ; University of Bristol, Centre for Exercise, Nutrition and Health Sciences Cooper, Ashley; University of Bristol, Centre for Exercise, Nutrition and Health Sciences Andrews, Robert; University of Bristol, Henry Wellcome Laboratories for Integrative
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Nutrition and metabolism
Keywords:	Type 2 diabetes, Dietary analysis, Dietary change

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3 **Dietary changes and associations with metabolic improvements in**
4 **adults with Type 2 diabetes during a patient-centred dietary**
5 **intervention: an exploratory analysis**
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36 Running title: Dietary change in adults with Type 2 diabetes
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38 *Keywords: Type 2 diabetes, dietary analysis, dietary change*
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43 Bath Research Ethics Committee (05/Q2001/5)
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45
46 Word count
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48 Abstract: 299
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50 Main text: 3758
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3 1 Abstract
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5 2 *Objectives:* Describe dietary intake of participants enrolled in a non-prescriptive dietary
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7 3 intervention and dietary changes at 6 months and explore whether these changes had a role in
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9 4 observed improvements in HbA1c, weight, lipids and blood pressure.

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11 5 *Design:* Secondary analysis of data from the Early ACTivity in Diabetes randomised
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13 6 controlled trial.

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15 7 *Participants* 262 patients with newly diagnosed Type 2 diabetes randomised to the dietary
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17 8 intervention.

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19 9 *Outcomes and analysis:* Changes in energy intake, macronutrients, fibre and alcohol and in
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21 10 weight, waist circumference, lipids, HbA1c and blood pressure at baseline and 6 months.
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23 11 Multivariate models were used to examine associations between dietary changes and
24
25 12 metabolic variables.

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27 13 *Results:* Men reported reducing mean energy intake from 1903 ± 462 kcal to 1685 kcal \pm
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29 14 439 kcal ($p < 0.001$), increasing carbohydrate intake from $42.4 \pm 6.6\%$ to $43.8 \pm 6.6\%$
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31 15 ($p = 0.002$) and reducing median alcohol intake from 13 (0-27)g to 5 (0-18)g ($p < 0.001$).
32
33 16 Women reported reducing mean energy intake from 1582 ± 379 kcal to 1459 ± 326 kcal
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35 17 ($p < 0.001$) with no change to macronutrient distribution and alcohol. Fibre intake was
36
37 18 maintained. In men ($n = 148$) weak and clinically insignificant associations were found
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39 19 between increased carbohydrates and reduction in HbA1c ($\beta = -0.003$ [-0.006, -0.001];
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41 20 $p = 0.009$), increased fibre and reduction in total cholesterol ($\beta = -0.023$ [-0.044, -0.002];
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43 21 $p = 0.033$), decreased total fat and reduction in LDL-cholesterol ($\beta = 0.024$ [0.006, 0.001];
44
45 22 $p = 0.011$), and decreased alcohol and reduction in diastolic blood pressure ($\beta = 0.276$ [0.055,
46
47 23 0.497]; $p = 0.015$). In women ($n = 75$) associations were found between a decrease in trans-fats
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49 24 and reductions in waist circumference ($\beta = -0.029$ [0.006, 0.052]; $p = 0.015$), total cholesterol
50
51 25 ($\beta = 0.399$ [0.028, 0.770]; $p = 0.036$) and LDL cholesterol ($\beta = 0.365$ [0.042, 0.668]; $p = 0.028$).

52
53 26 *Conclusion:* Clinically important metabolic improvements observed in a patient-centred
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55 27 dietary intervention were not explained by changes in macronutrients. However, a non-
56
57 28 prescriptive approach may promote a reduction in total energy intake whilst maintaining fibre
58
59 29 consumption.
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30 Article summary31 Strengths and limitations

- 32 • Describes the dietary intake of people soon after diagnosis of Type 2 DM living in the
33 UK, the dietary changes made during a dietary intervention and explores associations
34 between dietary changes and changes in metabolic outcomes. This intervention was
35 based on the dietary advice that is given in routine clinical practice in the UK.
36
- 37 • Only 53% of the participants provided food diary data at the end of the trial and these
38 people showed greater improvements in metabolic outcomes than those who did not
39 return food diaries. It is probable that they were more motivated than a typical patient
40 group and this limits the generalizability of the findings.

41 Introduction

42 Dietary management is recognised as highly important in the treatment of Type 2 diabetes
43 (Type 2 DM). Based upon meta-analyses of exercise and diet studies, the American Diabetes
44 Association (ADA) and European Association for the Study of Diabetes (EASD) recommend
45 that lifestyle interventions should be initiated as the first step in treating new-onset Type 2
46 DM [1]. Over the last 3 years, The Look Ahead research group, the Lifestyle Over and Above
47 Drugs in Diabetes (LOADD) and Early Activity in Diabetes (Early ACTID) randomised
48 controlled trials (RCTs) have shown that dietary interventions which target weight reduction
49 are beneficial and improve glycaemic control [2-4]. These trials achieved reductions in
50 HbA1c comparable to reductions demonstrated in patients starting metformin or a gliptin as
51 monotherapies [5] and, although the Look Ahead trial showed no reduction in cardiovascular
52 events after 9.6 years, participants in the intervention arm were less likely to be treated with
53 insulin [6].

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55 It has been reported that changes to the macronutrient composition of the diet may impact
56 upon glycaemic control, blood lipids and weight [7], but the effect of specific dietary changes
57 on these metabolic outcomes are still unclear and no single ‘diet for diabetes’ has been
58 identified [8]. In recognition of this, both the 2012 ADA and EASD joint guidelines and 2011
59 Diabetes UK nutritional guidelines emphasise the importance of an individualised, patient-
60 centred approach to diet rather than a prescriptive approach [1,9]. This approach recognises
61 that different people have individual dietary habits and may find certain dietary changes more
62 straightforward than others. There is evidence that men and women living in the UK have
63 differing dietary patterns [10]. Men have been reported to drink more alcohol and consume
64 more meat but less fruit and diet soft drinks than women [11] Few studies have looked at what
65 changes are made to macronutrients in response to non-prescriptive dietary advice, whether
66 men and women make different changes and whether these changes impact on metabolic
67 control.

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69 The Early ACTID trial included a non-prescriptive, patient-centred dietary intervention. The
70 trial aimed to assess whether adding physical activity to a dietary intervention produced
71 greater benefit than diet alone or usual care in individuals newly diagnosed with Type 2 DM
72 [4]. Participants who received the lifestyle interventions had better HbA1c, lower body

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3 73 weight, less insulin resistance, and were on less medication than the control group at 6 and 12
4 74 months. During the intervention participants in this cohort reported small changes to higher
5 75 calorie, low fibre foods. Examination of the specific changes to foods and food groups
6 76 reported by participants has been previously published [12] and this current paper focuses on
7 77 macronutrients.
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14 79 The aim of this paper is to describe baseline energy and macronutrient intakes of men and
15 80 women who were enrolled into the dietary intervention in the Early ACTID study and to
16 81 examine reported dietary changes made after 6 months.
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20 82 We conducted exploratory analysis to examine the following hypotheses:
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23 83 • Men and women with Type 2 DM make different dietary changes in response to a
24 84 dietary intervention.
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26 85 • The changes to energy intake and macronutrients are associated with beneficial
27 86 changes to glycaemic control, weight, waist circumference, blood pressure and lipids.
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30 87 Subjects and methods

31 88 *Subjects*

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35 89 This paper is an exploratory analysis of data from the Early ACTID randomised controlled
36 90 trial. Early ACTID was a diet and physical activity trial involving patients living in the South
37 91 West of England who were recruited within 5 to 8 months of a diagnosis of Type 2 DM from
38 92 December 2005 to September 2008. Full trial procedures with the CONSORT diagram and
39 93 results are described elsewhere [4 ,13 ,14]. The analysis is limited to participants in the
40 94 intervention arms who returned valid food diary data.
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45 95 *Overview of the dietary intervention*

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48 96 Patients in the diet alone and the diet and physical activity groups received the same dietary
49 97 intervention. For the first 6 months the intervention aimed to promote dietary change. At
50 98 randomisation patients attended a one-hour appointment with a study dietitian followed by 2
51 99 further visits of 30 minutes. These visits were supported by 6 additional visits with a research
52 100 nurse, where 15 minutes were used to discuss dietary matters for both groups, reinforcing
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3 101 dietary goals, and 15 minutes to discuss either physical activity or other matters pertinent to
4 102 the patient, depending upon intervention group allocated to. Maintenance was the primary
5 103 goal of the second 6 months and consisted of 2 more 30 minute dietitian visits and 4
6 104 additional visits with the research nurses.
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10 105 The dietary intervention was based upon the 2003 Diabetes UK healthy eating guidelines [15]
11 106 and employed goal oriented motivational interviewing [16]. Patients were encouraged to
12 107 discuss their reasons for change, any ambivalence about change and to set their own dietary
13 108 goals and identify their own strategies for achieving these goals. Prescriptive daily
14 109 requirements for energy or macronutrients were not calculated unless requested by the patient
15 110 and prescriptive meal plans or food lists were not used. Instead patients received study
16 111 specific written dietary information at each visit (available here:
17 112 <http://jcrubristol.org.uk/EA/ACTID%20patients%20Handbook/Forms/AllItems.aspx>) and
18 113 were encouraged to use this to evaluate their own eating habits. The materials included
19 114 information on maintaining a regular meal pattern and including starchy carbohydrates as a
20 115 part of each meal, reducing total, saturated and *trans* fat intake, limiting non-milk extrinsic
21 116 sugars, aiming for 5 portions a day of fruit and vegetables and gave guidance on portion
22 117 control. Specific food choices were discussed and participants were advised on choosing
23 118 wholegrain and higher fibre foods, reducing fatty and processed meats and high fat dairy
24 119 products, and increasing oily fish and limiting foods like cakes, biscuits, salty snacks and
25 120 take-away meals. The benefit of aiming for a 5 to 10% weight loss by reducing overall
26 121 energy intake was discussed with everyone. Goals were reviewed at each appointment and
27 122 successes, difficulties and new strategies discussed. Patients were encouraged to self-monitor
28 123 their weight and diet.
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43 *Measurements*

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45 125 Measures were taken at baseline (prior to randomisation) and repeated 6 and 12 months later.
46 126 Baseline and 6 month data were used in the current analysis, since outcomes at 6 months
47 127 were defined as the primary endpoint of the study. Measurements used in this analysis were
48 128 weight, height (to calculate body mass index (BMI)), waist circumference, blood pressure,
49 129 HbA1c, fasting lipids and minutes of moderate to vigorous physical activity (MVPA)
50 130 measured using accelerometry and defined as activity expending greater than 3kcal/kg/hour .
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52 131 As previously described, blood measurements and anthropometric measures were carried out
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3 132 using standardised procedures [13]. Smoking habits and use of dietary supplements were
4 133 assessed by a research nurse. The UK Index of Multiple Deprivation (IMD) 2007 was
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6 134 calculated from home postcode and used as an indicator of socio-economic position [17].
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9 135 *Dietary assessment and analysis*

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11 136 Patients in the intervention arms were asked to complete 4-day food diaries, to include 2
12 137 weekdays and 1 weekend day, prior to each dietitian appointment, recording all foods and
13 138 drinks consumed during those 4 days. Portion sizes were estimated using household measures
14 139 and package weights and brands indicated where appropriate. The diaries were discussed
15 140 during the appointments and used to identify potential areas for change, difficulties in making
16 141 change, and for patients to observe change in their diets over time. Patients were asked to
17 142 return all the diaries at the final visit for further analysis. Those who did not return diaries at
18 143 the visit were reminded by telephone and e-mail to post outstanding diaries to the research
19 144 team after the visit.
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21 145 Baseline and 6-month food diaries were coded by one coder and checked for accuracy and
22 146 agreement by a second coder, using the dietary coding programme Diet in Data Out (DIDO),
23 147 developed at the Medical Research Council Human Nutrition Unit in Cambridge, UK [18].
24 148 Diaries were analysed with the nutrient analysis programme Bristol General Analysis of
25 149 Dietary Experiments (BRIGADE) [19]. The nutrient database is based on *McCance and*
26 150 *Widdowson's Composition of Foods, 5th edition* [20], updated with the supplements to that
27 151 edition, new data from the 6th edition and manufacturers' data. Additional nutrient data from
28 152 the INTERMAP nutrient database for the UK were also used [21]. If no portion size
29 153 information was given, age-appropriate portion sizes were assigned [22]. The mean daily
30 154 consumption of each nutrient was calculated for each participant.
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32 155 *Statistical analysis*

33 156 As the dietary intervention was designed to be identical for both intervention groups and
34 157 there were no difference in outcomes between the diet and diet and physical activity groups,
35 158 the data were analysed as a cohort. Patients in the usual care group were excluded from the
36 159 analysis since they did not receive the dietary intervention and were not asked to complete a
37 160 diary at 6 months. Descriptive statistics were used for patient characteristics and for intakes
38 161 of macronutrients at baseline and 6 months. Variables were checked for normal distribution;
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3 162 non-normal variables were log transformed prior to analysis. For ease of interpretation,
4 163 arithmetic means and back transformed variables are presented. Independent *t*-tests were used
5 164 to explore differences in continuous variables between men and women at baseline and
6 165 between those who did and did not return food diaries, and chi-squared tests were used to
7 166 explore differences in dichotomous variables. Paired sample *t*-tests were used to describe
8 167 differences in energy and macronutrient intake between baseline and 6 months. McNemar
9 168 tests were used to explore differences in numbers of people meeting recommendations at
10 169 baseline and 6 months. As alcohol variables could not be transformed, the Mann Whitney U
11 170 and paired sample Wilcoxon signed rank test were used to describe differences. Cases with
12 171 missing data were excluded listwise. Data were assumed to be randomly missing and table 1
13 172 includes numerical superscripts to indicate the number of participants with missing data for
14 173 the variable of interest.

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24 174 Multivariate regression models were used to conduct exploratory analysis to investigate
25 175 associations between changes in energy and macronutrient intake and the metabolic variables
26 176 at 6 months in those who provided valid physical activity data. Changes in energy intake
27 177 were explored using a standard multivariate model. Each macronutrient was explored
28 178 independently using a multivariate nutrient density model to adjust for change in energy
29 179 intake. Change in percentage energy from each macronutrient was calculated and entered into
30 180 the model with change in total energy included as a covariate. Change in fibre intake was
31 181 explored using a standard multivariate model and entered as an absolute intake (in grams)
32 182 with change to total energy intake as a covariate [23]. Models were adjusted for age, BMI,
33 183 time since diagnosis, minutes of moderate to vigorous physical activity (MVPA) and
34 184 dichotomous yes/no variables for smoking status, relevant lipid lowering, blood pressure and
35 185 diabetes medication and dietary supplement use at 6 months.

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45 186 Due to the number of different analyses that were conducted the results are interpreted in
46 187 terms of strength of evidence of associations [24]. This is an exploratory analysis and as such
47 188 has not been adjusted for multiple comparisons [25 ,26], consequently p values of <0.05 are
48 189 interpreted as some evidence of association, p<0.01 as increasing evidence and p<0.001 as
49 190 strong evidence.

50 191 Results

51 192 *Study participants*

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3 193 A total of 593 patients were recruited into the Early ACTID study, with 494 being assigned to
4 194 one of the intervention groups. 396 (80%) patients were recorded as completing food diaries
5 195 at both baseline and 6 months but only 262 (53%) patients returned them. Metabolic and
6 196 dietary outcomes at baseline and 6 months are presented for these 262 patients. At 6 months
7 197 491 (99%) patients assigned to one of the intervention arms remained in the study, with 434
8 198 (88%) attending all scheduled visits up to that point and a further 37 (8%) attending all except
9 199 one.

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15 200 Mean age was 62.4 (9.0) years, 97% of patients were white, 83% were married or with a long
16 201 term partner and 41% were in the lowest IMD quartile. At baseline 104 (40%) of participants
17 202 were on oral hypoglycaemic medication, 170 (65%) on lipid lowering medication and 174
18 203 (66%) on blood pressure medication. Only 6% of patients were current smokers at baseline.
19 204 Men and women had similar characteristics, although there was some evidence that men were
20 205 more likely to be on lipid lowering medication than women (69% vs. 56%, $p=0.041$). At 6
21 206 months, 105 (40%) of participants were on oral hypoglycaemic medication, although 12 (5%)
22 207 participants had increased the dose and 4 (2%) had decreased; 177 (68%) were on lipid
23 208 lowering medication and 175 (67%) were on blood pressure medication.

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31 209 Compared to the patients who did not return food diaries, those who did were older (62 years
32 210 vs 57 years, $p<0.001$), with a lower mean weight (88.2 kg vs 93.3 kg, $p=0.001$), lower mean
33 211 BMI (30.7 vs 32.5, $p=0.001$) and lower mean waist circumference (105 cm vs 108 cm,
34 212 $p=0.025$), but there was no difference in glycaemic control, lipids and blood pressure.

35 213 *Metabolic outcomes*

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42 214 Table 1 shows the metabolic outcomes at baseline and 6 months for those who returned food
43 215 diaries. There was no difference in glycaemic control or blood pressure between men and
44 216 women, but women had higher total ($p<0.001$), LDL ($p<0.001$) and HDL ($p=0.015$)
45 217 cholesterol levels.

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49 218 Weight, waist circumference and BMI improved at 6 months for both men and women
50 219 ($p<0.001$). Men and women improved their HbA1c (men: $p=0.006$; women: $p<0.001$). Men
51 220 improved their fasting blood glucose ($p=0.006$) and there is some evidence that women
52 221 increased their HDL cholesterol ($p=0.033$).

222 At 6 months those who returned food diaries had lost more weight (2.4 kg vs 1.3 kg,
223 $p=0.001$), reduced waist circumference more (2.7 cm vs 1.3 cm, $p=0.022$) and reduced
224 HbA1c (0.18% (2 mmol/l) vs 0% (0 mmol/l), $p=0.02$).

225 *Nutrient analysis*

226 Table 2 shows the mean reported energy and nutrient intakes at baseline and 6 months and
227 their mean reported changes.

228 At baseline participants reported generally good dietary habits. 61% of women and 59% of
229 men reported the recommended total fat intake (less than 35% of energy from total fat) and
230 55% of women and 66% of men reported a low to moderate carbohydrate intake (<45% of
231 energy). Men were more likely to drink alcohol and more likely to drink to excess than
232 women with 49% of women and 28% of men recording no alcohol during the 4 days and 8%
233 of women and 19% of men reporting more than 30g of alcohol per day ($p=0.022$).

234 At 6 months mean daily reported energy intake was reduced by 187 kcal ($p<0.001$). Men
235 reduced their energy intake more than women (218 ± 332 vs. 123 ± 270 kcal/day, $p=0.022$).
236 This was achieved by small reductions in all macronutrients, whilst maintaining fibre intake.
237 The mean percentage energy from macronutrients was unchanged for women whilst men
238 reported a small mean increase of $1.4 \pm 5.9\%$ ($p<0.001$) of energy from carbohydrates. Men
239 reported reducing median alcohol intake ($p<0.001$), with 40% reporting no alcohol during the
240 4 days and 15% reporting more than 30g per day. There was no reported median change in
241 alcohol intake for women. Despite no mean change to energy from saturated fat, more men
242 met recommendations at 6 months (35% men at baseline vs. 49% at 6 months reporting less
243 than 10% energy from saturated fat, $p=0.007$). There was no change in the number of women
244 meeting recommendations (40% baseline vs 44% at 6 months, $p=0.71$).

245 Valid physical activity data and dietary data were provided by 223 (45%) participants. Table
246 3 shows the regression coefficients and confidence intervals for changes in energy and
247 macronutrients that show evidence for associations with specific metabolic variables. In men
248 a 1% reduction in energy from alcohol was associated with a 0.276 mmHg reduction in
249 diastolic blood pressure (95% CI= 0.055 to 0.497). In women a 1% reduction in energy from
250 trans-fat was associated with a decrease in cholesterol of 0.399 mmol/l (95% CI= 0.028 to
251 0.770). In men a 1% increase in energy from carbohydrate was associated with a decrease in

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3 252 HbA1c of 0.003% (95% CI= -0.006 to -0.001). There were no associations between change
4 253 in energy intake and the metabolic variables.
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10 255 Discussion

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12 256 *Main findings*

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14 257 The main findings from this exploratory analysis are that patients who were randomised to
15 258 the intervention arms in the Early ACTID study and returned food diaries reported a good
16 259 diet at baseline but still achieved small dietary changes. They reported a mean decrease in
17 260 energy intake of around 200 kcal per day, during the first 6 months. This is a modest
18 261 reduction in calorie intake but, if sustained, will have an impact on weight and glycaemic
19 262 control. It has been argued that long-term small changes are more effective for weight
20 263 management than short-term large changes [27]. Men reported a reduced alcohol intake that
21 264 produced a greater reduction in energy and reported a small increase in the percentage energy
22 265 from carbohydrate. Women reported modest reductions to all macronutrients but made no
23 266 changes to alcohol, their energy reduction was less and the macronutrient ratio of their diets
24 267 did not change. Both sexes maintained fibre intake. Although changes in percentage intake of
25 268 macronutrients were associated with metabolic outcomes, these effect sizes were too small to
26 269 be of clinical significance
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37 270 *Comparison with other studies*

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39 271 The Early ACTID dietary intervention was a pragmatic, 'real world' intervention, in which
40 272 participants discussed dietary advice with dietitians and nurses to decide on their own dietary
41 273 changes. The approach contrasts with dietary studies where participants are asked to make
42 274 specific, prescribed changes to the macronutrient composition, by lowering carbohydrate and
43 275 increasing protein [28-30] or to lower the glycaemic index [31 ,32]. The LOADD trial [3]
44 276 based a successful dietary intervention in patients with poor glycaemic control on very
45 277 similar recommendations to those used in the Early ACTID intervention, but total energy
46 278 intake and macronutrient ratios for each participant were calculated and diets were prescribed
47 279 according to these calculations taking into account personal preference, budget and
48 280 sociocultural factors. The Early ACTID intervention did not compare a prescriptive with a
49 281 non-prescriptive approach so cannot be used to demonstrate that this is superior but
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3 282 reductions in weight, waist circumference and HbA1c were achieved that are comparable to
4 283 those achieved during these interventions. Withdrawal rates for prescriptive dietary
5 284 interventions range from 10% to 30% and these higher withdrawal rates may suggest that in
6 285 routine clinical care a more flexible approach can be advantageous in promoting retention. Of
7 286 those participants in Early ACTID who either did not attend all appointments or withdrew
8 287 completely, only one person stated that they did not see the benefit of the trial. The majority
9 288 could not schedule all 9 dietitian and nurse visits because of other commitments, 5 cited other
10 289 health issues, 3 moved too far away, 1 said they 'did not want to diet,' 1 wanted to take
11 290 orlistat from baseline and 3 gave no reasons. What is common to intervention trials in
12 291 diabetes is that patients receive individual support and attend multiple appointments with a
13 292 dietitian or a health practitioner who is expert in promoting dietary change. It is important to
14 293 emphasise that this model is not routinely replicated in primary care for patients with Type 2
15 294 DM.

16 295 Exploratory analysis of the associations between specific dietary changes and metabolic
17 296 outcomes found small effect sizes that are not clinically important, but they are consistent
18 297 with existing nutritional data on the benefits of a reduction in trans fats on lipids and waist
19 298 circumference [33], an increase in fibre on LDL cholesterol [34] and a reduction in alcohol
20 299 and blood pressure [35]. It is of interest that this analysis found that there was no benefit in
21 300 carbohydrate reduction in men with good glycaemic control who are already consuming a
22 301 low to moderate carbohydrate diet. It is not possible to determine whether there is an
23 302 optimum macronutrient distribution for T2 DM from this analysis, particularly in those with
24 303 poor glycaemic control, but there is no unequivocal evidence that low carbohydrate diets
25 304 produce better blood glucose control or weight loss than higher carbohydrate diets [36]. A
26 305 meta-analysis of low carbohydrate diets versus low fat diets conducted in 2012 [37]
27 306 concluded that there was evidence of a small but beneficial effect on lipid profiles of a low
28 307 (defined as <45% energy from carbohydrate) or very low carbohydrate (<60g carbohydrate)
29 308 diet but no difference in improvements to weight or glycaemic control. Larsen et al [29]
30 309 correlated dietary change with metabolic outcomes and found associations with energy
31 310 reduction and HbA1c and waist circumference.

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51 311 *Strengths and weaknesses*
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3 312 To our knowledge this is the first study to describe the dietary intake of people soon after
4 313 diagnosis with Type 2 DM living in the UK, the dietary changes made during an intervention
5 314 based on patient-centred, non-prescriptive dietary advice and that examines associations
6 315 between dietary change and metabolic variables. The demographics of the Early ACTID
7 316 participants included in this analysis suggest that these findings are only representative of the
8 317 white population; however the sample is socio-economically diverse with 40% of participants
9 318 living in areas of high economic deprivation. Ethical approval was granted to make no
10 319 changes to hypoglycaemic, lipid lowering or blood pressure medications during the first 6
11 320 months, unless absolutely necessary and this was controlled by a strict protocol. Due to small
12 321 numbers those participants who made medication changes were included in the analysis
13 322 without correction.

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16 323 The study has important weaknesses. Only 53% of the participants returned baseline and 6
17 324 month food diaries at the end of the trial and these people had a lower BMI and waist
18 325 circumference at baseline and achieved greater metabolic improvements. The participants
19 326 who did not return diaries reported mislaying them which may indicate less motivation and
20 327 less engagement with the trial. Participants who did return diaries could have been more
21 328 motivated to make dietary changes than a typical patient population, and, given that their
22 329 diets were good at baseline, may already have made dietary changes prior to entry into the
23 330 Early ACTID study. The relative lack of dietary data limits our ability to generalise these
24 331 findings to broader patient groups. Furthermore this was an exploratory analysis using an
25 332 existing dataset and as such an estimation of sample size was not conducted in advance. .
26 333 However, post hoc sample calculations indicate that the study was underpowered to detect small
27 334 associations between dietary changes and metabolic outcomes, having 15% power for women and
28 335 52% for men at an alpha of 0.05.

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46 337 The use of any self-reported measure of diet, including 4-day food diaries, is a recognised
47 338 limitation in dietary studies. Under-reporting of food intake and selective under-reporting or
48 339 under-eating of foods perceived to be 'bad' are commonly documented, especially in people
49 340 who are obese [38 ,39]. Measurement of alcohol can be problematic due to the episodic
50 341 nature of consumption, although including at least one weekend day can improve estimates
51 342 by including alcohol consumption of 'weekend-only' drinkers [40]. Methods exist to estimate
52 343 under-reporting, using calculated basal metabolic rate and estimates of physical activity [41

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3 344 ,42] but these methods assume that an individual's weight is stable and are consequently
4 345 inappropriate for use during a weight loss trial. It should be noted that other dietary
5 346 interventions in patients with Type 2 DM have reported similar energy intakes [28 ,31] and
6 347 an energy reduction of around 200kcal/day is plausible assuming a dynamic model of energy
7 348 balance [43] and given the modest weight reduction observed. It is also important to note that
8 349 this is a secondary analysis so cause and effect cannot be assumed. It was not possible to
9 350 perform a formal mediation analysis since participants from the control arm were not asked to
10 351 complete a food diary at 6 months.

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17 352 *Conclusion*

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19 353 The Early ACTID trial indicates that a flexible, non-prescriptive approach to dietary advice
20 354 based on standard healthy eating guidelines in Type 2 DM given soon after diagnosis may be
21 355 effective in promoting small dietary change, even in patients with good glycaemic control.
22 356 This supports current clinical practice and guidelines. The current analysis suggests that
23 357 changes in percentage intake of macronutrients did not have any clinically significant effect
24 358 on metabolic outcomes during the trial but this needs confirmation in a larger cohort, with
25 359 less good glycaemic control. Further research is needed on whether dietary changes made
26 360 using a non-prescriptive approach are sustainable and beneficial in the longer term in a more
27 361 typical patient population.
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Acknowledgements

We would like to acknowledge the participants in the Early ACTID trial, members of the Early ACTID team and steering committee, Dr Pauline Emmett for advice on dietary analysis, Dr Rosemary Greenwood for advice on statistical analysis and Professor Debbie Sharp for assistance in manuscript preparation.

Funding

The Early ACTID trial was supported by Diabetes UK, the UK Department of Health and Western Comprehensive Local Research Network. Pilot dietary analysis was supported by the Above and Beyond Foundation. C.Y. England is supported by NIHR Clinical Doctoral Research Fellowship 10-017.

Authors' contributions

This work forms part of the PhD of CYE which is supervised by RCA, JLT and RJ. RCA led the Early ACTID study and advised on clinical application of this work. CYE participated in data collection, data entry and was responsible for data analysis with guidance from JLT and RJ. ARC was responsible for the design of the ACTID physical activity intervention and for processing and analysis of the physical activity data. The first draft of the manuscript was prepared by CYE with critical input and revisions by all other authors. All authors approved the final manuscript.

Conflicts of interests

The authors declare that they have no conflict of interest

Data Sharing Statement

No additional data are available

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Table 1: Metabolic characteristics at baseline and 6 months

Metabolic characteristics	Baseline			6 months			Change (6 months - baseline)		
	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)
Weight, kg	88.2 (16.1)	83.1 (17.9)	90.7 (14.5)	85.9 (16.3)	80.7 (17.7)	88.5 (15.0)	- 2.3 (3.3) ^z	- 2.5 (3.3) ^z	- 2.3 (3.3) ^z
Body mass index, kg/m ²	30.7 (5.3)	31.9 (6.9)	30.2 (4.7) ^a	29.9 (5.4)	30.9 (6.2)	29.4 (4.9)	- 0.8 (1.2) ^z	- 1 (1.0) ^z	- 0.8 (1.1) ^z
Waist circumference, cm	105 (12)	102 (13) ¹	107 (11)	103 (12)	100 (13)	104 (12)	- 3 (4) ^z	- 3 (4) ^z	- 3 (4) ^z
HbA1c, % (mmol/l)	6.66 (0.94) (49.0 (10.3))	6.67 (0.91) (49.0 (9.9))	6.65 (0.95) (49.0 (10.4))	6.47 (0.89) (47.0 (9.7))	6.41 (0.63) (47.0 (6.9))	6.51 (0.99) ¹ (48.0 (10.8))	- 0.18 (0.72) ^z (- 2.0 (7.9))	- 0.27 (0.63) ^z (- 3.0 (6.9))	- 0.14 (0.75) ^x (- 1.5 (8.2))
Total cholesterol, mmol/l	4.33 (0.90)	4.66 (0.89) ¹	4.16 (0.86) ^{1c}	4.29 (0.93)	4.66 (0.98)	4.11 (0.84)	- 0.03 (0.69)	0.01 (0.79)	- 0.06 (0.63)
LDL-cholesterol, mmol/l	2.30 (0.78)	2.55 (0.81) ³	2.18 (0.74) ^{2c}	2.27 (0.81)	2.51 (0.88) ³	2.15 (0.75) ¹	- 0.03 (0.67)	- 0.03 (0.76)	- 0.03 (0.62)
HDL-cholesterol, mmol/l	1.29 (0.33)	1.37 (0.39) ¹	1.25 (0.29) ^{1a}	1.34 (0.37)	1.45 (0.47)	1.28 (0.30)	0.05 (0.27) ^y	0.09 (0.37) ^x	0.03 (0.21)
Systolic blood pressure, mmHg	134 (16)	133 (16)	134 (15)	134 (15)	135 (16)	134 (14)	1 (12)	2 (13)	0 (12)
Diastolic blood pressure, mmHg	79 (8)	78 (8)	79 (8)	78 (8)	78 (8)	78 (8)	0 (7)	0 (8)	0 (7)
Physical activity (n=223)	(n=223)	(n=75)	(n=148)	(n=223)	(n=75)	(n=148)	(n=223)	(n=75)	(n=148)
Minutes of moderate to vigorous physical activity / day (MVPA)	26 (21)	21 (18) ¹²	29 (22) ²⁷	33 (25)	21 (19)	38 (26)	7 (21)	1 (12)	10 (24)

a = p<0.05; b = p<0.005; c = p<0.001 women vs. men at baseline

x = p<0.05; y = p<0.005; z = p<0.001 baseline vs. 6 month

Numerical superscripts indicate number of participants with missing data for the variable of interest. Cases with missing data are excluded listwise

Table 2: Nutrient intake at baseline and 6 months

Mean daily intake nutrients	Baseline			6 months			Change (6 months - baseline)		
	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)
Energy (kcal)	1796 (461)	1582 (379)	1903 (462) ^c	1610 (418)	1459 (326)	1685 (439) ^c	-187 (315) ^z	- 123 (270) ^z	- 218 (332) ^{a,z}
Protein (g)	80 (19)	73 (16)	83 (20) ^c	74 (19)	68 (13)	77 (20) ^c	- 6 (17) ^z	- 5 (15) ^y	- 6 (19) ^z
Total carbohydrates (g)	202 (55)	186 (48)	211 (57) ^b	186 (53)	170 (39)	194 (58) ^b	- 17 (41) ^z	- 15 (33) ^z	- 17 (45) ^z
Total sugar (g)	81 (32)	77 (28)	83 (34)	75 (31)	71 (23)	77 (34)	- 6 (26) ^z	- 6 (21) ^x	- 6 (28) ^y
Starch (g)	119 (36)	105 (30)	126 (37) ^c	109 (31)	97 (26)	115 (32) ^c	-10 (28) ^z	- 9 (24) ^y	- 11 (30) ^z
Non-starch polysaccharide (g)	17 (5)	16 (5)	17 (5)	16 (5)	15 (4)	17 (5) ^a	- 1 (5)	- 1 (4)	0 (5)
Total fat (g)	69 (22)	61 (20)	73 (22) ^c	61 (20)	56 (19)	64 (20) ^b	- 8 (18) ^z	- 5 (17) ^x	- 9 (18) ^z
Saturated fat (g)	23 (9)	21 (8)	24 (9) ^b	20 (9)	19 (9)	21 (9)	- 3 (8) ^z	- 2 (7) ^x	- 3 (8) ^z
Trans fat (g)	2.3 (1.1)	2.0 (1)	2.4 (1.1) ^b	2.1 (1.1)	1.9 (1.1)	2.2 (1.1) ^a	- 0.2 (1.1) ^y	- 0.1 (1.1)	- 0.3 (1.2) ^y
Monounsaturated fat (g)	24 (8)	21 (8)	26 (8) ^c	22 (8)	20 (7)	23 (8) ^b	- 2 (7) ^z	- 1 (8) ^x	- 3 (7) ^z
Polyunsaturated fat (g)	13 (6)	12 (6)	14 (6) ^a	12 (4)	11 (4)	13 (5) ^a	- 1 (5) ^z	-1 (6)	- 1 (5) ^y
Alcohol, median (IQR)(g)	7 (0-23)	1 (0-12)	13 (0-27) ^a	4 (0-16)	0 (0-11)	5 (0-18) ^b	0 (-3-1) ^z	0 (-3-4)	-3 (-14-0) ^{c,z}
% Energy from protein	18.3 (3.6)	19.0 (3.7)	18.0 (3.5) ^a	18.8 (3.5)	19.0 (3.3)	18.7 (3.6)	0.5 (3.7) ^z	0.0 (3.6)	0.7 (3.8) ^y
% Energy from total carbohydrates	43.2 (6.6)	44.8 (6.4)	42.4 (6.6) ^a	44.1 (6.5)	44.7 (6.2)	43.8 (6.6)	0.9 (6.0) ^z	- 0.1 (6.2)	1.4 (5.9) ^y
% Energy from total fat	33.5 (5.6)	33.4 (5.8)	33.6 (5.5)	33.3 (5.8)	33.3 (6.4)	33.3 (5.4)	-0.2 (5.9)	- 0.1 (6.3)	- 0.3 (5.7)
% Energy from saturated fat	11.2 (3.1)	11.4 (3.4)	11.2 (3.1)	11.0 (3.4)	11.1 (3.6)	10.9 (3.2)	- 0.3 (3.3)	- 0.3 (3.1)	- 0.3 (3.5)
% Energy from trans fat	1.1 (0.4)	1.1 (0.43)	1.1 (0.5)	1.1 (0.5)	1.1 (0.4)	1.1 (0.5)	0.0 (0.5)	0.0 (0.5)	0.0 (0.5)
% Energy from monounsaturated fat	11.7 (2.5)	11.5 (2.6)	11.9 (2.5)	11.9 (2.5)	11.7 (2.7)	12.0 (2.5)	- 0.2 (2.8)	0.2 (3.2)	0.1 (2.6)
% Energy from polyunsaturated fat	6.5 (2.2)	6.7 (2.4)	6.4 (2.1)	6.6 (1.9)	6.6 (1.9)	6.6 (1.9)	0.1 (2.4)	0.0 (2.6)	0.2 (2.3)
% Energy from total sugar	17.2 (5.7)	18.7 (5.5)	16.5 (5.6) ^b	17.7 (5.7)	18.8 (5.4)	17.2 (5.8) ^a	0.5 (5.0)	0.2 (5.2)	0.7 (4.9)
% Energy from alcohol	3 (0-8)	1 (0-5)	5 (0-9) ^c	2 (0-7)	0 (0-6)	2 (0-7) ^a	0 (-3-1) ^z	0 (-1-2)	-1 (-4-0) ^{c,z}

a = p<0.05; b = p<0.005; c = p<0.001 women vs. men

y = p<0.005; z = p<0.001 baseline vs. 6 months

Table 3: Associations between macronutrients and metabolic outcomes in men (n=148) and women (n=75) who provided physical activity data.

Macronutrient		Metabolic outcomes	Regression coefficient, β (95% Confidence interval)	p value
Change to % energy from total carbohydrates	Men	HbA1c % (mmol/l)	-0.003 (-0.006, -0.001) (-0.005 (-0.009, -0.001))	0.009
	All	Total cholesterol	-0.023 (-0.044, -0.002)	0.033
Change to fibre (nsp) intake (g)	Men	Total cholesterol	-0.025 (-0.047, -0.003)	0.023
	All	LDL cholesterol	0.018 (0.003, 0.032)	0.016
Change to % energy from total fat	Men	LDL cholesterol	0.024 (0.006, 0.042)	0.011
	All	Waist circumference	0.014 (0.003, 0.024)	0.011
Change to % energy from trans fat	Women	Waist circumference	0.029 (0.006, 0.052)	0.015
		Total cholesterol	0.399 (0.028, 0.770)	0.036
		LDL cholesterol	0.365 (0.042, 0.688)	0.028
Change to % energy from monounsaturated fats	All	LDL cholesterol	0.036 (0.006, 0.065)	0.018
	All	Diastolic blood pressure	0.217 (0.020, 0.414)	0.031
Change to % energy from alcohol	Men	Diastolic blood pressure	0.276 (0.055, 0.497)	0.015

All models are adjusted for change in energy intake, outcome at baseline, age, BMI, time since diagnosis, relevant hypoglycaemic mediation (metformin, sulphonylureas, glitazones), lipid lowering medication or anti-hypertensives, dietary supplements, mean daily minutes of moderate to vigorous physical activity.

For each macronutrient listed a 1% (1g for fibre) increase is associated with the change in outcome listed

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3 **Dietary changes and associations with metabolic improvements in**
4 **adults with Type 2 diabetes during a patient-centred dietary**
5 **intervention: an exploratory-secondary analysis**
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17 The study was carried out at The University of Bristol, Senate House, Tyndall Avenue,
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36 Running title: Dietary change in adults with Type 2 diabetes

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39 *Keywords: Type 2 diabetes, dietary analysis, dietary change*

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43 Bath Research Ethics Committee (05/Q2001/5)

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46 Word count

47
48 Abstract: 299

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50 Main text: 3758

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3 1 Abstract

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5 2 *Objectives:* Describe dietary intake of participants enrolled in a non-prescriptive dietary
6 intervention and ~~Examine dietary dietary~~ changes at 6 months ~~reported during a non-~~
7 ~~prescriptive dietary intervention~~ and explore whether these changes had a role in observed
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9 4 improvements in HbA1c, weight, lipids and blood pressure.

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12 6 *Design:* Secondary analysis of data from the Early ACTivity in Diabetes randomised
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14 7 controlled trial.

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17 8 *Participants* 262 patients with newly diagnosed Type 2 diabetes randomised to the dietary
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19 9 intervention.

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21 10 *Outcomes and analysis:* Changes in energy intake, macronutrients, fibre and alcohol and in
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23 11 weight, waist circumference, lipids, HbA1c and blood pressure at baseline and 6 months.
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25 12 Multivariate models were used to examine associations between dietary changes and
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27 13 metabolic variables.

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29 14 *Results:* Men reported reducing mean energy intake from 1903 ± 462 kcal to 1685 kcal \pm
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31 15 439 kcal ($p < 0.001$), increasing carbohydrate intake from $42.4 \pm 6.6\%$ to $43.8 \pm 6.6\%$
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33 16 ($p = 0.002$) and reducing median alcohol intake from ~~138 (0-27)g \pm 20g~~ to ~~115 \pm 14g(0-18)g~~
34
35 17 ($p < 0.001$). Women reported reducing mean energy intake from 1582 ± 379 kcal to ~~1450~~ \pm
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37 18 326 kcal ($p < 0.001$) with no change to macronutrient distribution and ~~no reduction in~~ alcohol.
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39 19 Fibre intake was maintained. In men ($n = 148$) weak and clinically insignificant associations
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41 20 were found between increased carbohydrates and reduction in HbA1c ($\beta = -0.003$ [-0.006, -
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43 21 0.001]; $p = 0.009$), increased fibre and reduction in total cholesterol ($\beta = -0.023$ [-0.044, -
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45 22 0.002]; $p = 0.033$), decreased total fat and reduction in LDL-cholesterol ($\beta = 0.024$ [0.006,
46
47 23 0.001]; $p = 0.011$), and decreased alcohol and reduction in diastolic blood pressure ($\beta = 0.276$
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49 24 [0.055, 0.497]; $p = 0.015$). In women ($n = 75$) associations were found between a decrease in
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51 25 trans-fats and reductions in waist circumference ($\beta = -0.029$ [0.006, 0.052]; $p = 0.015$), total
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53 26 cholesterol ($\beta = 0.399$ [0.028, 0.770]; $p = 0.036$) and LDL cholesterol ($\beta = 0.365$ [0.042, 0.668];
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55 27 $p = 0.028$).

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58 28 *Conclusion:* Clinically ~~important~~ significant metabolic improvements observed in a patient-
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60 29 centred dietary intervention ~~were~~ are not explained by changes in ~~percentage intake of~~

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3 30 macronutrients. However, a non-prescriptive approach may promote a reduction in total
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5 31 energy intake whilst maintaining fibre consumption.
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For peer review only

32 Article summary33 Strengths and limitations

- 34 • Describes the dietary intake of people soon after diagnosis of Type 2 DM living in the
35 UK, the dietary changes made during a dietary intervention and explores amines
36 associations between dietary changes and changes in metabolic outcomes. This
37 intervention was based on the dietary advice that is given in routine clinical practice
38 in the UK.
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- 40 • Only 53% of the participants provided food diary data at the end of the trial and these
41 people showed greater improvements in metabolic outcomes than those who did not
42 return food diaries. It is probable that they were more motivated than a typical patient
43 group and this limits the generalizability of the findings.

44 Introduction

45 Dietary management is recognised as highly important in the treatment of Type 2 diabetes
46 (Type 2 DM). Based upon meta-analyses of exercise and diet studies, the American Diabetes
47 Association (ADA) and European Association for the Study of Diabetes (EASD) recommend
48 that lifestyle interventions should be initiated as the first step in treating new-onset Type 2
49 DM [1]. Over the last 3 years, The Look Ahead research group, the Lifestyle Over and Above
50 Drugs in Diabetes (LOADD) and Early Activity in Diabetes (Early ACTID) randomised
51 controlled trials (RCTs) have shown that dietary interventions which target weight reduction
52 are beneficial and improve glycaemic control [2-4]. These trials achieved reductions in
53 HbA1c comparable to reductions demonstrated in patients starting metformin or a gliptin as
54 monotherapies [5] and, although the Look Ahead trial showed no reduction in cardiovascular
55 events after 9.6 years, participants in the intervention arm were less likely to be treated with
56 insulin [6].

57
58 It has been reported that changes to the macronutrient composition of the diet may impact
59 upon glycaemic control, blood lipids and weight [7], but the effect of specific dietary
60 changes on these metabolic outcomes are still unclear and no single 'diet for diabetes' has
61 been identified [8]. In recognition of this, both the 2012 ADA and EASD joint guidelines and
62 2011 Diabetes UK nutritional guidelines emphasise the importance of an individualised,
63 patient-centred approach to diet rather than a prescriptive approach [1,9]. This approach
64 recognises that different people have different individual dietary habits and may find certain
65 dietary changes more straightforward than others. There is evidence that men and women
66 living in the UK have differing dietary patterns [10]. Men have been reported to drink more
67 alcohol and consume more meat but less fruit and diet soft drinks than women [11]. Few
68 studies have looked at what changes to macronutrients are made to macronutrients in
69 response to non-prescriptive dietary advice, whether men and women make different changes
70 this type of dietary advice and whether how these changes impact on metabolic control.

71
72 The Early ACTID trial included a non-prescriptive, patient-centred dietary intervention. The
73 trial aimed to assess whether adding physical activity to a dietary intervention produced
74 greater benefit than diet alone or usual care in individuals newly diagnosed with Type 2 DM
75 [4]. Participants who received the lifestyle interventions had better HbA1c, lower body

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3 76 weight, less insulin resistance, and were on less medication than the control group at 6 and 12
4 77 months. During the intervention participants in this cohort reported small changes to higher
5 calorie, low fibre foods. Examination of the specific changes to foods and food groups
6 reported by participants has been previously published [12] and this current paper focuses on
7 macronutrients.
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14 82 The aim of this paper is to describe baseline energy and macronutrient intakes of men and
15 women who were enrolled into the dietary intervention in the Early ACTID study and to
16 examine the reported dietary changes made after 6 months. by men and women newly
17 diagnosed with Type 2 DM who were enrolled into the dietary intervention in the Early
18 ACTID study.
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24 87 We conducted exploratory analysis to examine the following hypotheses:

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26
27 88 • Men and women with Type 2 DM make different dietary changes in response to a
28 dietary intervention.
29
30 90 • The changes to energy intake and macronutrients are associated with the
31 observed beneficial changes to glycaemic control, weight, waist circumference, blood
32 pressure and lipids. The associations between changes to energy, macronutrients and
33 metabolic outcomes were explored to determine the effect of dietary changes on the
34 metabolic variables.
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39 Subjects and methods

40 41 96 *Subjects*

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44 97 This paper is an exploratory secondary analysis of data from the Early ACTID randomised
45 98 controlled trial. Early ACTID was a diet and physical activity trial involving patients living in
46 99 the South West of England who were recruited within 5 to 8 months of a diagnosis of Type 2
47 100 DM from December 2005 to September 2008. Full trial procedures with the CONSORT
48 101 diagram and results are described elsewhere [4, 13, 14]. The analysis is limited to participants
49 102 in the intervention arms who returned valid food diary data.
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54 55 103 *Overview of the dietary intervention*

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3 104 Patients in the diet alone and the diet and physical activity groups received the same dietary
4 105 intervention. For the first 6 months the intervention aimed to promote dietary change. At
5 106 randomisation patients attended a one-hour appointment with a study dietitian followed by 2
6 107 further visits of 30 minutes. These visits were supported by 6 additional visits with a research
7 108 nurse, where 15 minutes were used to discuss dietary matters for both groups, reinforcing
8 109 dietary goals, and 15 minutes to discuss either physical activity or other matters pertinent to
9 110 the patient, depending upon intervention group allocated to. Maintenance was the primary
10 111 goal of the second 6 months and consisted of 2 more 30 minute dietitian visits and 4
11 112 additional visits with the research nurses.

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19 113 The dietary intervention was based upon the 2003 Diabetes UK healthy eating guidelines [15]
20 114 and employed goal oriented motivational interviewing [16]. Patients were encouraged to
21 115 discuss their reasons for change, any ambivalence about change and to set their own dietary
22 116 goals and identify their own strategies for achieving these goals. Prescriptive daily
23 117 requirements for energy or macronutrients were not calculated unless requested by the patient
24 118 and prescriptive meal plans or food lists were not used. Instead patients received study
25 119 specific written dietary information at each visit (available here:
26 120 <http://jcrubristol.org.uk/EA/ACTID%20patients%20Handbook/Forms/AllItems.aspx>) and
27 121 were encouraged to use this to evaluate their own eating habits. The materials included
28 122 information on maintaining a regular meal pattern and including starchy carbohydrates as a
29 123 part of each meal, reducing total, saturated and *trans* fat intake, limiting non-milk extrinsic
30 124 sugars, aiming for 5 portions a day of fruit and vegetables and gave guidance on portion
31 125 control. Specific food choices were discussed and participants were advised on choosing
32 126 wholegrain and higher fibre foods, reducing fatty and processed meats and; high fat dairy
33 127 products, e and increasing oily fish and limiting foods like cakes, biscuits, salty snacks and
34 128 take-away meals. The benefit of aiming for a 5 to 10% weight loss by reducing overall
35 129 energy intake was discussed with everyone. Goals were reviewed at each appointment and
36 130 successes, difficulties and new strategies discussed. Patients were encouraged to self-monitor
37 131 their weight and diet.

38 39 40 41 42 43 44 45 46 47 48 49 50 51 *Measurements*

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54 133 Measures were taken at baseline (prior to randomisation) and repeated 6 and 12 months later.
55 134 Baseline and 6 month data were used in the current analysis, since outcomes at 6 months

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3 135 were defined as the primary endpoint of the study. Measurements used in this analysis were
4 136 weight, height (to calculate body mass index (BMI)), waist circumference, blood pressure,
5 137 HbA1c, fasting lipids and minutes of moderate to vigorous physical activity (MVPA)
6 138 measured using accelerometry and defined as activity expending greater than 3kcal/kg/hour .
7
8 139 As previously described, blood measurements and anthropometric measures were carried out
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10 140 using standardised procedures [13]. Smoking habits and use of dietary supplements were
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12 141 assessed by a research nurse. The UK Index of Multiple Deprivation (IMD) 2007 was
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14 142 calculated from home postcode and used as an indicator of socio-economic position [17].
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17 143 *Dietary assessment and analysis*

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20 144 Patients in the intervention arms were asked to complete 4-day food diaries, to include 2
21 145 weekdays and 1 weekend day, prior to each dietitian appointment, recording all foods and
22
23 146 drinks consumed during those 4 days. Portion sizes were estimated using household measures
24
25 147 and package weights and brands indicated where appropriate. The diaries were discussed
26
27 148 during the appointments and used to identify potential areas for change, difficulties in making
28
29 149 change, and for patients to observe change in their diets over time. Patients were asked to
30
31 150 return all the diaries at the final visit for further analysis. Those who did not return diaries at
32
33 151 the visit were reminded by telephone and e-mail to post outstanding diaries to the research
34
35 152 team after the visit.

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37 153 Baseline and 6-month food diaries were coded by one coder and checked for accuracy and
38
39 154 agreement by a second coder, using the dietary coding programme Diet in Data Out (DIDO),
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41 155 developed at the Medical Research Council Human Nutrition Unit in Cambridge, UK [18].
42
43 156 Diaries were analysed with the nutrient analysis programme Bristol General Analysis of
44
45 157 Dietary Experiments (BRIGADE) [19]. The nutrient database is based on *McCance and*
46
47 158 *Widdowson's Composition of Foods, 5th edition* [20], updated with the supplements to that
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49 159 edition, new data from the 6th edition and manufacturers' data. Additional nutrient data from
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51 160 the INTERMAP nutrient database for the UK were also used [21]. If no portion size
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53 161 information was given, age-appropriate portion sizes were assigned [22]. The mean daily
54
55 162 consumption of each nutrient was calculated for each participant.

56 163 *Statistical analysis*

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3 164 As the dietary intervention was designed to be identical for both intervention groups and
4 165 there were no difference in outcomes between the diet and diet and physical activity groups,
5 166 the data were analysed as a cohort. Patients in the usual care group were excluded from the
6 167 analysis since they did not receive the dietary intervention and were not asked to complete a
7 168 diary at 6 months. Descriptive statistics were used for patient characteristics and for intakes
8 169 of macronutrients at baseline and 6 months. Variables were checked for normal distribution;
9 170 non-normal variables were log transformed prior to analysis. For ease of interpretation,
10 171 arithmetic means and back transformed variables are presented. Independent *t*-tests were used
11 172 to explore differences in continuous variables between men and women at baseline and
12 173 between those who did and did not return food diaries, and chi-squared tests were used to
13 174 explore differences in dichotomous variables. Paired sample *t*-tests were used to describe
14 175 differences in energy and macronutrient intake between baseline and 6 months. McNemar
15 176 tests were used to explore differences in numbers of people meeting recommendations at
16 177 baseline and 6 months. As alcohol variables could not be transformed, the Mann Whitney U
17 178 and paired sample Wilcoxon signed rank test were used to describe differences. Cases with
18 179 missing data were excluded listwise. Data were assumed to be randomly missing and table 1
19 180 includes numerical superscripts to indicate the number of participants with missing data for
20 181 the variable of interest.

21 182 Multivariate regression models were used to conduct exploratory analysis to investigate
22 183 associations between changes in energy and macronutrient intake and the metabolic variables
23 184 at 6 months in those who provided valid physical activity data. Changes in energy intake
24 185 were explored using a standard multivariate model. Each macronutrient was explored
25 186 independently using a multivariate nutrient density model to adjust for change in energy
26 187 intake. Change in percentage energy from each macronutrient was calculated and entered into
27 188 the model with change in total energy included as a covariate. Change in fibre intake was
28 189 explored using a standard multivariate model and entered as an absolute intake (in grams)
29 190 with change to total energy intake as a covariate [23]. Models were adjusted for age, BMI,
30 191 time since diagnosis, minutes of moderate to vigorous physical activity (MVPA) and
31 192 dichotomous yes/no variables for smoking status, relevant lipid lowering, blood pressure and
32 193 diabetes medication and dietary supplement use at 6 months.

33 194 Due to the number of different analyses that were conducted the results are interpreted in
34 195 terms of strength of evidence of associations [24]. This is an exploratory analysis and as such

196 | has not been adjusted for multiple comparisons [25,26], consequently p values of <0.05 are
197 | interpreted as some evidence of association, p<0.01 as increasing evidence and p<0.001 as
198 | strong evidence.

199 | Results

200 | *Study participants*

201 | A total of 593 patients were recruited into the Early ACTID study, with 494 being assigned to
202 | one of the intervention groups. 396 (80%) patients were recorded as completing food diaries
203 | at both baseline and 6 months but only 262 (53%) patients returned them. Metabolic and
204 | dietary outcomes at baseline and 6 months are presented for these 262 patients. ~~and 223 of~~
205 | ~~these had valid accelerometry data at both time points.~~ At 6 months 491 (99%) patients
206 | assigned to one of the intervention arms remained in the study, with 434 (88%) attending all
207 | scheduled visits up to that point and a further 37 (8%) attending all except one.

208 | Mean age was 62.4 (9.0) years, 97% of patients were white, 83% were married or with a long
209 | term partner and 41% were in the lowest IMD quartile. At baseline 104 (40%) of participants
210 | were on oral hypoglycaemic medication, 170 (65%) on lipid lowering medication and 174
211 | (66%) on blood pressure medication. Only 6% of patients were current smokers at baseline.

212 | Men and women had similar characteristics, although there was some evidence that men were
213 | more likely to be on lipid lowering medication than women (69% vs. 56%, p=0.041). At 6
214 | months, 105 (40%) of participants were on oral hypoglycaemic medication, although 12 (5%)
215 | participants had increased the dose and 4 (2%) had decreased; 177 (68%) were on lipid
216 | lowering medication and 175 (67%) were on blood pressure medication.

217 | Compared to the patients who did not return food diaries, those who did were older (62 years
218 | vs 57 years, p<0.001), with a lower mean weight (88.2 kg vs 93.3 kg, p=0.001), lower mean
219 | BMI (30.7 vs 32.5, p=0.001) and lower mean waist circumference (105 cm vs 108 cm,
220 | p=0.025), but there was no difference in glycaemic control, lipids and blood pressure.

221 | *Metabolic outcomes*

222 | Table 1 shows the metabolic outcomes at baseline and 6 months for those who returned food
223 | diaries. There was no difference in glycaemic control or blood pressure between men and

224 women, but women had higher total (p<0001), LDL (p<0.001) and HDL (p=0.015)
225 cholesterol levels.

226 Weight, waist circumference and BMI improved at 6 months for both men and women
227 (p<0.001). Men and women improved their HbA1c (men: p=0.006; women: p<0.001). Men
228 improved their fasting blood glucose (p=0.006) and there is some evidence that women
229 increased their HDL cholesterol (p=0.033).

230 At 6 months those who returned food diaries had lost more weight (2.4 kg vs 1.3 kg,
231 p=0.001), reduced waist circumference more (2.7 cm vs 1.3 cm, p=0.022) and reduced
232 HbA1c (0.18% (2 mmol/l) vs 0% (0 mmol/l), p=0.02).

233 *Nutrient analysis*

234 Table 2 shows the mean reported energy and nutrient intakes at baseline and 6 months and
235 their mean reported changes.

236 At baseline participants reported generally good dietary habits. 61% of women and 59% of
237 men reported the recommended total fat intake (less than 35% of energy from total fat) and
238 55% of women and 66% of men reported a low to moderate carbohydrate intake (<45% of
239 energy). Men were more likely to drink alcohol and more likely to drink to excess than
240 women with 49% of women and 28% of men recording no alcohol during the 4 days and 8%
241 of women and 19% of men reporting more than 30g of alcohol per day (p=0.022).

242 At 6 months mean daily reported energy intake was reduced by 187 kcal (p<0.001). Men
243 reduced their energy intake more than women (218 ± 332 vs. 123 ± 270 kcal/day, p=0.022).
244 This was achieved by small reductions in all macronutrients, whilst maintaining fibre intake.
245 The mean percentage energy from macronutrients was unchanged for women whilst men
246 reported a small mean increase of 1.4 ± 5.9% (p<0.001) of energy from carbohydrates. Men
247 reported reducing ~~mean~~ median alcohol intake (p<0.001), with 40% reporting no alcohol
248 during the 4 days and 15% reporting more than 30g per day. There was no reported
249 median~~mean~~ change in alcohol intake for women. Despite no mean change to energy from
250 saturated fat, more men met recommendations at 6 months (35% men at baseline vs. 49% at 6
251 months reporting less than 10% energy from saturated fat, p=0.007). There was no change in
252 the number of women meeting recommendations (40% baseline vs 44% at 6 months,
253 p=0.71).

254 | Valid physical activity data and dietary data were provided by 223 (45%) participants. Table
255 | 3 shows the regression coefficients and confidence intervals for changes in energy and
256 | macronutrients that show evidence for associations with specific metabolic variables. In men
257 | a 1% reduction in energy from alcohol was associated with a 0.276 mmHg reduction in
258 | diastolic blood pressure (95% CI= 0.055 to 0.497). In women a 1% reduction in energy from
259 | trans-fat was associated with a decrease in cholesterol of 0.399 mmol/l (95% CI= 0.028 to
260 | 0.770). In men a 1% increase in energy from carbohydrate was associated with a decrease in
261 | HbA1c of 0.003% (95% CI= -0.006 to -0.001). There were no associations between change
262 | in energy intake and the metabolic variables.

264 | Discussion

265 | *Main findings*

266 | The main findings from this exploratory analysis are that patients who were randomised to
267 | the intervention arms in the Early ACTID study and returned food diaries reported a good
268 | diet at baseline but still achieved small dietary changes. They reported a mean decrease in
269 | energy intake of around 200 kcal per day, during the first 6 months. This is a modest
270 | reduction in calorie intake but, if sustained, will have an impact on weight and glycaemic
271 | control. It has been argued that long-term small changes are more effective for weight
272 | management than short-term large changes [27]. Men reported a reduced alcohol intake that
273 | produced a greater reduction in energy and reported a small increase in the percentage energy
274 | from carbohydrate. Women reported modest reductions to all macronutrients but made no
275 | changes to alcohol, their energy reduction was less and the macronutrient ratio of their diets
276 | did not change. Both sexes maintained fibre intake. Although changes in percentage intake of
277 | macronutrients were associated with metabolic outcomes, these effect sizes were too small to
278 | be of clinical significance.

279 | ~~These results suggest that current recommendations that dietary advice is personalised,
280 | flexible and focuses on realistic, achievable, and sustainable reductions in intake may
281 | promote dietary change in people with T2-DM.~~

282 | *Comparison with other studies*

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3 283 The Early ACTID dietary intervention was a pragmatic, ‘real world’ intervention, in which
4 284 participants discussed dietary advice with dietitians and nurses to decide on their own dietary
5 285 changes. The approach contrasts with dietary studies where participants are asked to make
6 286 specific, prescribed changes to the macronutrient composition, by lowering carbohydrate and
7 287 increasing protein [28-30] or to lower the glycaemic index [31 ,32]. The LOADD trial [3]
8 288 based a successful dietary intervention in patients with poor glycaemic control on very
9 289 similar recommendations to those used in the Early ACTID intervention, but total energy
10 290 intake and macronutrient ratios for each participant were calculated and diets were prescribed
11 291 according to these calculations taking into account personal preference, budget and
12 292 sociocultural factors. The Early ACTID intervention did not compare a prescriptive with a
13 293 non-prescriptive approach so cannot be used to demonstrate that this is superior but
14 294 reductions in weight, waist circumference and HbA1c were achieved that are comparable to
15 295 those achieved during these interventions. Withdrawal rates for prescriptive dietary
16 296 interventions range from 10% to 30% and these higher withdrawal rates may suggest that in
17 297 routine clinical care a more flexible approach can be advantageous in promoting retention. Of
18 298 those participants in Early ACTID who either did not attend all appointments or withdrew
19 299 completely, only one person stated that they did not see the benefit of the trial. The majority
20 300 could not schedule all 9 dietitian and nurse visits because of other commitments, 5 cited other
21 301 health issues, 3 moved too far away, 1 said they ‘did not want to diet,’ 1 wanted to take
22 302 orlistat from baseline and 3 gave no reasons. What is common to intervention trials in
23 303 diabetes is that patients receive individual support and attend multiple appointments with a
24 304 dietitian or a health practitioner who is expert in promoting dietary change. It is important to
25 305 emphasise that this model is not routinely replicated in primary care for patients with Type 2
26 306 DM.

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44 307 Exploratory analysis of the associations between specific dietary changes and metabolic
45 308 outcomes found small have not, as far as we are aware, previously been examined in patients
46 309 with Type 2 DM. Effect sizes were small and not that are not clinically important, significant
47 310 but they are consistent with existing nutritional data on the benefits of a reduction in trans fats
48 311 on lipids and waist circumference [33], an increase in fibre on LDL cholesterol [34] and a
49 312 reduction in alcohol and blood pressure [35]. It is of interest that this analysis found that there
50 313 was no benefit in carbohydrate reduction in men with good glycaemic control who are
51 314 already consuming a low to moderate carbohydrate diet. It is not possible to determine

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3 315 whether there is an optimum macronutrient distribution for T2 DM from this analysis,
4 316 particularly in those with poor glycaemic control, but there is no unequivocal evidence that
5 317 low carbohydrate diets produce better blood glucose control or weight loss than higher
6 318 carbohydrate diets [36]. A meta-analysis of low carbohydrate diets versus low fat diets
7 319 conducted in 2012 [37] concluded that there was evidence of a small but beneficial effect on
8 320 lipid profiles of a low (defined as <45% energy from carbohydrate) or very low carbohydrate
9 321 (<60g carbohydrate) diet but no difference in improvements to weight or glycaemic control.
10 322 Larsen et al [29] correlated dietary change with metabolic outcomes and found associations
11 323 with energy reduction and HbA1c and waist circumference.

12 324 *Strengths and weaknesses*

13 325 To our knowledge this is the first study to describe the dietary intake of people soon after
14 326 diagnosis with Type 2 DM living in the UK, the dietary changes made during an intervention
15 327 based on patient-centred, non-prescriptive dietary advice and that examines associations
16 328 between dietary change and metabolic variables. The demographics of the Early ACTID
17 329 participants included in this analysis suggest that these findings are only representative of the
18 330 white population; however the sample is socio-economically diverse with 40% of participants
19 331 living in areas of high economic deprivation. Ethical approval was granted to make no
20 332 changes to hypoglycaemic, lipid lowering or blood pressure medications during the first 6
21 333 months, unless absolutely necessary and this was controlled by a strict protocol. Due to small
22 334 numbers those participants who made medication changes were included in the analysis
23 335 without correction.

24 336 The study has important weaknesses. Only 53% of the participants returned baseline and 6
25 337 month food diaries at the end of the trial and these people had a lower BMI and waist
26 338 circumference at baseline and achieved greater metabolic improvements. The participants
27 339 who did not return diaries reported mislaying them which may indicate less motivation and
28 340 less engagement with the trial. Participants who did return diaries could have been more
29 341 motivated to make dietary changes than a typical patient population, and, given that their
30 342 diets were good at baseline, may already have made dietary changes prior to entry into the
31 343 Early ACTID study. The relative lack of dietary data limits our ability to generalise these
32 344 findings to broader patient groups. Furthermore this was an exploratory analysis using an
33 345 existing dataset and as such an estimation of sample size was not conducted in advance. .

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3 346 However, post hoc sample calculations indicate that the study was underpowered to detect small
4 347 associations between dietary changes and metabolic outcomes, having 15% power for women and
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6 348 52% for men at an alpha of 0.05.
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11 350 The use of any self-reported measure of diet, including 4-day food diaries, is a recognised
12 351 limitation in dietary studies. Under-reporting of food intake and selective under-reporting or
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14 352 under-eating of foods perceived to be ‘bad’ are commonly documented, especially in people
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16 353 who are obese [38 ,39]. Measurement of alcohol can be problematic due to the episodic
17 354 nature of consumption, although including at least one weekend day can improve estimates
18 355 by including alcohol consumption of ‘weekend-only’ drinkers [40]. Methods exist to estimate
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20 356 under-reporting, using calculated basal metabolic rate and estimates of physical activity [41
21 357 ,42] but these methods assume that an individual’s weight is stable and are consequently
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23 358 inappropriate for use during a weight loss trial. It should be noted that other dietary
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25 359 interventions in patients with Type 2 DM have reported similar energy intakes [28 ,31] and
26 360 an energy reduction of around 200kcal/day is plausible assuming a dynamic model of energy
27
28 361 balance [43] and given the modest weight reduction observed. It is also important to note that
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30 362 this is a secondary analysis so cause and effect cannot be assumed. It was not possible to
31 363 perform a formal mediation analysis since participants from the control arm were not asked to
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33 364 complete a food diary at 6 months.
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36
37 365 *Conclusion*
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39 366 The Early ACTID trial indicates that a flexible, non-prescriptive approach to dietary advice
40 367 based on standard healthy eating guidelines in Type 2 DM given soon after diagnosis may be
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42 368 effective in promoting small dietary change, even in patients with good glycaemic control.
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44 369 This supports current clinical practice and guidelines. The current analysis suggests that
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46 370 changes in percentage intake of macronutrients did not have any clinically significant effect
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48 371 on metabolic outcomes during the trial but this needs confirmation in a larger cohort, with
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50 372 less good glycaemic control. Further research is needed on whether dietary changes made
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52 373 using a non-prescriptive approach are sustainable and beneficial in the longer term in a more
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54 374 typical patient population.
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Acknowledgements

We would like to acknowledge the participants in the Early ACTID trial, members of the Early ACTID team and steering committee, Dr Pauline Emmett for advice on dietary analysis, Dr Rosemary Greenwood for advice on statistical analysis and Professor Debbie Sharp for assistance in manuscript preparation.

Funding

The Early ACTID trial was supported by Diabetes UK, the UK Department of Health and Western Comprehensive Local Research Network. Pilot dietary analysis was supported by the Above and Beyond Foundation. C.Y. England is supported by NIHR Clinical Doctoral Research Fellowship 10-017.

Authors' contributions

This work forms part of the PhD of CYE which is supervised by RCA, JLT and RJ. RCA led the Early ACTID study and advised on clinical application of this work. CYE participated in data collection, data entry and was responsible for data analysis with guidance from JLT and RJ. ARC was responsible for the design of the ACTID physical activity intervention and for processing and analysis of the physical activity data. The first draft of the manuscript was prepared by CYE with critical input and revisions by all other authors. All authors approved the final manuscript.

Conflicts of interests

The authors declare that they have no conflict of interest

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Table 1: Metabolic characteristics at baseline and 6 months

Metabolic characteristics	Baseline			6 months			Change (6 months - baseline)		
	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)
Weight, kg	88.2 (16.1)	83.1 (17.9)	90.7 (14.5) ^e	85.9 (16.3)	80.7 (17.7)	88.5 (15.0)	- 2.3 (3.3) ^z	- 2.5 (3.3) ^z	- 2.3 (3.3) ^z
Body mass index, kg/m ²	30.7 (5.3)	31.9 (6.9)	30.2 (4.7) ^a	29.9 (5.4)	30.9 (6.2)	29.4 (4.9)	- 0.8 (1.2) ^z	- 1 (1.0) ^z	- 0.8 (1.1) ^z
Waist circumference, cm	105 (12)	102 (13) ¹	107 (11) ^b	103 (12)	100 (13)	104 (12)	- 3 (4) ^z	- 3 (4) ^z	- 3 (4) ^z
HbA1c, % (mmol/l)	6.66 (0.94) (49.0 (10.3))	6.67 (0.91) (49.0 (9.9))	6.65 (0.95) (49.0 (10.4))	6.47 (0.89) (47.0 (9.7))	6.41 (0.63) (47.0 (6.9))	6.51 (0.99) ¹ (48.0 (10.8))	- 0.18 (0.72) ^z (- 2.0 (7.9))	- 0.27 (0.63) ^z (- 3.0 (6.9))	- 0.14 (0.75) ^x (- 1.5 (8.2))
Total cholesterol, mmol/l	4.33 (0.90)	4.66 (0.89) ¹	4.16 (0.86) ^{1c}	4.29 (0.93)	4.66 (0.98)	4.11 (0.84)	- 0.03 (0.69)	0.01 (0.79)	- 0.06 (0.63)
LDL-cholesterol, mmol/l	2.30 (0.78)	2.55 (0.81) ³	2.18 (0.74) ^{2c}	2.27 (0.81)	2.51 (0.88) ³	2.15 (0.75) ¹	- 0.03 (0.67)	- 0.03 (0.76)	- 0.03 (0.62)
HDL-cholesterol, mmol/l	1.29 (0.33)	1.37 (0.39) ¹	1.25 (0.29) ^{1a}	1.34 (0.37)	1.45 (0.47)	1.28 (0.30)	0.05 (0.27) ^y	0.09 (0.37) ^x	0.03 (0.21)
Systolic blood pressure, mmHg	134 (16)	133 (16)	134 (15)	134 (15)	135 (16)	134 (14)	1 (12)	2 (13)	0 (12)
Diastolic blood pressure, mmHg	79 (8)	78 (8)	79 (8)	78 (8)	78 (8)	78 (8)	0 (7)	0 (8)	0 (7)
Physical activity (n=223)	(n=223)	(n=75)	(n=148)	(n=223)	(n=75)	(n=148)	(n=223)	(n=75)	(n=148)
Minutes of moderate to vigorous physical activity / day (MVPA)	26 (21)	21 (18) ¹²	29 (22) ²⁷	33 (25)	21 (19)	38 (26)	7 (21)	1 (12)	10 (24)

a = p<0.05; b = p<0.005; c = p<0.001 women vs. men at baseline

x = p<0.05; y = p<0.005; z = p<0.001 baseline vs. 6 month

Numerical superscripts indicate number of participants with missing data for the variable of interest. [Cases with missing data are excluded listwise](#)

Table 2: Nutrient intake at baseline and 6 months

Mean daily intake nutrients	Baseline			6 months			Change (6 months - baseline)		
	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)	Total (n=262) Mean (SD)	Women (n=87) Mean (SD)	Men (n=175) Mean (SD)
Energy (kcal)	1796 (461)	1582 (379)	1903 (462) ^c	1610 (418)	1459 (326)	1685 (439) ^c	-187 (315) ^z	- 123 (270) ^z	- 218 (332) ^{az}
Protein (g)	80 (19)	73 (16)	83 (20) ^c	74 (19)	68 (13)	77 (20) ^c	- 6 (17) ^z	- 5 (15) ^y	- 6 (19) ^z
Total carbohydrates (g)	202 (55)	186 (48)	211 (57) ^b	186 (53)	170 (39)	194 (58) ^b	- 17 (41) ^z	- 15 (33) ^z	- 17 (45) ^z
Total sugar (g)	81 (32)	77 (28)	83 (34)	75 (31)	71 (23)	77 (34)	- 6 (26) ^z	- 6 (21) ^x	- 6 (28) ^y
Starch (g)	119 (36)	105 (30)	126 (37) ^c	109 (31)	97 (26)	115 (32) ^c	-10 (28) ^z	- 9 (24) ^y	- 11 (30) ^z
Non-starch polysaccharide (g)	17 (5)	16 (5)	17 (5)	16 (5)	15 (4)	17 (5) ^a	- 1 (5)	- 1 (4)	0 (5)
Total fat (g)	69 (22)	61 (20)	73 (22) ^c	61 (20)	56 (19)	64 (20) ^b	- 8 (18) ^z	- 5 (17) ^x	- 9 (18) ^z
Saturated fat (g)	23 (9)	21 (8)	24 (9) ^b	20 (9)	19 (9)	21 (9)	- 3 (8) ^z	- 2 (7) ^x	- 3 (8) ^z
Trans fat (g)	2.3 (1.1)	2.0 (1)	2.4 (1.1) ^b	2.1 (1.1)	1.9 (1.1)	2.2 (1.1) ^a	- 0.2 (1.1) ^y	- 0.1 (1.1)	- 0.3 (1.2) ^y
Monounsaturated fat (g)	24 (8)	21 (8)	26 (8) ^c	22 (8)	20 (7)	23 (8) ^b	- 2 (7) ^z	- 1 (8) ^x	- 3 (7) ^z
Polyunsaturated fat (g)	13 (6)	12 (6)	14 (6) ^a	12 (4)	11 (4)	13 (5) ^a	- 1 (5) ^z	-1 (6)	- 1 (5) ^y
Alcohol median (IQR) (g)	7 (0-23) 14 (18)	1 (0-12) 7 (11)	13 (0-27) 18 (20) ^a	4 (0-16) 10 (13)	0 (0-11) 7 (9)	5 (0-18) 11 (14) ^b	0 (-3-1) -5 (14) ^z	0 (-3-4) 10	-3 (-14-0) -7 (15) ^{cz}
% Energy from protein	18.3 (3.6)	19.0 (3.7)	18.0 (3.5) ^a	18.8 (3.5)	19.0 (3.3)	18.7 (3.6)	0.5 (3.7) ^z	0.0 (3.6)	0.7 (3.8) ^y
% Energy from total carbohydrates	43.2 (6.6)	44.8 (6.4)	42.4 (6.6) ^a	44.1 (6.5)	44.7 (6.2)	43.8 (6.6)	0.9 (6.0) ^z	- 0.1 (6.2)	1.4 (5.9) ^y
% Energy from total fat	33.5 (5.6)	33.4 (5.8)	33.6 (5.5)	33.3 (5.8)	33.3 (6.4)	33.3 (5.4)	-0.2 (5.9)	- 0.1 (6.3)	- 0.3 (5.7)
% Energy from saturated fat	11.2 (3.1)	11.4 (3.4)	11.2 (3.1)	11.0 (3.4)	11.1 (3.6)	10.9 (3.2)	- 0.3 (3.3)	- 0.3 (3.1)	- 0.3 (3.5)
% Energy from trans fat	1.1 (0.4)	1.1 (0.43)	1.1 (0.5)	1.1 (0.5)	1.1 (0.4)	1.1 (0.5)	0.0 (0.5)	0.0 (0.5)	0.0 (0.5)
% Energy from monounsaturated fat	11.7 (2.5)	11.5 (2.6)	11.9 (2.5)	11.9 (2.5)	11.7 (2.7)	12.0 (2.5)	- 0.2 (2.8)	0.2 (3.2)	0.1 (2.6)
% Energy from polyunsaturated fat	6.5 (2.2)	6.7 (2.4)	6.4 (2.1)	6.6 (1.9)	6.6 (1.9)	6.6 (1.9)	0.1 (2.4)	0.0 (2.6)	0.2 (2.3)
% Energy from total sugar	17.2 (5.7)	18.7 (5.5)	16.5 (5.6) ^b	17.7 (5.7)	18.8 (5.4)	17.2 (5.8) ^a	0.5 (5.0)	0.2 (5.2)	0.7 (4.9)
% Energy from alcohol	3 (0-8) 5.0 (6.1)	2.9 (4.3) 1 (0-5)	6.1 (6.6) 5 (0-9) ^c	3.9 (4.9) 2 (0-7)	0 (0-6) 3.0 (3.9)	4.3 (5.3) 2 (0-7) ^a	-1.2 (4.7) 0 (-3-1) ^z	0.2 (4.0) 0 (-1-2)	-1.8 (5.0) -1 (-4-0) ^{cz}

a = p<0.05; b = p<0.005; c = p<0.001 women vs. men
y = p<0.005; z = p<0.001 baseline vs. 6 months

Table 3: Associations between macronutrients and metabolic outcomes in men (n=148) and women (n=75) who provided physical activity data.

Macronutrient		Metabolic outcomes	Regression coefficient, β (95% Confidence interval)	p value
Change to % energy from total carbohydrates	Men	HbA1c % (<u>mmol/l</u>)	-0.003 (-0.006, -0.001) <u>(-0.005 (-0.009, -0.001))</u>	0.009
	All	Total cholesterol	-0.023 (-0.044, -0.002)	0.033
Change to fibre (nsp) intake (g)	Men	Total cholesterol	-0.025 (-0.047, -0.003)	0.023
	All	LDL cholesterol	0.018 (0.003, 0.032)	0.016
Change to % energy from total fat	Men	LDL cholesterol	0.024 (0.006, 0.042)	0.011
	All	Waist circumference	0.014 (0.003, 0.024)	0.011
Change to % energy from trans fat	Women	Waist circumference	0.029 (0.006, 0.052)	0.015
		Total cholesterol	0.399 (0.028, 0.770)	0.036
		LDL cholesterol	0.365 (0.042, 0.688)	0.028
Change to % energy from monounsaturated fats	All	LDL cholesterol	0.036 (0.006, 0.065)	0.018
Change to % energy from alcohol	All	Diastolic blood pressure	0.217 (0.020, 0.414)	0.031
	Men	Diastolic blood pressure	0.276 (0.055, 0.497)	0.015

All models are adjusted for change in energy intake, outcome at baseline, age, BMI, time since diagnosis, relevant hypoglycaemic mediation (metformin, sulphonylureas, glitazones), lipid lowering medication or anti-hypertensives medication, dietary supplements, mean daily minutes of moderate to vigorous physical activity. For each macronutrient listed a 1% (1g for fibre) increase is associated with the change in outcome listed