The effect of physical activity on weight loss is mediated by eating self-regulation

Ana M. Andrade, Silvia R. Coutinho, Marlene N. Silva, Jutta Mata, Paulo N. Vieira, Cláudia S. Minderico, Kathleen J. Melanson, Fátima Baptista, Luís B. Sardinha, Pedro J. Teixeira

A R T I C L E   I N F O
Article history:
Received 1 September 2009
Received in revised form 31 December 2009
Accepted 7 January 2010

Keywords:
Eating self-regulation
Physical activity
Exercise
Obesity
Women

A B S T R A C T

Objective: This study tested whether different forms of physical activity (PA) were associated with eating self-regulation during weight control, and if changes in eating behavior mediated the relationship between PA and weight loss, in overweight/obese women.

Methods: 239 women (37.6 ± 7.0 years; 31.3 ± 4.1 kg/m²) participated. The intervention group received a 12-month group behavioral treatment designed to increase autonomy and self-regulation for weight control. Controls received a health education program. Assessments included body weight, structured and lifestyle exercise/PA, and eating self-regulation.

Results: Moderate + vigorous and lifestyle PA were associated with 12-month change in most eating variables (p < 0.05) and with body weight change (p < 0.01). Mediation analysis showed that flexible cognitive restraint and emotional eating fully mediated the relation between lifestyle PA and weight change (effect ratio: 0.63). About 34% of the effect of moderate + vigorous PA on weight change was explained by these same mediators (partial mediation).

Conclusion: Exercise and PA may positively influence weight control through eating self-regulation. Flexible dietary control and reduced emotional overeating are mechanisms by which an active lifestyle can contribute to long-term weight management.

Practice implications: Regular exercise and PA can contribute to improved eating behaviors during weight management. This could represent an important incentive for people seeking weight control.

© 2010 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Obesity is a disorder of energy imbalance and highly dependent on variations in both dietary energy intake and energy expenditure. As such, weight management almost always involves the successful regulation of several energy balance-related behaviors, particularly eating and physical activity. While epidemiological and experimental studies show that physically active people tend to adopt more healthful diets than less active people [1–3], the extent, consequences, and underlying mechanisms of such behavioral covariance are largely unknown. Regarding the causal direction of the relationship, different research lines suggest a positive influence of physical activity on eating behavior. For instance, regular exercise may improve homeostatic control of appetite; active people have improved hunger–satiety mechanisms resulting in better appetite regulation [4]. Exercise may also help control urges to binge and eat in response to negative emotions [5], suggesting that psychological mechanisms are also involved. Regular exercise consistently improves mood and affect [6], which in itself is likely to influence self-regulatory skills and behavioral adherence in other areas [7]. While some individuals may increase their energy intake following exercise – whether responding to metabolic or behavioral adaptations to increased physical activity [8] – the preponderance of evidence suggests a neutral or positive effect of increased exercise on appetite regulation resulting in negative energy balance [4]. However, practically all available studies are of short duration (days or weeks) and the large majority used normal weight subjects (see [9] for a review). The potential of an exercise-eating relationship for the success of obesity treatment is easy to understand. Interventions that cause increases in physical activity would also improve participants' eating self-regulation with aggregate benefits in the ability to reach and maintain a reduced weight. In fact, this could partially explain the consistent associations between regular exercise/physical activity and successful long-term weight control [10].

Success and failure in the self-regulation of eating involve multiple psychological and behavioral facets [11,12]. In the context of obesity and weight control, some of the variables most

Notes:
- This trial is registered at ClinicalTrials.gov (NCT00513084).
- Corresponding author at: Faculty of Human Kinetics, Technical University of Lisbon, Estrada da Costa, 1495-688 Cruz Quebrada, Portugal.
Tel.: +351 21 414 9134.
E-mail address: pteixeira@fmh.utl.pt (P.J. Teixeira).

0738-3991/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pec.2010.01.006
commonly employed to evaluate eating self-regulation are cognitive restraint, disinhibition, perceived hunger, eating self-efficacy, internal/external eating, and binge/emotional eating [13,14]. Studies generally show that increases in eating self-efficacy and cognitive restraint, and decreases in emotional and disinhibited eating are predictive of successful weight control [15–19]. For instance, a high disinhibition score is clearly a risk factor for obesity as it is consistently associated with total energy intake and poorer food choices [20]. Using food to regulate affect (emotional eating) is reported by weight relapsers to a higher extent than by weight maintainers [21]. Regarding the role of cognitive restraint for successful eating and weight control, epidemiological [22–25] and intervention studies [26,27] clearly point to the relative advantage of flexible restraint of calorie intake over rigid control. Considering their importance for weight control, studying what predicts positive change in some of these eating behavior variables is clearly warranted. For instance, we have recently shown that increases in exercise motivation predict positive changes in eating self-regulation variables such as cognitive restraint and eating self-efficacy [28].

When studying physical activity, both as an outcome or as an exposure, it is important to distinguish between different types of activity, namely purposeful and more structured exercise (e.g., fitness classes, running), typically involving higher intensity and higher energy expenditure rates, and physical activities within daily living (e.g., walking for transportation, taking the stairs), which can be named spontaneous or lifestyle physical activity. In the context of obesity, both structured and lifestyle physical activity have been positively associated with successful long-term weight control [29]. However, there is a paucity of research looking at both predictors and consequences of different forms of physical activity behavior. For instance, motivational mechanisms underlying the adoption of structured exercise appear to differ from those associated with lifestyle physical activity in overweight women [30]. Indeed, behavioral and physiological correlates of different forms of physical activity may also be specific, at least to some degree.

The aims of this study were (i) to test if structured (moderate or vigorous) and lifestyle physical activity were associated with critical eating self-regulation variables during weight control in women, and (ii) whether this association mediated the relationship between physical activity and 1-year weight control. Since physical activity can directly influence body weight regulation by changing energy balance, we predicted partial mediation effects at best through eating-related mechanisms, especially for the impact of moderate and vigorous physical activity on weight change. For lifestyle physical activity, which typically involves a lower energy requirement compared to structured exercise, stronger indirect effects through eating self-regulation were expected.

2. Methods

2.1. Study design and intervention

The study was part of a randomized controlled trial including a 1-year behavior change intervention. Participants were split into two randomly-assigned groups, intervention and control. The intervention group attended 30 sessions in groups of 25–30 women while the control group received a general health education curriculum, in groups of similar size. Details of the study’s theoretical rationale, protocol, and a description of the intervention curriculum are available elsewhere [31,32]. In brief, primary targets of the intervention included increasing physical activity and energy expenditure, adopting a diet consistent with a moderate energy deficit, and ultimately establishing exercise and eating patterns that would support weight maintenance. Cognitive and behavioral aspects such as identifying personal barriers, overcoming lapses, establishing adequate goals, and implementing self-monitoring were emphasized. The program’s principles and style of intervention were based on Self-Determination Theory [33,34] with a special focus on increasing competence and autonomous self-regulation towards exercise and weight control. The control group attended 29 sessions grouped into “thematic courses” such as preventive nutrition, stress management, self-care, and effective communication skills, without addressing topics specific to weight control.

For the present study, subjects in both groups were pooled together for analyses since the relationships under scrutiny are hypothesized to be independent of the type of weight control program; additionally, pooling both groups led to a larger variability in values for the dependent and independent variables. The intervention team consisted of 6 Ph.D. or M.S. level exercise physiologists, nutritionists/dietitians, and psychologists. The Faculty of Human Kinetics Ethics Committee reviewed and approved the study, and all subjects signed informed consents.

2.2. Participants

Participants were recruited through newspapers, flyers, and TV advertisements to join a university-based behavioral weight loss program. To be included in the study, participants had to be female, between 25 and 50 years old, premenopausal, have a BMI between 25 and 40 kg/m², be willing to attend weekly meetings (during 1 year), be free from major illnesses, be not pregnant or lactating, and not take medications known to interfere with body weight regulation. This particular age group was selected for consistency with previous research studies in our Laboratory, which have largely focused on premenopausal adult women. Of all women who entered the study (N = 258), 19 women were subsequently excluded from all analyses because they started taking medication susceptible to affect weight (e.g., antidepressants, anxiolytics, antiepileptics; n = 10), had a serious chronic disease diagnosis or severe illness/injury (n = 4), became pregnant (n = 2) or entered menopause (n = 3). These women were of similar age (p = 0.575) and BMI (p = 0.418) as the 239 participants considered as the effective initial sample.

Participants were 37.6 ± 7.0 years old, overweight or mildly obese (BMI: 31.3 ± 4.1 kg/m²), and 67% had at least some college education. Women in the intervention group did not differ from those in the control group in terms of BMI, age, education, and marital status. There were also no differences between the women who completed the 12-month assessments and those who quit the program, for any demographics or psychosocial variable at baseline, except age; women who stayed in the program were on average four years older (p = 0.01).

2.3. Measurements

Weight was measured twice at each assessment, to the nearest 0.1 kg (average was used) using an electronic scale (SECA model 770, Hamburg, Germany) and height was also measured twice, to the nearest 0.1 cm (average was used). Body mass index (BMI) in kilograms per meter squared was calculated from weight (kg) and height (m).

Cognitive restraint, disinhibition, and perceived hunger were assessed with the 51-item Eating Inventory, also known as the Three-Factor Eating Questionnaire (TFEQ [35]). The cognitive restraint scale (21 items) measures conscious attempts to monitor and regulate food intake, the disinhibition scale (16 items) measures uncontrolled eating in response to cognitive or emotional clues, and the perceived hunger scale (14 items) measures the extent to which respondents experience feelings...
of hunger in their daily lives. Higher scores indicate higher levels of cognitive restraint, disinhibition, and perceived hunger. Two additional scores, flexible restraint and rigid restraint, were calculated from the TFEQ [22,36]. Flexible cognitive restraint (7 items) is associated with low emotional and disinhibited eating, with a higher score indicating a more graduated approach to eating and weight control. Rigid cognitive restraint (7 items) is associated with a dichotomous, all-or-nothing eating pattern and with higher disinhibition. The Dutch Eating Behavior Questionnaire [37] was used to measure external eating (sensitivity to external cues such as sight and smell of food), and emotional eating or eating in response to affective states (diffuse and clearly-identified emotions). It consists of 31 questions and answers are given on a 5-point scale from “never” to “very frequently”. Eating self-efficacy, the belief in one’s capacity for resisting opportunities to overeat and for self-regulating one’s dietary intake, was assessed with the Weight Management Efficacy Questionnaire [38]. Statements were evaluated on a 10-point scale from “not at all confident” to “very confident”.

Subjects completed psychosocial assessments at baseline and 12 months, following a standard protocol with a study technician attending every assessment period. In brief, forward and backward translations between English and Portuguese were performed for all questionnaires cited above. Two bilingual Portuguese researchers subsequently reviewed the translated Portuguese versions and minor adjustments were made to improve grammar and readability. Cronbach’s alphas for baseline and 12-month measurements were acceptable (above 0.70), except for rigid and flexible restraint, which were slightly lower [27].

Minutes per week of leisure-time moderate and vigorous physical activities were estimated with the 7-Day Physical Activity Recall interview [39,40]. Habitual activities with a MET value above 3.0 and performed during the last 7 days (or on a typical week of the past month) were quantified to produce this variable. A lifestyle physical activity index was specifically developed for this study as a simple self-administered instrument for measuring habitual lifestyle physical activities typical of the last month. This is a variable typically not available in existing physical activity questionnaires. To calculate the lifestyle physical activity index we used a score based on the mean value of 7 questions, such as “Using stairs or escalators”; “Walking instead of using transportation”; “Parking away from destination”; “Using work breaks to be physically active”. The response options ranged from never (1) to always (5) on a Likert scale. The internal consistency (Cronbach’s alpha) of this scale was 0.84.

2.4. Statistical analyses

For correlation, regression, and mediation analyses, psychosocial variables and body weight were expressed as residuals of the 12-month value regressed on the baseline score. This method is preferable to the use of subtraction scores, which can induce overcorrection of the post by the pre-score [41]. For physical activity, we used 12-month values as the independent variable. Previous experience in our laboratory has shown considerable overestimation of physical levels at baseline assessments, possibly as a result of little previous/current experience with these behaviors on the part of participants. Hence, we opted for using the final value for lifestyle and moderate and vigorous physical activity as indicators of change through the course of the 1-year program [32].

Pearson correlations were used to test for bivariate relations. For the mediation analyses (see Fig. 1 for the overall model), we used a novel procedure to calculate total, direct, and indirect effects of physical activity on weight change through selected mediators, as described by Shrout and Bolger [42]. Preacher and Hayes [43] have recently provided a SPSS macro that calculates total, direct, and indirect effects (total and specific for each mediator), including tests of significance using both normal theory and bootstrap procedures. The latter are considered preferable because they do not assume normality of the distribution of the indirect effects and hence provide stronger protection against type II errors, compared to normal procedures such as the Sobel test [42]. We report results for both normal theory and bootstrap tests, with a resample procedure of 5000 bootstrap samples (bias corrected and accelerated estimates and 95% CI). Effect ratios were calculated to express the amount of the total effect that is explained by the (total) indirect effects via the mediators. For example, an effect ratio of 0.5 would mean that half of the total effects of the independent on the dependent variable is explained by the mediator(s), assuming no suppressing variables are present in the model [42].

3. Results

Retention rates in the intervention and control groups were 93% and 80%, respectively (87% overall). Intervention effects on physical activity, eating behavior, and body weight have been reported elsewhere [27,32]. Briefly, moderate and vigorous physical activity reached 300 ± 179 min (from 110 ± 150 min at baseline) in the intervention group and 162 ± 171 min (from 88 ± 122 min at baseline) in the control group (p < 0.001 for between-group changes). The between-group effect size for the lifestyle physical activity score was 1.13 (3.84 ± 0.69 vs. 2.98 ± 0.81, respectively for intervention and controls, p < 0.001). Twelve-month change effect size for eating behavior variables ranged from –0.36 (emotional eating) to 1.42 (flexible restraint) in the intervention group and from 0.03 (emotional eating) and 0.61 (total and rigid restraint) in controls, p < 0.01 for all between-group comparisons. Body weight changed by –7.3 ± 5.9% and by –1.7 ± 5.0% in the intervention and control groups, respectively (p < 0.001).

Table 1 shows bivariate correlations among physical activity, eating, and body weight variables at 12 months. Both lifestyle as well as moderate and vigorous physical activity were significantly correlated with all eating behavioral variables. As hypothesized, body weight change was also predicted by both eating and physical activity measures; flexible (and total) cognitive restraint, emotional eating, and eating self-efficacy were the strongest eating behavior predictors, while moderate and vigorous physical activity was a stronger correlate of body weight change than lifestyle physical activity.

Before testing for mediation effects, we ran a multiple regression model with weight change as the dependent variable, followed by eating-related variables significantly associated with weight change in stepwise fashion. Considering some degree of covariance among all eating variables, this was conducted to identify the strongest independent predictors within eating variables to be included in multiple mediation models. It should be noted that a stepwise option is not available in the multiple
The aims of this study were to describe the long-term relationship between two types of self-reported physical activity and several eating behavior variables that generally describe dietary self-regulation and, secondly, to analyze whether eating behavior was among the mechanisms explaining the relationship between physical activity and weight change, in overweight and mildly obese women. Results confirmed that individuals reporting higher levels of physical activity after the program were also those displaying more substantial (and positive) changes in eating self-regulation. More importantly, eating variables appeared to mediate the association between physical activity, particularly lifestyle types of physical activity, and 1-year body weight change. This indicates that the adoption of physical activity may predict weight loss success partially due to its effects on important markers of eating behavior such as a more flexible dietary restraint pattern and lower levels of emotional eating.

Two forms of physical activity were analyzed in this study. As expected, structured, moderate and vigorous exercise was more strongly associated with change in body weight than lifestyle activity, which typically involves a lower caloric expenditure. However, in both cases, a significant portion of the effects (of exercise on body weight) was, according to mediation analysis, explained by changes occurring in eating behavior. For self-reported structured exercise, about one-third of the effect was shown as being indirect, mediated by flexible cognitive restraint and emotional eating. While the direct effect is easy to justify by the relatively high energy expenditure induced by purposeful exercise of at least moderate intensity, the indirect effect through eating behavior is open to several possible explanations. They may range from psycho-biological aspects related to appetite regulation as increased self-efficacy and motivation as increased self-efficacy and motivation, to exercise-induced effects on mood, affect, and psychological well-being [47]. These metabolic (automatic) and behavioral (mostly volitional) aggregate effects are made even more complex because they may change with time, as described by King and colleagues [9]. Thus far, very few studies have analyzed long-term effects of exercise on eating behavior variables.

### 4. Discussion and conclusion

#### 4.1. Discussion

The aims of this study were to describe the long-term relationship between two types of self-reported physical activity and several eating behavior variables that generally describe dietary self-regulation and, secondly, to analyze whether eating behavior was among the mechanisms explaining the relationship between physical activity and weight change, in overweight and mildly obese women. Results confirmed that individuals reporting higher levels of physical activity after the program were also those displaying more substantial (and positive) changes in eating self-regulation. More importantly, eating variables appeared to mediate the association between physical activity, particularly lifestyle types of physical activity, and 1-year body weight change. This indicates that the adoption of physical activity may predict weight loss success partially due to its effects on important markers of eating behavior such as a more flexible dietary restraint pattern and lower levels of emotional eating.

Two forms of physical activity were analyzed in this study. As expected, structured, moderate and vigorous exercise was more strongly associated with change in body weight than lifestyle activity, which typically involves a lower caloric expenditure. However, in both cases, a significant portion of the effects (of exercise on body weight) was, according to mediation analysis, explained by changes occurring in eating behavior. For self-reported structured exercise, about one-third of the effect was shown as being indirect, mediated by flexible cognitive restraint and emotional eating. While the direct effect is easy to justify by the relatively high energy expenditure induced by purposeful exercise of at least moderate intensity, the indirect effect through eating behavior is open to several possible explanations. They may range from psycho-biological aspects related to appetite regulation as increased self-efficacy and motivation, to exercise-induced effects on mood, affect, and psychological well-being [47]. These metabolic (automatic) and behavioral (mostly volitional) aggregate effects are made even more complex because they may change with time, as described by King and colleagues [9]. Thus far, very few studies have analyzed long-term effects of exercise on eating behavior variables.
In today’s environment, with abundant food stimuli, “hedonic hunger” can easily disrupt physiological eating regulation [48]. Indeed, disinhibition and opportunistic eating in the presence of high incentive value foods may cause overeating and weight gain [20]. Additionally, negative emotional states are known to affect eating behavior, for instance by depleting cognitive resources needed for habitual restraint [49]. Thus, processes that strengthen the regulation of emotional states should predict more healthful eating choices and improved weight control. Exercise/physical activity could be such a process. In a recent review, Martins et al. concluded that exercise improves appetite regulation and does not result in increased perception of hunger and/or energy intake, at least in the short-term [4]. Others have observed that adding three times per week of structured exercise to cognitive-behavioral therapy for binge eating resulted in fewer episodes of uncontrolled eating [5]. These authors appeared to attribute most of the exercise effect to improvements in psychological function resulting from the added regular exercise. Indeed, exercise may improve psychological well-being [30] and decrease anxiety and stress sensitivity [51], which could aid in successfully controlling emotional overeating. The present results add to the literature by showing that fewer emotional (or internal) overeating episodes may be one mechanism by which exercise indirectly contributes to weight control during weight loss treatment.

Recent studies have also highlighted the fact that individuals engaging in regular structured exercise display an enhanced capacity to compensate for larger preloads by eating fewer calories at the following meal [52]. This enhanced compensatory capacity for the regulation of food intake is similar to (or at least included in) what is captured by the flexible cognitive restraint scale of the TFEQ. Flexible cognitive restraint is an interesting facet of eating behavior, and one that could be of primary relevance for people in need of losing and/or maintaining weight. On the one hand it is a form of dietary restraint, thus effectively resulting in decreased energy intake if implemented successfully; this is almost always a requirement for the overweight/obese person involved in a weight management program. On the other hand, it is a moderate and graduated approach to cutting calories from food, quite distinct from the “all-or-nothing” dieting approach where eating forbidden foods and lapses are introjected as failures and strict dietary prescriptions are adhered to rigidly [36]. We have recently shown that increases in flexible cognitive restraint, but not in rigid restraint, predicted 24-month weight loss after treatment [27], in line with results from previous studies [23,24,26]. Additional putative mechanisms related to how regular exercise affects body weight regulation (through flexible eating control) are increases in exercise self-efficacy and motivation. If a person believes he/she can substantially increase energy expenditure using exercise/physical activity in periods when energy intake has occasionally increased, this is likely to decrease internal pressure to strictly diet and reduce feelings of guilt after (over)eating. Both self-efficacy and exercise intrinsic motivation have been shown to predict long-term weight control in women [16,27].

Cognitive and motivational factors may also underlie our result showing that the effect of lifestyle physical activity on weight change was almost completely mediated by measured changes in eating behavior variables. Small changes in daily life such as parking further away from the destination or regularly taking the stairs may add to daily total energy expenditure but are unlikely to carry the physiological significance needed to influence mood-stabilizing neurotransmitters or influence appetite regulation biological cascades. However, in our program, women who effectively internalized the motivation to be more physically active to the point of automatically (and consistently) adopting the more energy-costly option in daily routines discarding the more sedentary behavior (e.g., standing instead of sitting when waiting, taking a walk during a short break), may have also displayed a more internal and steady drive to adopt other weight-heathful behaviors, such as a balanced eating pattern and self-monitoring. Motivational factors may predict eating self-regulation to the degree that motivation is internally regulated or autonomous [28,53]. We have observed that general, treatment, and exercise autonomous motivation were associated with higher eating self-efficacy and cognitive restraint, and with lower disinhibition, internal, and external eating [28]; furthermore, autonomous motivation partially mediated the effects of physical activity level on eating self-regulation. Underlying mechanisms should include accepting the regulation of behavior change as one’s own as opposed to being externally controlled. Participation in regular exercise will enhance self-determined regulation if it induces a shift in regulatory motives from external to more internal [54], following the internalization process described by Self-Determination Theory [34]. As we and others have shown, self-motivation, self-efficacy, and intrinsic reasons to lose weight are significant predictors of successful weight loss and maintenance [13,14,55–57].

Limitations of this study include the fact that it is based on a post-hoc analysis of an existing RCT not primarily aimed at studying the relationship between exercise and eating behaviors [31]. Future studies specifically planned and powered to study these effects are needed to further confirm or refute the present results. Nevertheless, we did plan to study predictors (e.g., self-regulatory processes) associated with successful weight control; this analysis opens up exciting new hypotheses for future research. Also, by design, we cannot fully exclude the existence of interaction/moderation effects by the intervention on the relationships under analysis. According to our analysis adjusting for group membership, if they are present, these effects should be stronger for the results involving lifestyle physical activity. Participants in this study volunteered for a weight loss program and may thus represent a self-selected group of overweight and obese women (e.g., more motivated to reduce their weight), which could affect the generalizability of the findings. Finally, it is unknown if the mechanisms suggested by the present results would also occur in the long-term, after the intervention has ended, i.e. whether they may additionally contribute to weight loss maintenance.

4.2. Conclusion

In summary, the present study adds empirical evidence to the contention that exercise and physical activity may positively influence weight control through direct but also indirect mechanisms, including eating self-regulation. Adopting a flexible control over one's eating behavior and reducing emotional overeating are likely mechanisms by which physical activity contributes to successful weight management in women, in the context of a behavioral weight loss program.

4.3. Practice implications

When assisting overweight and obese participants, clinicians and health professionals can use the present findings in several ways. First, ensuring that physical activity, both structured and unstructured, is effectively promoted early on in the treatment program will not only directly contribute to energy expenditure but is also likely to contribute to behavioral self-regulation in other areas such as eating behavior. Thus, practitioners should also discuss with participants the multiple roles of exercise and physical activity in weight control, not only for health benefits (e.g., reducing obesity co-morbidities) but also for its facilitating role in the multiple changes in lifestyle that are often required. People seeking weight control are often discouraged with the modest
effects of exercise alone on weight control; knowing that an active lifestyle can also help them regulate their dietary intake could be an important additional incentive. Finally, for participants with specific difficulties in dietary control (e.g., women with a tendency to rigidly control their eating or with frequent overeating episodes), practitioners should be mindful that regular physical activity could be a useful intervention aid, along with nutrition education and other types of behavior change counseling.

**Conflict of interest**

All authors read and approved the final manuscript and have no competing interests to declare.

**Role of the funding source**

This study was partially funded by the Portuguese Science and Technology Foundation (grant number FCT-POCI/DES/57705/2004) and the Calouste Gulbenkian Foundation (grant number 65565/2004). The Oeiras City Council, Nestlé Portugal, and IBESA Portugal provided additional financial support. The funding sources had no involvement in the study design, in data collection, analysis and interpretation, in the writing of the report, and in the decision to submit the paper for publication.

**Acknowledgements**

The authors are grateful to all the participants in this study. They also acknowledge Teresa Santos and Mariana Pessoa for their help in implementing the PESO trial and in project coordination and supervision.

**References**


