Healthy Behavior Change and Cardiovascular Outcomes in Newly Diagnosed Type 2 Diabetes Patients: A Cohort Analysis of The ADDITION-Cambridge Study

OBJECTIVE
To examine whether improvements in health behaviors are associated with reduced risk of cardiovascular disease (CVD) in individuals with newly diagnosed type 2 diabetes.

RESEARCH DESIGN AND METHODS
Population-based prospective cohort study of 867 newly diagnosed diabetes patients aged between 40 and 69 years from the treatment phase of the ADDITION-Cambridge study. Because the results for all analyses were similar by trial arm, data were pooled, and results were presented for the whole cohort. Participants were identified via population-based stepwise screening between 2002 and 2006, and underwent assessment of physical activity (European Prospective Investigation into Cancer-Norfolk Physical Activity Questionnaire), diet (plasma vitamin C and self-report), and alcohol consumption (self-report) at baseline and 1 year. A composite primary CVD outcome was examined, comprised of cardiovascular mortality, nonfatal myocardial infarction, nonfatal stroke, and revascularization.

RESULTS
After a median (interquartile range) follow-up period of 5.0 years (1.3 years), 6% of the cohort experienced a CVD event (12.2 per 1,000 person-years; 95% CI 9.3–15.9). CVD risk was inversely related to the number of positive health behaviors changed in the year after diabetes diagnosis. The relative risk for primary CVD event in individuals who did not change any health behavior compared with those who adopted three/four healthy behaviors was 4.17 (95% CI 1.02–17.09), adjusting for age, sex, study group, social class, occupation, and prescription of cardioprotective medication (P for trend = 0.005).

CONCLUSIONS
CVD risk was inversely associated with the number of healthy behavior changes adopted in the year after the diagnosis of diabetes. Interventions that promote early achievement of these goals in patients with newly diagnosed diabetes could help reduce the burden of diabetes-related morbidity and mortality.

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Healthy behaviors are associated with a reduced risk of mortality and cardiovascular disease (CVD) in the general population (1–3). The benefits of a healthy lifestyle for individuals at high risk for type 2 diabetes (4–7), or for those with newly diagnosed (8,9) and longstanding (10,11) diabetes are well-established. In those individuals at high risk of diabetes, interventions aimed at promoting healthy behavior changes can prevent or delay the development of diabetes (5,7) and retinopathy (12), and can lead to sustained health benefits (6). Among individuals with newly diagnosed diabetes, behavior change interventions reduce CVD risk factor levels (9) and promote weight loss (8), independent of prescribed medication. While these studies support the hypothesis that lifestyle changes early in the diabetes disease trajectory may confer long-term health benefits, they are too small and of insufficient follow-up time to confirm that lifestyle changes reduce CVD events.

Interventions among individuals with clinically diagnosed diabetes have demonstrated reductions in CVD risk factor levels (10) and CVD events (13–15). However, most of these studies have focused on the benefits of intensive pharmacological treatment (13,14). There is insufficient evidence to confirm whether improvements in health behaviors after diabetes diagnosis reduce CVD outcomes, or whether health behavior change has an impact over and above the effects of medical prescribing. This is important to elucidate at a time when many health care systems are introducing national screening programs (16), which may lead to an increase in the numbers of patients with newly diagnosed diabetes. Using data from the ADDITION-Cambridge study, a cluster-randomized trial in patients with screen-detected diabetes, we examined changes in physical activity, diet, and alcohol consumption in the year after diabetes diagnosis, and their association with CVD outcomes using 5-year follow-up data.

**RESEARCH DESIGN AND METHODS**

**Participants and Study Population**

The ADDITION-Cambridge study consisted of the following two phases: a stepwise screening program and a cluster-randomized trial comparing the effects of intensive multifactorial treatment (IT) with routine care (RC) in individuals with screen-detected type 2 diabetes (17). Data from the second treatment phase of the study are reported here. Because results for all analyses were similar by trial arm (study group), data were pooled, and results are presented for the whole cohort. Briefly, 49 general practices (GPs) in Eastern England were cluster randomized to screening, followed by IT (n = 26) or RC (n = 23). Eligible participants were aged 40 to 69 years, not known to have diabetes, and with a Cambridge Diabetes Risk Score ≥0.17, corresponding to the top 25% of participants’ risk distribution (18). Exclusion criteria were pregnancy, lactation, illness with a prognosis of death in ≤1 year, or a psychiatric illness likely to preclude involvement/informed consent. In total, 33,539 eligible individuals were invited to partake in the screening program. Diabetes was diagnosed according to World Health Organization criteria (19). Details on ADDITION-Cambridge study participant recruitment have been published (17). A total of 867 individuals with diabetes were identified and agreed to participate. This report conforms with the Strengthening the Reporting of Observational Studies in Epidemiology statement. Ethical approval was obtained from the Eastern Multi-Centre Research Ethics Committee (reference number 02/5/54), and all participants gave written informed consent. The ADDITION-Cambridge trial is registered as ISRCTN86769081.

Patients with newly diagnosed diabetes were managed according to the treatment regimen to which their practice was allocated. Patients in the IT group received theory-based health promotion materials concerning diet, physical activity, tobacco use, and medication adherence. Practitioners in the IT group were encouraged to follow a stepwise target-led treatment regimen to reduce and control CVD risk factors, including blood glucose level, blood pressure, and lipids levels (17,20). RC practices followed U.K. national guidelines for diabetes management (21).

**Measurements**

Baseline and 1-year health assessment included anthropometric (height and weight) and clinical measurements (blood glucose, blood pressure, and lipids) by trained staff following standard operating procedures (17). Standardized self-report questionnaires collected information on sociodemographic characteristics (age, sex, occupation, and ethnicity), alcohol consumption, smoking status, and prescribed medications. Social class was defined according to the Registrar General’s occupation-based classification and comprised the following three categories: “professional, managerial, and technical”; “skilled—manual and nonmanual”; and “partly skilled or unskilled.” Physical activity was assessed by past year total physical activity energy expenditure (net MET hours · day⁻¹) using the previously validated European Prospective Investigation into Cancer-Norfolk Physical Activity Questionnaire (38). Dietary behavior was assessed using a validated food-frequency questionnaire (22). Plasma vitamin C level, an objective biomarker of fruit and vegetable consumption, was measured using a fluorometric assay. A plasma vitamin C concentration of ≥70 μmol · L⁻¹ roughly equates to the daily consumption of five servings of fruit and vegetables (23).

The primary end point was the composite of first cardiovascular event, including cardiovascular mortality, cardiovascular morbidity (nonfatal myocardial infarction and nonfatal stroke), and revascularization. Participants were tagged for mortality at the Office of National Statistics. Electronic searches of GP records were conducted. Additional information was obtained from hospital records and coroner offices as required. All primary end-point events of interest were independently adjudicated by two experts, who were unaware of group allocation, according to an agreed protocol using standardized case report forms.

**Statistical Analysis**

Participant characteristics at baseline and 1 year were summarized separately by sex using means (SD) and percentages
(number). To minimize the possibility that subclinical disease affected behavior change, individuals experiencing a CVD event in the first year were excluded from analyses (n = 10). Change in physical activity and dietary behavior (daily intake of total energy, fat as a percentage of energy, fiber, alcohol, and plasma vitamin C) comprised the six primary exposures, quantified by generating binary variables denoting an increase or decrease in each individual behavior between baseline and 1 year. For all behaviors, the unhealthy behavior was the reference category and scored as 0. A binary “change in alcohol” variable categorized patients into those who continued to drink/increased their alcohol intake (coded 0) and those who abstained/decreased their alcohol intake (coded 1) between baseline and 1 year. The low number of patients reporting smoking cessation between baseline and 1 year (n = 15) precluded analyses examining change in smoking status. Thus, baseline smoking status was adjusted for in analyses, where appropriate.

A “health behavior change score” summed the number of healthy behavior changes in the year after diabetes diagnosis. One point was assigned to each category of four health behavior change factors: increasing physical activity; decreasing/stopping alcohol consumption; increasing both daily fiber and vitamin C intake; and decreasing both daily energy and total fat intake. These health behaviors were chosen based on the reported benefits of physical activity (24,25) and diet (26,27) on diabetes progression, and to reduce problems with collinearity through the use of multiple measures of the same underlying behavior. Health behavior change scores (ranging from 0 to 4) were calculated for those individuals with complete data on all four health behavior categories, with higher scores reflecting adoption of healthier behaviors between baseline and 1 year.

Cox proportional hazards regression calculated the rate of primary composite CVD events for categories of health behavior change and the health behavior change score. Age was used as the underlying time scale in all models (28), with person-time for each participant calculated from age at study entry (baseline) to age at death or the censor date (31 December 2009), whichever came first. Clustering of individuals within GP was accounted for in all analyses by using cluster-correlated robust estimates of variance to obtain variance-corrected incidence rates and rate ratios (RRs). Sex, age at study entry, baseline level of relevant health behavior, and study group were considered a priori confounders, and were included in all models. Model 1 examined whether any of the six health behavior change variables were independently associated with 5-year CVD events. In Model 2, stepwise forward regression was used to identify the health behavior changes that were most strongly associated with the composite primary CVD outcome, additionally adjusted for social class and occupation. Only health behaviors that improved model fit, determined via likelihood ratio testing, were included. Model 3 further adjusted for self-reported antihypertensive, glucose- and lipid-lowering (cardioprotective) medications at 1 year. A similar analytic approach was used to investigate the association between the health behavior change score and CVD risk.

Both BMI and waist circumference were omitted from multivariable analyses as they are likely to lie on the causal pathway between behavior change and CVD risk. To ascertain whether any behavior change variables mediate their effects through BMI or waist circumference, models were also run with and without these covariates, and the percentage change in RR associated with CVD risk for each health behavior change was assessed. Competing-risks regression estimated the risk of a composite cardiovascular end point in the presence of the competing risk of non-CVD death, while adjusting for potential confounders. The population-attributable fraction (29) estimated the proportion of CVD events that could be prevented if everyone adopted three or four health behaviors in the year after diagnosis, adjusting for all known confounders (Model 3). Because the results for all analyses were similar by trial arm, data were pooled and results presented for the whole cohort, adjusting for trial arm (study group). The relation between missing data and other variables was investigated using t-tests or χ² tests, where appropriate. Sensitivity analyses were carried out to test the robustness of estimates: 1) multiple imputation of missing health behavior (ordered categorical variable) and self-reported drug prescription (binary variable) were carried out by conditioning via multinomial logistic regression or via logistic regression respectively, on the observed predictor variables to generate five imputed data sets (30); sensitivity analyses 2) omitting revascularization from the composite CVD end point 3) omitting abstainers, and 4) including the ratio of polyunsaturated to saturated fats rather than the percentage of energy from total fat intake were also run. Data were analyzed using STATA version 13.1 (Stata, College Station, TX).

RESULTS

The mean age (SD) of participants was 61.1 years (7.2 years). The majority of participants were male (61%), Caucasian (97%), and reported being in a professional or skilled occupation (79%) (Table 1). Between baseline and 1 year, improvements were seen in the majority of health behaviors and CVD risk factors across study groups, including significant reductions in alcohol intake, total energy, and fat intake, and reductions in BMI, mean cholesterol, and HbA1c levels in both men and women (Table 1). Ten people experienced a CVD event before the 1-year follow-up, and 2 people withdrew from the study, leaving a total of 855 participants for analysis. The median follow-up time (interquartile range) was 5.0 years (1.3 years; 4,361 person-years at risk), during which time 6% of the cohort experienced a composite primary CVD event (53 of 855 participants), corresponding to an incidence rate of 12.2 per 1,000 person-years (95% CI 9.3–15.9). The CVD events comprised 21% of CVD deaths (11 deaths), 23% of myocardial infarctions (12 infarctions), 23% of strokes (12 strokes), and 34% of revascularizations (18 revascularizations).
The proportion of people achieving a healthy behavior change is shown in Table 2, along with the mean change in each of the individual health behaviors. No significant differences in any CVD risk factors were found at baseline between categories of health behavior score (data not shown). As shown by Model 1, alcohol consumption was the only health behavior that was independently associated with CVD incidence over 5 years, adjusting for age and sex. Individuals who continued to drink alcohol, or who increased their consumption in the year after diagnosis, had a higher rate of CVD than those who abstained or reduced their alcohol consumption. Additionally adjusting for social class and occupation, and mutually adjusting for changes in other health behaviors strengthened the association between change in physical activity, alcohol intake, and CVD risk. Individuals who increased their physical activity levels, or abstained or reduced their alcohol intake, had a lower CVD risk compared with those who decreased their activity levels (RR 0.53; 95% CI 0.36–0.78), a similar decrease in the RR for the association between change in alcohol consumption, and physical activity and CVD risk was observed once baseline waist circumference was included in the final model (4% decrease in both cases), but did not qualitatively alter the association between health behavior change and CVD risk. These reductions in RR suggest that changes in body composition may, at least in part, mediate the association between behavior change and CVD risk. There was a significant inverse association between the health behavior change score and incident CVD events (Table 3 and Fig. 1). Only twenty people changed all health behaviors, so
<table>
<thead>
<tr>
<th>Change category*</th>
<th>Health score</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
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<tr>
<td></td>
<td>Mean (SD)</td>
<td>n</td>
<td>D Y RR (95% CI)</td>
<td>P</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Decreased 0</td>
<td>0.4 (4.4)</td>
<td>361</td>
<td>23</td>
<td>1.87</td>
</tr>
<tr>
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<td>4.2 (5.1)</td>
<td>380</td>
<td>23</td>
<td>1.93</td>
</tr>
<tr>
<td>Increased 0 +</td>
<td>2.9 (5.7)</td>
<td>262</td>
<td>25</td>
<td>1.34</td>
</tr>
<tr>
<td>Decreased 1 +</td>
<td>3.0 (5.6)</td>
<td>458</td>
<td>20</td>
<td>2.35</td>
</tr>
<tr>
<td>Increased 0 +</td>
<td>351 (368)</td>
<td>243</td>
<td>17</td>
<td>1.23</td>
</tr>
<tr>
<td>Decreased 1 +</td>
<td>554 (474)</td>
<td>489</td>
<td>29</td>
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<tr>
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<td>5.1 (3.9)</td>
<td>268</td>
<td>17</td>
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</tr>
<tr>
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<td>464</td>
<td>29</td>
<td>2.38</td>
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<tr>
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<td>307</td>
<td>17</td>
<td>1.57</td>
</tr>
<tr>
<td>Increased 1 +</td>
<td>5.5 (5.2)</td>
<td>425</td>
<td>29</td>
<td>2.18</td>
</tr>
<tr>
<td>Decreased 0 +</td>
<td>16.2 (13.9)</td>
<td>295</td>
<td>18</td>
<td>1.51</td>
</tr>
<tr>
<td>Increased 1 +</td>
<td>17.7 (16.6)</td>
<td>340</td>
<td>20</td>
<td>1.69</td>
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<td>smoker NA NA</td>
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<td>10</td>
<td>0.76</td>
<td>1 0.71</td>
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<tr>
<td>Never/former NA</td>
<td>703</td>
<td>43</td>
<td>3.59</td>
<td>0.88 (0.47–6.95)</td>
</tr>
<tr>
<td>Increased 0 +</td>
<td>0.90 (0.8)</td>
<td>183</td>
<td>11</td>
<td>0.93</td>
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<tr>
<td>Decreased 1 +</td>
<td>1.89 (1.7)</td>
<td>541</td>
<td>34</td>
<td>2.78</td>
</tr>
</tbody>
</table>

All models were adjusted for age, sex, baseline value of relevant change variable, and study group. Multivariable model 1 presents the independent effects of each change in health behavior adjusted for baseline values of relevant change variable and change in physical activity, alcohol intake, and plasma vitamin C. Model 2 is for Model 1 and additionally adjusted for social class, education and mutually adjusted for change in physical activity, alcohol intake, and plasma vitamin C. Model 3 is for Model 1 and additionally adjusted for social class, education and mutually adjusted for change in physical activity, alcohol intake, and plasma vitamin C. Model 4 is for Model 1 and additionally adjusted for social class, education and mutually adjusted for change in physical activity, alcohol intake, and plasma vitamin C.

† Values at baseline (n) omitted from multivariable analysis as may be on causal pathway. Change denotes an increase or decrease in health behavior from baseline to 1 year of follow-up.
individuals with a health behavior change score of three or four were combined in these analyses. Participants who improved three or four health behaviors (n = 176 of 600 participants, 30%) had the lowest rate of CVD events. Participants who did not change any health behaviors (n = 37 of 600 participants, 6%) had a 3.71 times higher CVD event rate (95% CI 1.02–13.56, P for trend = 0.03), and this association remained significant after adjusting for prescription of antihypertensive, glucose-lowering, and lipid-lowering medication (P for trend = 0.04). CVD events occurred more often in men than in women (44 of 53 CVD events in men, 83%), which prevented examination of a differential effect of health behavior change on CVD risk by sex. Assuming the association between unhealthy behavior and CVD outcome is causal, 50.2% (95% CI 4.9–76.4%) of CVD events in this population could be attributed to not changing three of four health behaviors in the year after diabetes diagnosis, and 35.4% (95% CI 0.44–58.1%) of CVD events could be attributed to not changing two health behaviors (the population attributable fraction for CVD).

Compared with those who had complete health behavior data, participants with missing data were more likely to have a lower socioeconomic status (social class: x² = 18.9, P = 0.001; occupation: x² = 16.5, P = 0.01), but were similar with respect to other baseline variables (P > 0.05, data not shown). The hazard ratios for risk of composite CVD outcome from analyses with imputed missing health behavior and drug prescription data differed by an average of 10% (range 3–22%) from those obtained with original list-wise deleted models (Supplementary Table 1). Sensitivity analyses omitting revascularization from the composite CVD end point (n = 18), omitting abstainers (n = 173), and using the ratio of polyunsaturated to saturated fat rather than the percentage of energy from total fat did not qualitatively change these results (data not shown).

CONCLUSIONS

Patients with newly diagnosed type 2 diabetes who increased their physical activity levels and abstained or reduced their alcohol intake in the year after diagnosis of diabetes had a lower risk of CVD events over 5 years compared with individuals who did not change their behavior. The association between modifying these health behaviors early in the disease trajectory and reduced CVD risk were independent of age, sex, study group, social class, occupation, and the prescription of cardioprotective medication. The greater the number of healthy behavior changes made in the year after diabetes diagnosis, the lower the CVD risk. We demonstrate that the association between health behavior change and reduced CVD risk is likely, in part, mediated through changes in body composition.

Our results support and extend the results of previous research showing the beneficial effects of healthy behaviors on cardiovascular risk in the general population (1–3) and among individuals with diabetes. Studies in individuals with newly diagnosed diabetes showed that positive behavior changes can reduce CVD risk factor levels (9) and promote weight loss (8), but their effect on hard CVD outcomes remained unclear. In the Look-AHEAD trial in clinically diagnosed obese/overweight diabetes patients, an intensive lifestyle

<table>
<thead>
<tr>
<th>Health score</th>
<th>n</th>
<th>D</th>
<th>Y</th>
<th>Model 1 RR (95% CI)</th>
<th>Model 2 RR (95% CI)</th>
<th>Model 3 RR (95% CI)</th>
</tr>
</thead>
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<td>3 or 4</td>
<td>176</td>
<td>6</td>
<td>0.87</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>230</td>
<td>11</td>
<td>1.17</td>
<td>1.30 (0.54–3.15)</td>
<td>1.53 (0.62–3.81)</td>
<td>1.70 (0.64–4.50)</td>
</tr>
<tr>
<td>1</td>
<td>157</td>
<td>16</td>
<td>0.77</td>
<td>2.91 (1.17–7.19)</td>
<td>3.42 (1.31–8.92)</td>
<td>3.78 (1.32–10.77)</td>
</tr>
<tr>
<td>0</td>
<td>37</td>
<td>4</td>
<td>0.19</td>
<td>3.11 (0.90–10.68)</td>
<td>3.71 (1.02–13.56)</td>
<td>4.17 (1.02–17.09)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td>0.04</td>
<td>0.03</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Model 1 was adjusted for age, sex, and study group. Model 2 was additionally adjusted for social class and occupation. Model 3, as for Model 2 and additionally adjusting for cardioprotective medication at 1 year. Clustering of individuals within GPs was accounted for in all models. D, primary composite CVD outcome; Y, person-years at risk (per 1,000). Health score range, 0–4 possible points.
intervention led to improved CVD risk factor levels (10) and mobility (11), but did not significantly reduce CVD risk (31). Although these findings may mean that healthy behavior change is not effective at reducing CVD incidence in clinically diagnosed patients, other explanations (32) include the possibility that the protective effects of lifestyle change were reduced by a lower rate of prescribed cardioprotective medication in the intervention compared with the control group. It is also possible that the magnitude of the between-group differences in behavior between trial arms in the Look-AHEAD trial were smaller than the differences between categories of health behavior change variables in this observational study. Finally, health behavior change may have a larger effect earlier in the diabetes disease trajectory. Early improvements in health behaviors in the ADDITION-Cambridge cohort were associated with a reduction in incident CVD over 5 years, emphasizing the importance for practitioners to encourage healthy behavior change immediately after diagnosis.

Our findings suggest that the biggest effects on CVD risk came from changes in physical activity and alcohol consumption, rather than diet. Results from a recent trial emphasized the beneficial effects of dietary changes on intermediate outcomes after 1 year, with increased physical activity conferring no additional benefit (9). Explanations for our contrasting results include the possibility that the increases in activity achieved in the Early ACTID (Early Activity in Type 2 Diabetes) trial were insufficient to conclusively exclude a beneficial effect. Indeed, no clinically significant differences between trial arms in moderate-to-vigorous physical activity at 1 year were observed; between-group moderate-to-vigorous physical activity differences ranged from 0.9 to 5.6 minutes (9). Alternatively, physical activity and alcohol may be stronger determinants of CVD events (rather than CVD risk factor levels) than diet in the first 5 years after diagnosis. The beneficial effects of physical activity on CVD risk factor levels in patients with clinically diagnosed diabetes have previously been reported (33,34). While low alcohol consumption levels are associated with reduced CVD risk, the deleterious effect of heavy alcohol consumption on glycemia levels is well-established (35). In addition to reduced CVD risk, healthy behavior change may be associated with a range of health benefits in individuals with type 2 diabetes, including reductions in sarcopenia (36) and cognitive decline (37). A better understanding of the magnitude and types of behavior change needed to benefit health, coupled with improved interventions to help patients achieve and maintain behavior change, are needed to tackle the growing burden of disease caused by diabetes and associated comorbidities.

The strongest evidence for etiology and effectiveness comes from randomized control trials. However, as habitual behaviors are strongly environmentally patterned, most behavioral interventions rarely achieve large sustained differences in behavior between trial arms, and therefore assess the effects of the behavior change intervention, rather than the behavior change itself. Consequently, carefully conducted observational analyses of well-characterized cohorts significantly contribute to our current understanding of the importance of lifestyle (smoking, physical activity, diet, and alcohol consumption) and will continue to add to our limited understanding of the health impacts of behavior change.

We showed that the greater the number of healthy behavior changes adopted, the lower the risk of CVD events. But is it realistic to expect such changes in health behavior outside of a clinical trial setting? For physical activity, the net difference in average activity levels between the people who increased their activity (approximately half the cohort) compared with those who decreased their activity in the year after diagnosis was 8.4 net MET hr·day⁻¹, which equates to ~1 h of brisk walking per day. This net difference in activity was associated with a 51% reduction in CVD risk. However, such substantial effects are unlikely to be realized in clinical practice given that the average physical activity changes in the year after diagnosis in men and women were 0.5 and ~0.47 net MET h·day⁻¹, respectively (Table 1). This illustrates both the potential of health behavior change interventions, as well as the challenges faced in terms of motivating people to adopt and maintain such behaviors.

**Strengths and Limitations**

We recruited participants from a large, population-based sample, covering an extensive geographical area in the East Anglia region of the U.K., ensuring generalizability to similar settings. The study population exhibited socioeconomic, but not ethnic, diversity. The duration of follow-up, repeat measurement of lifestyle behaviors, and high participant retention (93% of those alive at 1 year) allowed us to quantify the effects of behavior change early in the diabetes trajectory. We achieved 99.8% end-point ascertainment, and all end points were independently adjudicated. Results from a number of sensitivity analyses, including those imputing missing data, were qualitatively the same as those from the complete case analyses, supporting the robustness of our estimates. Baseline CVD risk factor levels did not differ significantly between categories of health behavior score, suggesting that the benefit of behavior change was not attributable to pre-existing characteristics of participants. Use of self-reported physical activity, dietary, and alcohol data could introduce some measurement error and bias. However, we used previously validated questionnaires (22,38), and such error, if introduced, is likely to underestimate the strength of the association.

Furthermore, given the reliability of the measures, repeat use of the same instruments should reduce bias and allow changes in behavior to be quantified (39). Smoking status is a well-known modifiable risk factor for early death (40), but the low number of patients who reported smoking cessation between baseline and 1 year (n = 15) precluded analysis of the impact of a change in smoking status on 5-year CVD risk. A simple pragmatic health behavior change score was constructed
in this study (1,2). It may be possible to weight different health behaviors according to the strength of their association with CVD outcome, but this will always be limited by differences in measurement error associated with each health behavior. Dichotomizing change in healthy behaviors into individuals who increased or decreased their behaviors ensured an adequate number of events and sample sizes for all analyses, but could exaggerate the magnitude of associations and obscure the gradient of association between behavior change and CVD risk. The low number of events and the potential for differential measurement error in the self-reported behaviors also precluded us from a detailed quantification of the magnitude of behavior change needed to reduce CVD risk. However, we highlight that there was a clear separation of the CVD survival curves, even with our relatively crude measure of behavior change, supporting our interpretation of the findings.

This is the first study to show that healthy behavior changes in the year after diagnosis of diabetes are associated with significant reductions in the risk of incident CVD over 5 years, independent of cardioprotective medication use. Our results suggest that a combined approach that includes early improvements in health behaviors and cardioprotective medications is a beneficial strategy for reducing long-term CVD risk. The year after diagnosis of diabetes is an important period for encouraging change, and maintaining healthy behaviors and habit formation, which should continue to be a major focus for practitioners. How best to help patients achieve and maintain these changes remains uncertain, and should be the focus of future research.

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**Author Contributions.** G.H.L. conceived the study question, contributed to the analysis plan, carried out all statistical analyses, interpreted the data, and drafted and critically revised the manuscript. A.J.M.C. participated in the interpretation of data and in the critical revision of the report for important intellectual content. N.J.W. participated in the interpretation of data and in the critical revision of the report for important intellectual content, designed the ADDITION-Cambridge study, and is one of the principal investigators. S.J.G. conceived the study question, contributed to the analysis plan, interpreted the data, drafted and critically revised the manuscript, designed the ADDITION-Cambridge study, and is one of the principal investigators. R.K.S. conceived the study question, contributed to the analysis plan, interpreted the data, and drafted and critically revised the manuscript. All authors read and approved the final manuscript. G.H.L. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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