Title: **Evaluation of long-term diabetes outcomes for high-risk patients eligible to attend the 'Walking Away from Diabetes' educational intervention; a retrospective cohort study.**

Running title: **Long-term outcomes for Walking Away from Diabetes programme.**

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Abstract

Aims To retrospectively assess the efficacy of a pragmatic education programme called Walking Away from Diabetes (WAD), a single-session intervention aimed at patients who are at risk of developing type 2 diabetes mellitus (T2DM).

Methods Baseline and follow-up data for 6116 patients, identified as 'at risk of diabetes' in the period April 2012 to March 2016, were assessed for T2DM status in January 2018. Any differences in outcome between WAD attenders and non-attenders was explored using Kaplan-Meier, Log rank testing and Cox regression analyses.

Results During the follow-up period, 426 out of 3470 (12.3%) WAD attenders and 349/2646 (13.2%) non-attenders were diagnosed with T2DM (p-value 0.068, Log rank test). Cox regression shows that HbA1C (hazard ratio [HR] 1.23, p-value <0.001) and HDL levels (HR 0.67, p-value <0.001), rather than WAD attendance (HR 0.89, p-value 0.11), were the main two factors associated with progress from 'at risk' to T2DM.

Conclusions Although the wider health impact of the WAD programme was not considered here, session attendance does not appear to reduce the risk of developing T2DM. However, other factors influence the risk of developing T2DM. It is essential for educational programmes, designed to have a preventative effect for people at risk of diabetes, to be assessed for short- and long-term efficacy.

Key Words: diabetes, education, exercise, lifestyle, patient education, diabetes risk.

Introduction

Lifestyle interventions can enable a reduction in risk of developing T2DM.[1,2] This has been shown in various randomised controlled trials in a variety of populations.[1,3,4,5] The aim of the cited studies was to promote more intense physical activity in conjunction with an improvement in healthy diet adherence and weight management for overweight and obese patients. 'Walking Away from Diabetes' (WAD) is a theory driven, structured education programme for people identified at increased risk of T2DM. WAD has been developed within the NHS and is based on a previously published study.[6,7,8]

To date there is only clinical outcome data available on the WAD programme from a controlled clinical trial and one-year follow-up.[6] In that study, WAD did have a statistically significant positive effect on biomedical and lifestyle outcomes. Therefore, investigating the long-term outcomes related to WAD is indicated, to appraise whether WAD intervention impacts on the risk of at risk people progressing to diabetes.

Material & Methods

Study design

This concerns a retrospective cohort study, and is classed as a service evaluation in accordance with UK Health Research Authority guidelines. Therefore, individual informed consent was not obtained from patients to use their data. Caldicott approval was obtained from the NHS Trust that holds the data to analyse and publish it.

WAD programme details

The WAD programme is described in more detail elsewhere.[6,8] In summary, it provides three hours of structured education for up to 10 people (and a partner/friend) led by two trained educators. The programme is aimed at promoting walking and to further enhance the physical activity through walking message, patients are issued with a pedometer to self-monitor the steps they take daily. Other information provided to attendees involve the causes, complications and timelines for glucose intolerance and diabetes. Patient at risk of developing diabetes as determined by Leicester Diabetes Risk Assessment and/or pre-diabetic Hba1c levels (42 to 47 mmol/mol).[7] This study cohort includes patients referred to WAD by GPs between 1 April 2012 and 31 March 2016, and end date for follow-up was 1 January 2018 .

Data sources and analysis

Baseline demographic and clinical measures were taken in the GP surgery when a patient was classified as being at risk of diabetes. These included a patient's residence postcode, sex, age, HbA1C, HDL, cholesterol, and blood pressure. Patient ethnicity was not recorded, but the study sample is from a county in England where 96.5 % of the population is White British.[9] Index of multiple deprivation deciles were calculated from patients' postcodes[10] , with 1 being the highest degree of deprivation, and data on T2DM diagnosis was extracted from a national database maintained by the University of Exeter. For continuous and ordinal data, the mean and median, respectively, plus the 95% confidence interval (95% CI) was calculated. Differences between WAD attender and non-attender cohorts were assessed with Chi-squared test (binary and nominal data) and Mann-Whitney U-test (ordinal and continuous data). The rate of diagnosis of T2DM over time was considered with a Kaplan-Meier plot accompanied by Log rank test for WAD as a factor on its own, and Cox regression

analysis for all variables. Data was collated using Microsoft Excel and analysed using SPSS v20, and a p-value of 0.05 was considered significant.

Results

Across the period that the WAD programme ran in this particular NHS Trust, a total of 7916 patients were identified as being eligible for attendance in primary care, and referred to the WAD team in the diabetes department. Of those, 4420 patients attended and 3496 did not (56% attendance rate). Complete datasets, baseline demographic, clinical measurements data and diabetes outcome data were available for 6116 people who were identified as being at risk of developing T2DM. Therefore, all further data analysis was conducted using the dataset for these patients. The mean follow-up time was 52.0 months (95% CI 51.4-52.5) for attenders and 48.3 months (95% CI 47.7 – 49.0) for non-attenders (p-value <0.001, Mann-Whitney U-test). In total, 426 out of 3470 (12.3%) attenders and 349/2646 (13.2%) non-attenders were eventually diagnosed with T2DM during the follow-up period. The baseline variable measurements were not identical between the WAD attendance and non-attendance cohorts. Table 1 summarises that they differed in average age, degree of deprivation, HDL level, and cholesterol levels. Those who attended WAD were significantly older, less deprived, and had a better cardiovascular health profile.

When diabetes diagnosis in relation to solely WAD attendance is considered, Log rank analysis and Kaplan-Meier plotting (Figure 1) of diabetes diagnosis cases shows that there is no significant difference in the number of diabetes cases diagnosed during the follow-up period (p-value 0.068, Log rank test). Since this kind of analysis does not take into account any confounding factors that may influence whether someone develops diabetes, Cox

regression analysis was conducted to determine if any variables are associated with diabetes, and if this influences any impact that WAD attendance may have on diabetes developing during the follow-up period. Table 2 shows that HbA1C and HDL levels are associated most significantly with diabetes risk, both in terms of magnitude (hazard ratio [HR]) and statistical significance (p-value). A higher HbA1C level is associated with an increased risk of T2DM, whereas conversely a higher HDL level is associated with a lower risk of developing diabetes. Variables significantly associated with T2DM risk but with a negligible hazard ratio are deprivation score, patient age, and cholesterol. On the other hand, WAD attendance is not significantly linked to the risk of developing diabetes, though there appears to be a trend to lower risk of diabetes if a patient attends a session (not significant at p-value of 0.11).

Discussion

This retrospective evaluative study set out to appraise if real-life application of the WAD programme is significantly associated with a reduction in subsequent T2DM diagnosis in subsequent years. At first sight this does not seem to be the case. However, there are a few caveats to bear mind mind. Although the sample size is large and average follow-up period is considerable, this study is hamstrung by being a retrospective evaluation of the effectiveness of the WAD programme. Consequently, fasting glucose, low-density lipid profiles and some anthropometric measures such as body mass index are not included in the analysis. Neither is any data on pre- and post-attendance exercise levels achieved by people in this cohort; this is where a prospective epidemiological study would be

advantageous. From the available data it is observed that the non-significant reduction seen in T2DM in the WAD attenders can probably be attributed to a multitude of factors. There is a difference in baseline composition of the WAD attenders and non-attenders, both in terms of clinical and non-clinical parameters. Because the patients were able to choose whether to attend or not, rather than being allocated to a specific treatment arm, this could not be controlled for. Both high HbA1C and low HDL levels are recognised risk factors for T2DM as identified in controlled trials and through meta-analysis.[14,15,16] In absolute terms the average follow-up period for non-attenders is 3.7 months shorter, which equates to a 7% relative difference in follow-up time 'to the benefit' of the non-attendance arm. Despite the potential confounding role of HDL and relative difference in follow-up time between attenders and non-attenders, the long-term impact of attending a WAD session on diabetes risk appears modest and inconclusive. This contrasts to a Finnish diabetes prevention programme where short-, medium- *and* long-term outcomes have been positive.[1, 13] The main difference between the Finnish and WAD programme is the number of times the patient attended an education session: seven sessions with a nutritionist in first year alone vs one single session with a session practitioner, respectively. The achieved attendance rates are similar for both programmes, with a >50% participation rate recorded. In this present study we did not explore the medium- to long-term wider positive impact that the WAD programme may have from a patient-perspective, and therefore one has to be mindful that it may have other unintended positive effects bar prevention of T2DM.

National policy means that the WAD programme has been superseded by the Healthier You: NHS Diabetes Prevention Programme that is rolled out across England, using various programme delivery providers.[18,19] The limited effectiveness observed in this present

evaluation for the WAD programme may be due to a number of reasons, but the intensity of the intervention may be the key reason. Similar to the Finnish programme on which it is based[20], the 'Healthier You' programme involves at numerous (at least 13) education and exercise sessions of one to two hours each. The potential role of confounding factors – demographic, anthropometric and clinical – should be taken into account when evaluating the new 'Healthier You' programme. Early indications are that similar trends are observed as in the WAD cohort, with older, female patients more likely to attend.[21]

Conclusions

The single-session WAD education programme may not significantly slow down the rate of T2DM manifesting in people at risk of diabetes. More recent published data suggest that extended and more intense education programmes may be more effective in preventing progression to diabetes. However, evaluations of programmes need to be mindful of confounding variables such as patients' lipid profiles, and potential non-intended health benefits that a programme may bring.

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3-5 very short Key messages. Abbreviations and acronyms list (don't state in full in text).

Key messages

- Evaluative data on the long-term diabetes prevention effect of a single educational session for at risk people is lacking.
- The protective effect of attending the NHS-developed Walking Away from Diabetes (WAD) programme appears to be limited, though effectiveness analysis should take into account the role of confounding factors.
- More intense educational programmes have been introduced in the NHS recently; however, as for WAD their effectiveness should be measured with other variables (including e.g. high density lipid levels) taken into account.

Abbreviations and acronyms list

- HbA1C, haemoglobin A1C
- HDL, high density lipids
- HR, Hazard Ratio
- NHS, National Health Service
- T2DM, Type 2 diabetes mellitus
- WAD, Walking Away from Diabetes

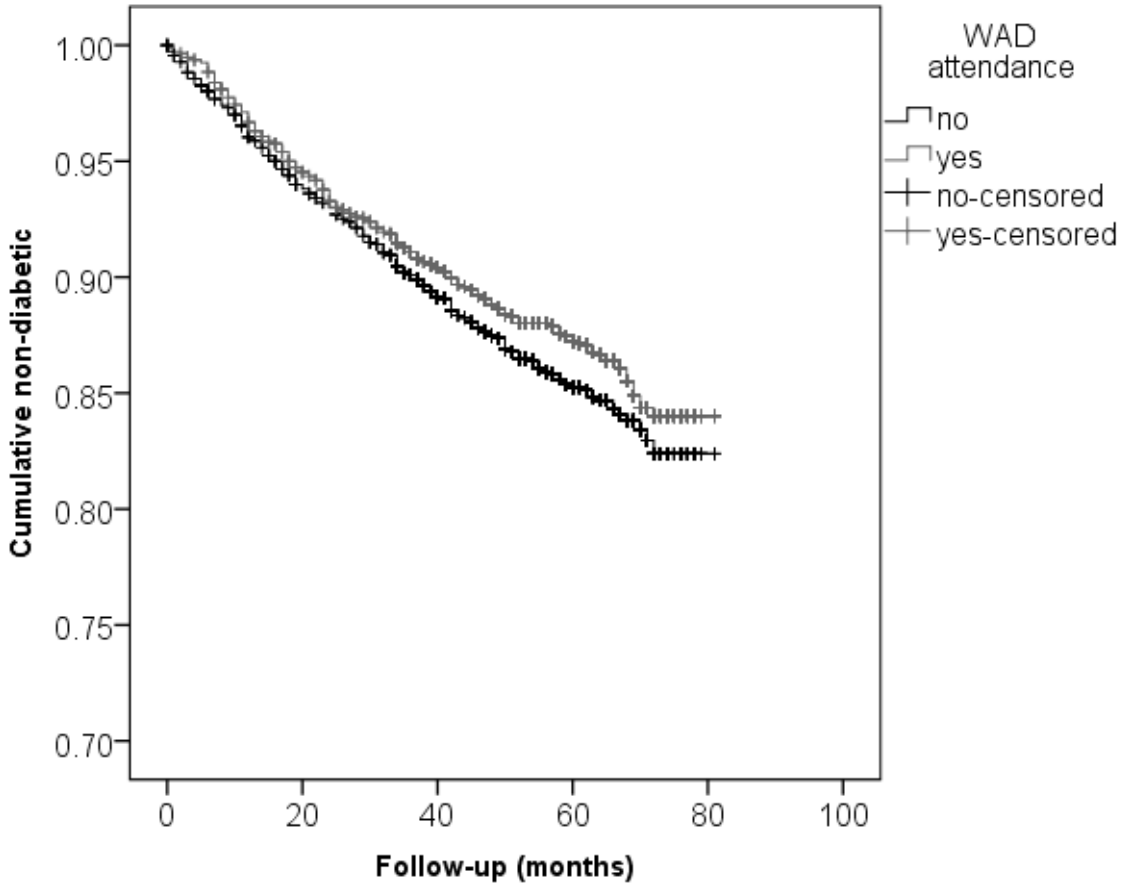
WAD attendance
no
yes
no-censored
yes-censored
Cumulative non-diabetic
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0
20
40
60
80
100
Follow-up (months)

Table 1, baseline demographics and clinical measures for patients referred to Walking Away from Diabetes programme.

Variable	**WAD attenders (n = 3470)**	**WAD non-attenders (n = 2646)**	**p-value**
Age, years, mean (95% CI)	66 (66-67)	63 (63-64)	<0.001~
Sex, n, male / female (%)	1527 / 1943 (44% / 56%)	1228 / 1418 (46% / 54%)	0.061#
Index of Multiple Deprivation, decile , median (95% CI)	6 (5.81-5.98)	6 (5.44-5.64)	<0.001~
HbA1C, mmol/mol, mean	44.2	44.2	0.16~

(95% CI)	(44.1-44.3)	(44.1-44.2)	
Blood pressure systolic, mmHg, mean (95% CI)	133.9 (133.4-134.4)	133.9 (133.3-134.5)	0.81~
Blood pressure diastolic, mmHg, mean (95% CI)	78.1 (77.7-78.4)	78.4 (78.0-78.8)	0.30~
HDL, mmol/L, mean (95% CI)	1.48 (1.46-1.50)	1.43 (1.41-1.45)	<0.001~
Total Cholesterol, mmol/L, mean (95% CI)	4.91 (4.86-4.95)	4.99 (4.84-5.04	0.007~

#Chi-squared test; ~Mann-Whitney U-test; 95% CI, 95% confidence interval

Table 2, Cox regression analysis for diabetes as outcome and follow-up in months as time factor.

Variable	**Hazard Ratio[#]**	**95% CI**	**p-value**
Deprivation index rating (1 = most deprived, to 10 = least deprived)	0.97	0.94 – 0.99	0.018*
Patient sex (0 = male; 1 = female)	1.16	0.99 – 1.35	0.056
Patient age (years)	0.99	0.98 – 1.00	0.019*
WAD attendance (0 = non-attendance; 1 = attendance)	0.89	0.77 – 1.03	0.11
Blood pressure systolic (mmHg)	1.00	0.99 – 1.01	0.78

Blood pressure diastolic (mmHg)	1.01	0.99 – 1.01	0.31
HbA1C (mmol / mol)	1.23	1.21 – 1.24	<0.001*
HDL (mmol/L)	0.67	0.56 – 0.81	<0.001*
Cholesterol (mmol/L)	0.91	0.86 – 0.96	0.001*

*Statistically significant, p-value <0.05. #HR score of > 1 indicates that increased value for variable is associated with increased risk of developing diabetes; conversely, HR of < 1 indicates that increased value of variable is associated with decreased risk of developing diabetes.