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Baseline characteristics associated with different BMI trajectories in weight loss trials: a case for better targeting of interventions

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Abstract

Background/Objectives: Dietary weight loss interventions have heterogeneous outcomes in long-term studies, with many participants regaining part or all of the lost weight. Growth mixture modelling is a novel analytic approach that can be used to identify different trajectories of weight change during a trial rather than focussing on the total amount of weight lost. Subjects/Methods: Data were pooled from two 12-month dietary weight loss studies where no significant difference was detected between the treatment and control arms, thus allowing analysis independent of treatment. The data set included 231 subjects (74.5% female), with a mean weight loss of 6.40 kg (4.96). Growth mixture models were used to identify participants with similar trajectories of change in body mass index (BMI). Results: Three subgroups were identified. A rapid and continuing BMI loss over the study period (rapid, n=53), a rapid initial weight loss in the first 3 months with a slowing rate over the remaining 9 months (maintainers, n=146) and those with an initial loss trajectory, which slowed and began to increase at 9 months (recidivists, n=53). Age (s.d.) and BMI (s.d.) were significantly different between the three groups (rapid 53 years (7), 28.99 kg/m2 (3.30); maintainers 47 years (9), 30.90 kg/m2 (2.95); recidivists 44 years (7), 34.84 kg/m2 (1.92), both P<0.001). Conclusions: Older subjects with lower BMIs were more likely to have a rapid and continuing weight loss in a 1-year dietary-based weight loss intervention. Different interventional approaches may be necessary for different ages and baseline BMIs and stratification prior to randomisation may be necessary to prevent confounding in weight loss trials.

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Running head: BMI trajectories in weight loss trials

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Abstract

Background/Objectives

Dietary weight loss interventions have heterogeneous outcomes in long term studies with many participants regaining part or all of lost weight. Growth mixture modelling is a novel analytic approach which can be used to identify different trajectories of weight change during a trial rather than focussing on the total amount of weight lost.

Subjects/Methods

Data were pooled from two 12 month dietary weight loss studies where no significant difference was detected between the treatment and control arms, thus allowing analysis independent of treatment. The dataset included 231 subjects (74.5% female), with a mean weight loss of 6.40kg(4.96). Growth mixture models were used to identify participants with similar trajectories of change in BMI.

Results

Three subgroups were identified. A rapid and continuing BMI loss over the study period (rapid, n=53), a rapid initial weight loss in the first three months with a slowing rate over the remaining nine months (maintainers, n=146) and those with an initial loss trajectory which slowed and began to increase at nine months (recidivists, n=53). Age(SD) and BMI(SD) were significantly different between the 3 groups (rapid 53years(7), 28.99kg.m^{-2}(3.30); maintainers 47years(9), 30.90 kg.m^{-2} (2.95); recidivists 44years(7), 34.84 kg.m^{-2} (1.92), both P<0.001).

Conclusions

Older subjects with lower BMIs were more likely to have a rapid and continuing weight loss in a one year dietary based weight loss intervention. Different interventional approaches may be necessary for different ages and baseline BMIs and stratification prior to randomisation may be necessary to prevent confounding in weight loss trials.

Introduction

Obesity is a growing health concern globally[1]. While considerable research demonstrates the efficacy of many weight loss strategies in the short term (~12 weeks) weight regain after this initial loss remains the largest difficulty in weight management[2]. As the length of follow-up in weight loss research increases, it is important to determine what represents successful weight loss and what are the factors associated with success. The current paradigm of success of a weight loss intervention focusses on the total weight loss at the end of the study period. The proportion of participants achieving a 5% weight loss has been accepted for some time as a clinically important criterion for success[3]. This single criterion does not acknowledge that individuals can have very different trajectories of weight loss over time to achieve this 5% and does not distinguish between those continuing to lose and those regaining at the end of the trial. Investigating these trajectories is important as regainers have been shown to have less favourable metabolic outcomes than those who continue to lose weight during the trial[4].

Growth mixture modelling is widely used in the psychology literature to investigate different trajectories of behavioural and psychological variables [5] however its' use in tracking empirically measured health outcomes is underutilised. This may be related to software limitations as while specialised packages exist (such as MPlus) routines in more conventional packages are more limited. There have been some examples of application of this method to outcomes of randomised clinical trials, for example, in studies examining responses to depression medication independent of the therapeutic intervention[6].

The current research aimed to investigate weight loss trajectories using change in body mass index (BMI) in two weight loss studies for which there was no demonstrated intervention effect, and to investigate the characteristics of the participants in the different groups which may be contributing to heterogeneous responses over time. The objective was to establish patterns, or trajectories, of change and to identify characteristics associated with these patterns that may assist with weight management and trial design. The focus on this form of analysis represents a move towards a person-centred approach to analysis as opposed to the more traditional variable form of analysis[5, 7]. Given the ineffectiveness of sustained interventions for weight loss different approaches need to be adopted. Investigating individual characteristics associated with weight loss patterns represents a new approach to both developing interventions and improving trial design.

Subjects and Methods

The current analysis pooled data from two previously published 12 month weight loss studies [8, 9]. In both studies there was no treatment effect of the primary intervention observed on weight and responses in the amount of weight lost were heterogeneous. One study involved a treatment arm focussing on increasing vegetable intake compared with standard dietary advice based on the Australian Guide to Healthy Eating[8]. The second study again had a control arm based on the Australian Guide to Healthy Eating. The treatment arms in this study involved increasing fish intake alone or in combination with a supplement to increase the amount of long chain n3 polyunsaturated fatty acids[9]. Both trials had similar inclusion criteria which included BMI 25-35kg/m^2 and age 18-65 years[8], or BMI 25-37kg/m^2, age 18-60 years and with a waist circumference >80cm for men or >94cm for women[9]. Exclusion criteria for both studies included major illnesses or voluntary weight loss proceeding the study period. Institutional ethics approval was granted for both initial studies and for this pooled analysis. Data extracted from the studies included the weight and BMI at each time point, the age, gender, education level, occupation and baseline physical activity using the Baecke questionnaire[10]. Study dropout was also recorded. Both studies were registered (www.anzctr.org.au ACTRN12610000784011 and ACTRN12608000425392).

Statistical Analysis

Groups of BMI change trajectories were identified using a growth mixture model (GMM). The analysis was performed using MPlus (Version 7.2 Muthén and Muthén, LA, CA). A priori it was decided to base the analysis on BMI rather than weight in order to minimise any sex effect related to differences in baseline weights between the genders. As we anticipated the change over time may not be linear both quadratic and cubic terms were initially considered in the models. Given the aim of determining clinically relevant interpretations of the groups, class numbers between 2-4 were compared. The best model was determined by considering the following model fit indices; entropy, the Bayesian Information Criterion and the Bayesian Likelihood Ratio test. Additionally the theoretical assumption (differences in BMI trajectory), interpretability and parsimony was used to decide between models with similar fit indices [11-13]. Comparison of the classes from the growth mixture model was conducted using t tests or one-way ANOVA with multiple post hoc comparisons adjusted using the Bonferroni procedure. Categorical comparisons between the groups were conducted using the Pearson Chi Square statistic. Exact tests were used when the minimum expected cell frequency assumption (n=5) was violated. Post hoc analysis of the categorical tests was conducted using z-tests to compare column proportions. The adjusted standardised residuals were used to determine the influence of individual cells. Class comparisons were conducted using SPSS (Version 21, IBM Inc Armonk, NY).

Results

The dataset contained 231 subjects (113 and 118 from the two studies respectively [8, 9]). Baseline characteristics for the total sample are shown in table 1. Mean weights (SD) and BMI (SD) respectively for the entire sample at baseline were 86.91kg(11.97), 30.65kg/m^2(3.20), at 3 months 81.99kg(11.65), 28.87kg/m^2(3.02), at 6 months 80.35kg(11.26), 28.22kg/m^2(2.44) at 9 months 79.25kg(11.00), 27.89kg/m^2(2.77) and at 12 months 79.70kg(11.33), 28.05kg/m^2(2.97). Mean overall weight loss was 6.40kg(4.96), within the 4.5 to 7.5kg (4.8-8.0%) range reported in a meta-analysis of different weight loss interventions with a minimum of 1 year follow up [14]. Weight loss was similar in the pooled treatment (-6.61kg(4.89)) and control groups (-6.25kg(5.03)) over the one year period (P=0.656, independent samples t test)

The final model had 3 classes and included a quadratic term. Residual variances were fixed over time as the GMM assumes increasing variance and this was not the case with this data. The entropy was 0.710, with a Bayesian Information Criterion of 2826 and a P value for the Bayesian Likelihood Ratio Test of <0.0001. Figure 1 shows the BMI trajectories over the study period of the 3 groups. Three distinct patterns of change over time can be seen, the largest group (n=146) demonstrate most of the weight loss in the first 3 months with a decline in the rate of loss over the last 9 months of the study (Maintainers). The second group (n=32) are the most successful (Rapid) demonstrating a rapid loss in the first 3 months, followed by a slower rate in the last 9 months, but with the greatest overall change from baseline. Group 3 (n=53) are the least successful group (Recidivists). While again showing most of their weight loss occurring in the first 3 months, this reduction slows between 3-9 months and BMI then starts increasing in the final three months.

Table 1 verifies these results by showing significant differences in weight change between the 3 groups at the different study timepoints. Those in the rapid weight loss group were significantly older than the other two groups, had a significantly lower rate of dropout and showed a greater proportion of retired participants than expected (adjusted standardised residual 4.2). The participants in the recidivist group in contrast were significantly younger than the other two groups, had a higher baseline BMI, a higher dropout rate and a higher proportion of participants employed in a trade or home duties than expected (adjusted standardised residuals 2.2 and 2.4 respectively). There was no difference between the groups in gender, education level, and baseline physical activity. The BMI groups did not differ in the proportions in the treatment and control groups in the studies P=0.208, χ^2 =3.15, df=2.

Of the 156 who completed the study, 51 (33%) had lost less than 5% body weight at 1 year, 106 (67%) of participants lost 5% or more, and 10 (6%) had a finishing weight in excess of their baseline weight. The proportion of participants in each of the 3 trajectory groups meeting the 5% weight loss criteria was significantly different (P<0.001, χ^2 =29.86, df=2). In the rapid weight loss group 29/29 (100%) met the criteria compared with 68/101 (67%) in the maintainers group, and 8/26 (31%) in the recidivist group (study completers only reported). The percent weight change from baseline for each of the three groups is represented in Figure 2.

Discussion

The aim of this study was to determine if different trajectories of change in BMI were evident in weight loss trials where an intervention effect was not demonstrated. A secondary aim was to determine if certain participant characteristics were associated with these different trajectories. If different trajectories could be identified this could suggest an underlying pattern which may confound intervention effects. Additionally if particular characteristics are associated with these patterns they can be accounted for in study randomisation and may suggest that specific approaches are needed for these target groups.

Three distinct BMI trajectories were identified, each associated with specific participant characteristics. The results of this study suggest that younger participants with higher a baseline BMI were less successful in both the amount of initial weight loss and their ability to sustain this weight loss overtime. Older subjects were more likely to achieve and sustain weight loss over the one year period. Although the number of participants in each employment category was small a significant relationship was found between employment category and the trajectory group with those who were retired being more likely to be in the rapid weight loss group and those employed in trades or home duties more likely to be in the recidivist group. The recidivist group also had a higher proportion of dropouts. Together these results suggest that the older participants particularly those who are retired may have had less competing responsibilities and were able to better comply with the study protocol and thus achieve a better outcome.

This finding has two important implications. Firstly on a public health level this suggests that weight loss interventions need to target demographic characteristics of the population. Younger adults with higher BMIs and competing work and home commitments may require a different strategy to older participants who have more time to commit to interventions. Secondly, our analysis indicates that weight loss intervention studies may require participants to be stratified according to baseline characteristics of age and BMI. This may prevent these baseline characteristics from confounding an intervention effect of the weight loss treatment.

Previously de Vos and colleagues[15] used growth mixture modelling to identify trajectories in a weight loss trial in overweight women which investigated the effectiveness of an individualised intervention for weight loss compared with a control who received no intervention. Their study differed from the present study in several ways. Mean weight losses in the treatment group were substantially smaller at one year (-0.6kg0.4SE) than those in our study population (-6.61kg0.52SE) and the control group gained weight (0.6kg0.4SE) whereas our control group lost a similar amount to the intervention group (-6.25kg0.61SE). Only 7.7% of their sample lost ≥5% of baseline weight at 12months compared with 67% in our sample (P<0.001). Their sample was restricted to women only within a narrow age range from 50-60 years, with a significantly higher baseline BMI compared with our cohort (32.36kg.m^{-2}(SD4.29) versus 30.65kg.m^{-2} (SD3.20) P<0.001). They also chose a model which identified 3 weight trajectories (steadies, gainers and losers) however in the previous study 2 of the 3 trajectories showed weight gain above baseline. Further, they demonstrated a significant effect of the intervention and the treatment group were significantly more likely to be in the losers group. That study was therefore limited in its ability to characterise the trajectory of weight loss independently of a particular type of intervention. The previous analysis showed that those with higher baseline weights were more likely to be losers, a finding distinctly different from ours where those with the highest baseline weights and BMIs were observed in the recidivist group. The lack of an effect of age in that study may be due to their limited age range of 50-60 years. Lastly, the previous study showed that those who had gained weight in the year prior to the study were more likely to be in the weight-losing group. Our trials excluded participants who had experienced a weight change in the 6 months prior to recruitment, again demonstrating that our results relate to a different population demographic and are therefore distinctly novel from those previously reported.

Other approaches to modelling weight loss trajectories have also been used in previous research of lifestyle interventions. Espeland et al (2009)[16] used principal component analysis to examine patterns of weight loss in the first year of the Look AHEAD study. This study compared an intensive lifestyle intervention with diabetes support and education only in overweight and obese subjects with type 2 diabetes. The first 6 months involved diet and physical activity advice to achieve a weight loss of 7% and if this was not achieved various strategies including pharmacological agents were used to individualise the weight loss plan. Thus the trial was not testing a single intervention per se. The results reported no evidence of clustering of subgroups of trajectories of weight loss, but rather demonstrated a continuum of varying patterns. Two principal components accounting for 97% of the variation represented a rapid weight loss and a curvilinear weight loss. The rapid component was more strongly associated with men, non-Hispanic whites, those with higher initial BMI, those with hypertension and those without cardiovascular disease as well as diabetes specific indicies of those with lower HbA1c and those not using insulin. A second analysis based again on principal components at 4 years of the LookAHEAD study found a similar relationship with the baseline characteristics. These results were extended to show that, within each component, a greater weight loss at the end of the first year showed the best weight outcomes at 4 years[4]. At one year 68% of the treatment group had lost ≥ 5% of baseline weight, which is similar to our cohort however only 13.3% of the control group met this criteria[17]. Clearly again the differing study population and intervention approach limit comparisons to our research. Importantly what this research does suggest is that this rapid weight loss is associated with longer term metabolic benefits and while it appears in our study there is a subgroup of older overweight subjects that can meet this criteria, further research is required to develop interventions for the younger higher BMI subgroup to promote longer term health.

While individual treatment response in randomised trials is known to vary, quantification of the amount and type of variability in weight loss trials and clinical trials in general is understudied[18, 19]. Limited research has demonstrated that the distribution of weight loss at the end of a trial is not normally distributed, shows large variance[20] and that there is a high proportion (30-40%) that may have weight gain[18]. Measuring the variability lends itself mathematically to covariance structure analysis or structural equation modelling of which the growth mixture model is a subtype[21]. The standard form of analysis of an intervention trial where treatment groups are specified by randomisation would be using a linear mixed, generalised linear mixed model or generalised estimating equation depending mainly on the distributional form of the response variable (see part II: Parametric modelling of longitudinal data [22]). Growth mixture modelling will not replace these forms of analysis however provides an important exploratory tool for following up the variation in treatment effects which can be done for the whole trial cohort or by treatment group[23].

Weight loss is a physiologically and biochemically heterogeneous process, and decreases in energy expenditure with weight loss have been shown to vary from -38% to -6% in a controlled experiment where subjects lost 10% of their weight [24, 25]. Strong hormonal influences drive weight regain after weight loss [26], and the individual variation in this process has yet to be characterised. However associations between success of initial weight loss and baseline leptin levels have been demonstrated [27]. Many genes may be involved in causing and/or promoting obesity and so it is not unexpected that the phenotypic presentation and response to treatments may vary substantially[28]. Growth mixture models provide a method for examining the effects of these different causal factors on the weight loss trajectory overtime. Given that current long term studies suggest initial weight loss is not sustained at the group level[17] it is necessary to determine what factors, other than those identified in this analysis, contribute to the group that continue to lose weight. Unanswered questions include whether these factors are psychological or lifestyle-related and whether they can they be extended to bring weight loss success to all or whether some genetic characteristics may be unresponsive to intervention?

This study has some limitations. Recently Thomas et al (2015)[29] used logistic regression modelling and Receiver Operating Curves to develop individualised models of predicting successful weight loss at one year based on modelling early individual weight loss at 1, 2 and 3 months along with age, sex, baseline weight, target dietary intake and difference between predicted and actual weight loss. This analysis was conducted on the POUNDS lost study which compared 4 dietary interventions varying in macronutrient composition. In this research incorporating the difference between predicted and actual weight loss addressed the mechanistic aspects of weight loss based on the first law of thermodynamics[30]. This normalisation of magnitude of weight loss relative to the predicted amount was not addressed in the current analysis and may address some of the unanswered questions above in future research.

Sample sizes in some of the categories were limited and these results need to be replicated in larger populations. The studies were overrepresented by males and those with a tertiary education. Seventy six percent of participants were Australian born and participants were primarily Caucasian of European descent. Comorbidities were an exclusion criteria which in part may explain some of the differences to the LookAHEAD study. Since comorbidities are common in overweight and obese populations, further investigations of which characteristics are associated with weight or BMI trajectories should include comorbidity data as covariates.

In summary growth mixture modelling was used to identify three different weight loss trajectories in weight loss trials with no intervention effect. The trajectories which represent successful rapid weight loss, weight loss maintainers and recidivists were associated with different baseline characteristics. These trajectories suggest firstly, that different treatment intervention may be warranted to manage obesity in the different demographic groups and secondly, that study designs must consider relevant covariates such as baseline BMI and age in randomisation to reduce the potential for the different trajectories to reduce the intervention effect. Further research in larger samples varying in baseline demographic and genetic characteristics is needed to determine additional factors associated with different weight loss trajectories.

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Conflict of Interest
The authors have no conflicts of interest to declare

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Table 1 Characteristics of the total sample and weight loss groups

	Maintainers (n=146)	Rapid (n=32)	Recidivists (n=53)	Total (n=231)	*P* Value
Gender	M 38(26%) F 108(74%)	M 10(31.2%) F 22(68.8%)	M 11(20.8%) F 42(79.2%)	M 59(25.5%) F 172(74.5%)	0.547
Age (years)	47(9) [a]	53(7) [b]	44(7) [c]	47(9)	<0.001
Education					
Secondary	29(20.1%)	10(32.3%)	17(32.1%)	56(24.6%)	0.214
Diploma	40(27.8%)	5(16.1%)	15(28.3%)	60(26.3%)	
Tertiary	75(52.1%)	16(51.6%)	21(39.6%)	112(49.1%)	
Profession					
Manager	23(17.4%)[a]	4(14.3%) [a]	4(8.3%) [a]	*31(14.9%)*	<0.001
Professional	25(18.9%) [a]	4(14.3%) [a]	9(18.8%) [a]	*38(18.3%0*	
Office work	39(29.5%) [a]	7(25%) [a]	15(31.2%) [a]	*61(29.3%)*	
Clerical	15(11.4%) [a*]	0(0%) [c]	2(4.2%) [a,b]	*17(8.2%)*	
Trade	14(10.6%) [a*]	5(17.8%) [a,b]	12(25.0%) [b*]	*31(14.9%)*	
Home duties	4(3.0%) [a]	0(0%) [a,b]	5(10.4%) [b*]	*9(4.3%)*	
Student	3(2.3%) [a]	0(0%) [a]	1(2.1%) [a]	*4(1.8%)*	
Retired	9(6.8%) [a]	8(28.6%) [b***]	0(0%) [a*]	*17(8.2%*	
Other[#]	*14(9.6%)*	*4(12.5%)*	*5(9.4%)*		
Weight change 0-3 (kg)	-3.95(2.46)[a] (n=123)	-8.29(2.34) [b] (n=31)	-3.71(3.19) [a] (n=41)	-4.59(3.06) (n=195)	<0.001
Weight change 3-12 (kg)	-1.04(2.86) [a] (n=101)	-5.15(3.76)[b] (n=28)	+1.13(2.94) [c] (n=26)	-1.42(3.60) (n=155)	<0.001
Weight change total (kg)	-5.32(3.30) [a] (n=101)	-13.12(4.57) [b] (n=29)	-3.07(4.14) [c] (n=26)	-6.40(4.96) (n=156)	<0.001
Baseline BMI (kg/m^2)	28.99(2.09) [a]	30.90(2.95) [b]	34.84(1.92) [c]	30.65(3.20)	<0.001
Dropout	45 (30.8%) [a]	3 (9.4%) [b]	27 (50.9%) [c]	75 (32.5%)	<0.001
Baecke activity score	7.6(1.4) (n=143)	7.0(1.1) (n=32)	7.3(1.4) (n=50)	7.4(1.4)	0.065

M male, F female. Groups which have different superscripts are significantly different using post hoc Bonferroni tests (anova) or z tests for proportions (chi square). Asterisks indicate statistically significant adjusted standardised residuals *<0.05, **<0.01, ***<0.001, [#] other not included in statistical analysis.

Figure 1 BMI trajectories of the 3 groups over 12 months

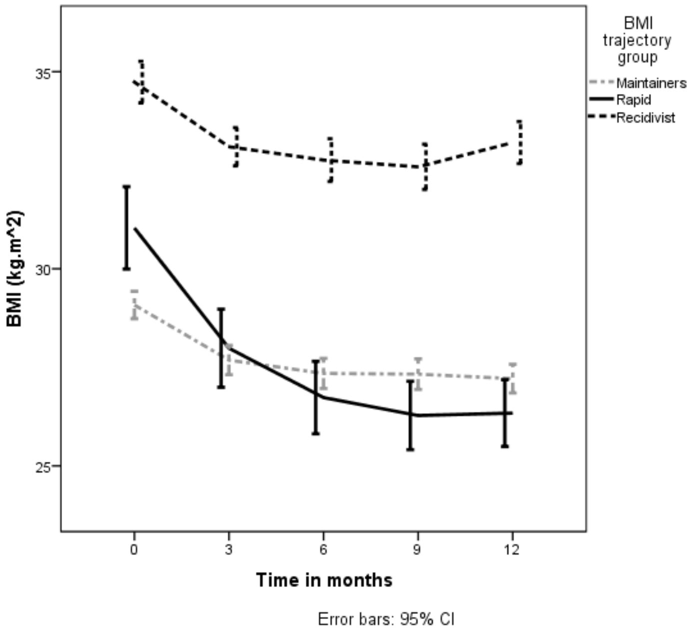

Figure 2 Mean percent weight loss at 3, 6, 9, and 12 months in the three BMI trajectory groups.