# Nutritional Interventions in Metabolic Syndrome A Systematic Review

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## Abstract

There is no consensus on the most appropriate nutritional strategy for treating metabolic syndrome (MS), such that cardiovascular risk is reduced. This study was designed to assess the strength of evidence of the benefits of various nutritional interventions in MS remission. Performed in Medline, Cochrane Library and PubMed databases, the virtual search consisted of randomized clinical trials published between 1999 and 2009 in any language, studies involving individuals aged 18 or older and diagnosed with MS, regardless of the criterion. The Boolean operator *and* was used in the combination of the MeSH terms "Metabolic Syndrome", "Metabolic x Syndrome" and "Metabolic Syndrome X", the entry terms "Dysmetabolic Syndrome X", Metabolic Cardiovascular Syndrome," "Metabolic X Syndrome" and "Syndrome X, Metabolic", plus the terms "diet", "intervention and diet", "treatment and diet" and "supplementation". For each study included in the review, we estimated the prevalence of MS and the calculation of effectiveness after the follow-up period. Relative risk measures for each study were described by Forest Plot. We identified 131 articles, which, after eligibility criteria, resulted in 15 studies. These studies were divided into four groups: normocaloric diet associated with exercise; isolated normocaloric diet, low-calorie diet combined with exercises; and isolated low-calorie diet. Tests with low-calorie diet associated with exercising revealed higher efficiency values, helping to emphasize the global aspects of lifestyle change in the treatment of MS, in which healthy and low-calorie diet should be complemented with the practice of physical activity.

## Keywords

Metabolic syndrome; clinical trials; exercise; diet fat-restricted; evidence - based medicine.

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## Introduction

Metabolic syndrome (MS) is a set of at least three abnormalities, either in blood pressure or metabolism of carbohydrates and lipids, usually associated with cardiovascular disease, the leading cause of morbidity and mortality in Brazil[1].

There is no consensus on the most appropriate nutritional strategy to treat MS. Although current proposals related to behavioral alterations such as changed eating habits and physical activity[2], nutritional recommendations were established from studies with healthy patients or those with isolated metabolic alterations[3-8]. Thus, since the treatment is effective only for one component of the syndrome, instead of diagnosis remission, represented by the normalization of at least three characteristics, cardiovascular protection would therefore be smaller.

In this context, the Guidelines Project of the Brazilian Society of Endocrinology[4] underscores the need for conducting research that contributes to define the type of intervention that is more effective in the treatment of individuals diagnosed with MS.

Due to lack of systematic review on this topics, this study was designed to assess the strength of evidence of the benefits of various nutritional interventions in MS remission.

## Methods

We performed a systematic review of studies with nutritional interventions in individuals with MS diagnosed by the presence of at least three alterations as recommended by the World Health Organization (WHO) in 1999[9]. In addition to this official publication, other diagnostic criteria suggested by the National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III)[10], American Heart Association (AHA)[11], International Diabetes Federation (IDF)[12] and European Group for the Study of Insulin Resistance (EGIR) [13] were also considered, as they represented adaptations or modifications of the official criterion.

The virtual search was performed on Medline, Cochrane Library and PubMed databases, to seek clinical trials published between 1999 and 2009 in any language. The evaluation of eligibility criteria was developed independently by two reviewers; in case of disagreements, advice was asked to a third researcher.

The Boolean operator *and* was used in the combination of the MeSH terms "Metabolic Syndrome", "Metabolic x Syndrome" and "Metabolic Syndrome X"; the entry terms "Dysmetabolic Syndrome X", Metabolic Cardiovascular Syndrome," "Metabolic

X Syndrome" and "Syndrome X, Metabolic", plus the terms "diet", "intervention and diet", "treatment and diet" and "supplementation". The type of publication was a randomized clinical trial for all combinations of words.

Abstracts of selected articles were analyzed to determine whether they met the inclusion criteria which included: presenting a randomized controlled clinical trial proposal for nutritional intervention in population older than 18 years of age, and consider the MS remission as the outcome. We excluded studies of interventions designed to treat only isolated MS alterations.

Wherever possible, we employed PRISMA[14] to report this systematic review. After reading the full articles, the results were summarized according to the MS diagnosis criterion, nutritional intervention, the control group, the intervention period and the prevalence of MS, the main outcome of this review.

To make comparison between studies easier, we calculated the effectiveness of interventions through the prevalence values of MS after the follow-up period, applied in the formula proposed by Szklo[15]: { [ (prevalence in the control group — prevalence in the intervention group) / prevalence in the control group] x 100}.

Relative risk measures for each study were described by Forest Plot, prepared in the statistical software Review Manager, version 5. However, statistical meta-analysis was not justified due to marked heterogeneity of studies included.

## Results

In the electronic search, 131 publications were obtained, of which, after reading the summaries and excluding some which involved drugs, 59 articles were selected for analysis. After exclusion of 44 articles that did not meet the inclusion criteria, 15 studies were included in the review (Figure 1).

All selected studies were randomized controlled trials and were published in English. As for the location, Italy[16-18] contributed with three studies; the United States[19-23] with five; Finland[24,25] with two; and Japan[26], Germany[27], Iran[28], Spain[29] and Norway[30], with one each.

The interventions had periods between six weeks and 31 months and involved 2,089 participants aged between 24 and 75 years with body mass index (BMI) between 26 and 43kg/m$^2$. Out of the 15 studies, only three mentioned run in period[16,25,28], and two with partially blind intervention[17,20].

As to the population, four trials studied outpatients from only one hospital[18,22]; two were multicentric[24,29]; two studied population representative of communities[16,30]; three studied patients picked up by newspaper advertisements[19,2526]; one studied university employees[20]; and three did not inform the population studied[21,23,27].

The prevalence of MS was the main outcome in six studies[16,24-26,29,30] and secondary when the prevalence of MS components[18-22,27,28], weight reduction[23] and behavior of inflammatory markers and endothelial function[17] function were the primary outcomes.

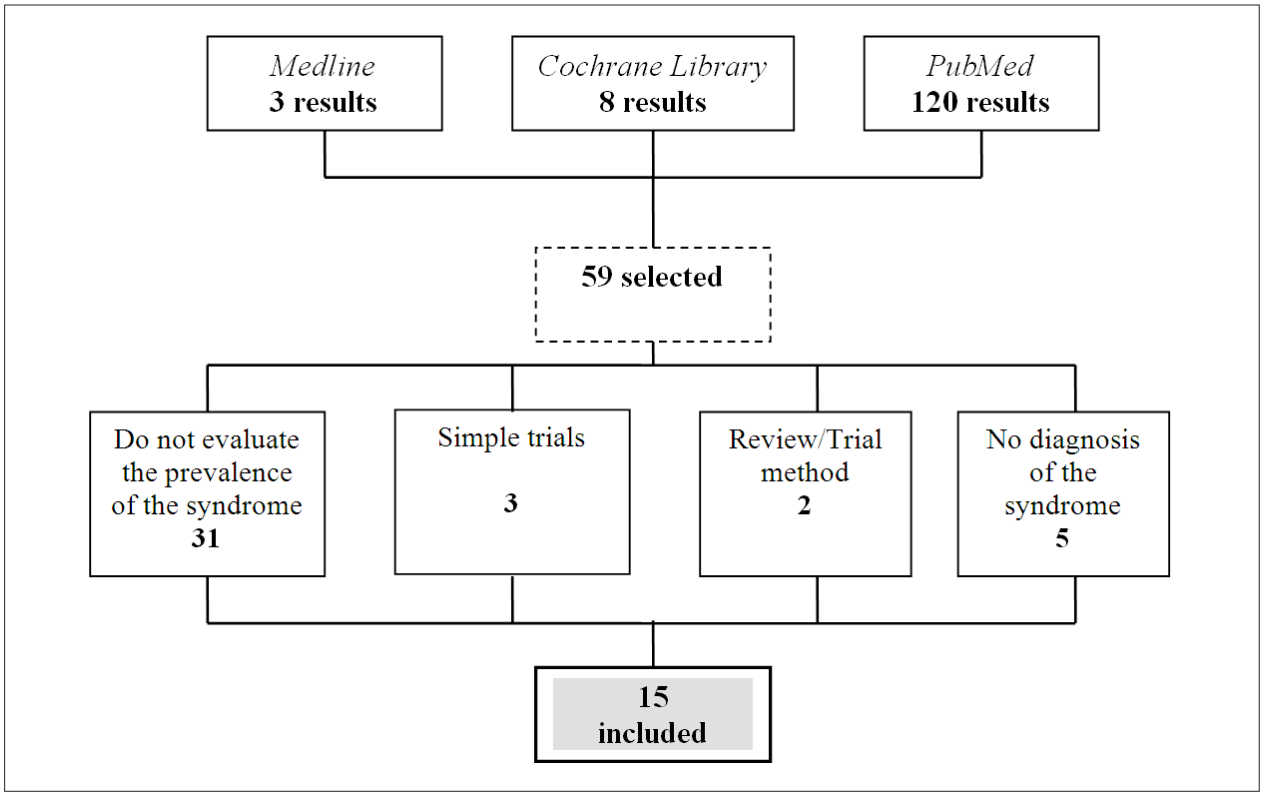


*Figure 1 - Electronic search and inclusion of articles of the study.*

The tests were grouped according to type of intervention, namely: normocaloric diet combined with exercise[16,19]; normocaloric diet[20,29], low-calorie diet combined with exercise[24,25], and low-calorie diet[22,27] (Table 1).

### Normocaloric diet combined with exercise

In the study by Stewart et al[16] the intervention group was asked to perform supervised aerobic exercise three times a week, besides the individual diet. Controls received only general guidelines on healthy diet. Similarly, Bo et al[17] instructed its control group with general information, while the intervention group received individualized nutritional counseling and exercise recommendations.

### Normocaloric Diet

In the study by Mutungi et al[20] the intervention was characterized by a diet without caloric restriction, low-carbohydrate, plus three liquid eggs (Vista®) per day. The control group consumed only a maintenance diet. It is noteworthy that although the diet proposal was normocaloric,

**Table 1 - Summary of studies included in the systematic review with their calculations of effectiveness**

| Author Year | Criteria for diagnosingMS | Intervention Group* | Control Group* | Duration (months) | Effectiveness of the study % |
|---|---|---|---|---|---|
| Stewart et al[19], 2005. | NCEP/ATPIII 2001 | Normocaloric diet + exercises (n=22) | General Guidelines (n=22) | 6 | 27.8% |
| Bo et al[16], 2007. | NCEP/ATPIII 2001 | Normocaloric diet + exercises (n=119) | General Guidelines (n=120) | 12 | 46.9% |
| Mutungi et al[20], 2008 | NCEP/ATPIII 2001 | Normocaloric diet + 3 eggs (n=11) | Normocaloric diet (n=7) | 3 | 100% |
| Salas-Salvadó et al[29], 2008. | NCEP/ATPIII 2001 | Normocaloric diet + olive oil (n=250)<br>Normocaloric diet + nuts (n=250) | Normocaloric diet (n=250) | 12 | 5.3%<br>13.8% |
| Kukkonen-Harjula et al[25], 2005. | NCEP/ATPIII 2001 modified | Low-calorie diet + exercises (n=10) | Low-calorie diet (n=13) | 31 | 25.7% |
| Villareal et al[21], 2006, | NCEP/ATPIII 2001 | Low-calorie diet + exercises (n=9) | General Guidelines (n=15) | 6.5 | 66.7% |
| Okura et al[26], 2007, | COMITÊ JAPONÊS 2005 | Low-calorie diet + exercises (n=38) | Low-calorie diet (n=21) | 3.5 | 81.5% |
| Anderssen et al[30], 2007, | IDF, 2006 | Low-calorie diet + exercises (n=43) | Low-calorie diet (n=34) | 12 | 49.6% |
| Ilanne-Parikka et al[24], 2008. | AHA, 2005 | Low-calorie diet + exercises (n=196) | General Guidelines (n=06) | 12 | 14.3% |
| Seshadri et al[22], 2004, | NCEP/ATPIII 2001 | Low-calorie high carbohydrates (n=19) | Low-calorie diet (n=17) | 6 | 16.4% |
| Esposito ET al[17], 2004, | NCEP/ATPIII 2001 | Mediterranean low-calorie diet (n=90) | General Guidelines (n=90) | 24 | 48.8% |
| Azadbakht et al[28], 2005, | NCEP/ATPIII 2001 | Low-calorie diet DASH (n=38) | Low-calorie diet (n=38) | 6 | 19.8% |
| Muzio et al[18], 2007, | NCEP/ATPIII 2001 | Low-calorie high carbohydrates (n=50) | Low-calorie high carbohydrates (n=50) | 5 | 23.3% |
| Katcher et al[23], 2008, | NCEP/ATPIII 2001 | Low-calorie diet with whole grains (n=24) | Low-calorie diet (n=23) | 3 | 0% |
| König et al[27], 2008. | NCEP/ATPIII 2001 | Low-calorie + soy-based meal replacement (n=22) | Low-calorie diet (n=8) | 1.5 | 11.9% |

*NCEP/ATPIII - National Cholesterol Education Program Adult Treatment Panel; IDF - International Diabetes Federation; AHA - American Heart Association; DASH - Dietary Approaches to Stop Hypertension; * Individuals diagnosed with metabolic syndrome.*

both groups reduced the energy content of the diet by the end of follow-up period.

In the trial by Salas-Salvadó et al[29] the two intervention groups consumed a Mediterranean diet supplemented with extra virgin olive oil (1.25L per week) or nuts (15g of walnuts per day; 7.5g of hazelnuts per day; 7.5g of almonds per day). The control group was guided only with normocaloric diet.

### Low-calorie diet combined with exercise

In the study by Kukkonen Harjula et al[20] participants underwent two phases: one which consisted of weight reduction and another which consisted of weight maintenance with the intervention of interest, diet plus walking, and one control group only with diet. In the study by Villareal et al[21] the intervention consisted of low-calorie diet combined with exercise, while the control group consumed only low-calorie diet. Okura et al[26] provided the control group a low-calorie diet with a food supplement (MicroDiet®). The intervention group consumed the same diet associated with exercise.

In the study by Anderssen et al[30] the group which combined exercise and diet was supervised to perform aerobic activity three times a week and calorie intake with energy restriction. The control group consumed only individualized low-calorie diet.

In the study by Ilanne-Parikka et al[24] the intervention consisted of guidelines to increase the level of physical activity, addition of 15g of fiber for each 1,000kcal and adoption of a diet low in fat and cholesterol. The control group received only general guidelines.

### Low-calorie diet

The study by Seshadri et al[22] offered balanced low-calorie diet to the control group, while the intervention group was instructed to consume low-calorie diet low in carbohydrates. Esposito et al[17] oriented the intervention group with a Mediterranean diet, while the control group followed general guidelines on healthy eating.

In the Azadbakht study[28] the intervention consisted of the DASH diet (Dietary Approaches to Stop Hypertension), with a deficit of 500 kcal/day, higher intake of fruits, vegetables, nonfat dairy foods and lower sodium content.

Muzio et al[18] conducted intervention with 48% carbohydrates and 65% control, both with a deficit of 500 kcal/day and monthly group sessions for nutritional guidance, while Katcher et al[23] compared a low-calorie diet group based on whole grains with another that consumed refined grains.

The study by König et al[27] instructed the control group to consume low-calorie diet and the intervention group to replace two meals a day for a soy yogurt with honey (Almased ®).

Considering all studies included in the review, as well as the different groups according to type of intervention and corresponding calculation of effectiveness, it was observed that the low-calorie diet combined with physical exercises performed better compared to other groups, followed by normocaloric diet with exercise, isolated low-calorie diet and isolated normocaloric diet.

However, regardless of the type of nutritional intervention, measures of effect expressed in the Forest Plot describe the protective effect on the risk of developing MS for all proposals for nutritional treatment analyzed (Figure 2).

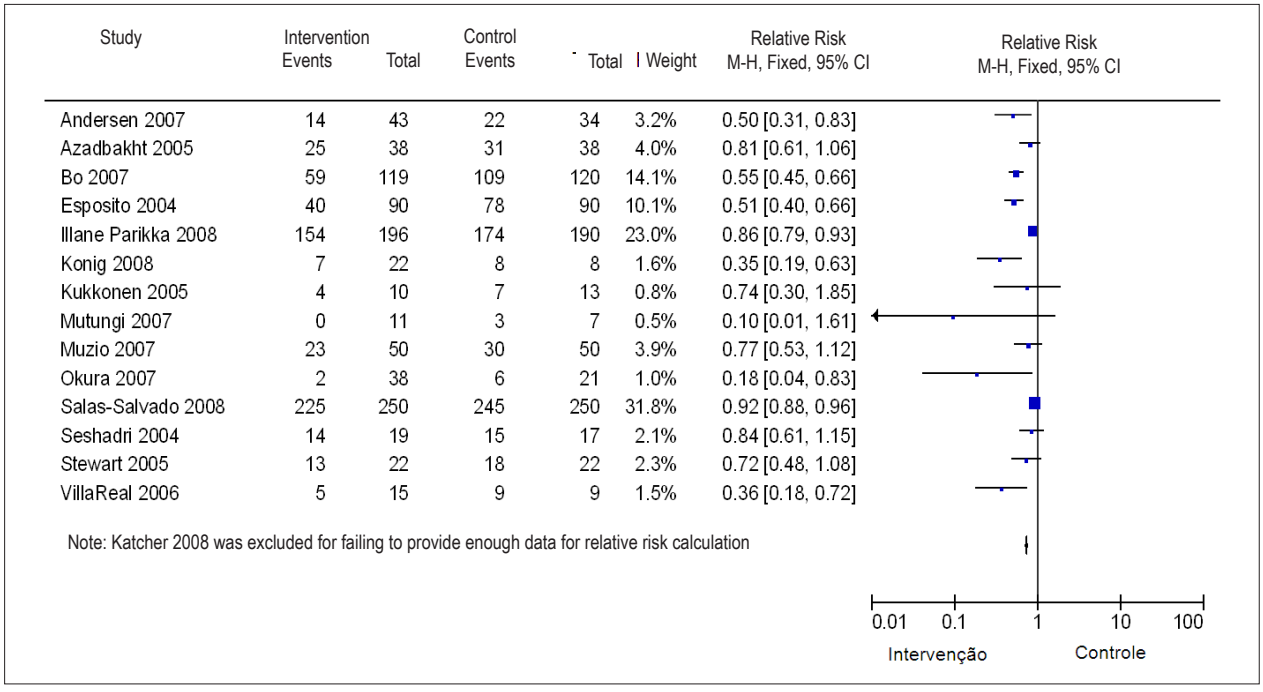


*Figure 2* - Forest plot of studies included in the systematic review and relevant measures of association.

## Discussion

As far as it is known, this is the only systematic review to evaluate the evidentiary strength of nutritional interventions in MS diagnosis remission. After an extensive search strategy, inclusion of only 15 studies stated the shortage of literature when it comes to assessing the diagnosis of MS as primary or secondary category-based outcome.

Besides the quantitative limitation, the low quality and heterogeneity of the studies were also noted. None of the authors conducted the trial according to the CONSORT guide (http://www.consort-statement.org/); there was high variability in the time of intervention. Some studies stipulated control groups based solely on general guidelines, while others, on calculated diet; and most of them compared groups with small samples (<30 participants).

These characteristics, associated with poor detailing of the methodology in most articles, prevented clarification on the sample size calculation, as well as specific information about the development of the intervention proposed, such as blinding and run in period, preventing a meta-analysis of the results presented.

However, the effectiveness of low-calorie proposals combined with physical activity was similar to the interventions performed in individuals with isolated alterations[31-34] and reinforce the suggestion by Reaven[35], who proposed a low-calorie diet combined with physical activity for the treatment of patients with MS.

We may consider that reducing diet calorie is the main strategy for the treatment of overweight[36], because reduced calorie intake promote reduced fat mass by means of negative energy balance, a condition in which energy expenditure exceeds energy intake. When calorie reduction is added to the practice of physical activities, the effect of weight reduction is enhanced, especially in individuals with MS, where the maintenance of lean body mass would increase sensitivity to insulin[37].

The importance of physical activity added to a diet plan, though normocaloric, was demonstrated in the studies by Stewart et al[16] and Bo et al[17]. Even with effectiveness inferior results comparing to interventions with low-calorie diet and exercise, similar characteristics of age and BMI in both groups and maintenance of energy consumption after the intervention reinforce the influence of physical activity on weight reduction. At the same time, reduced effectiveness of normocaloric diet not associated with physical activity of Salas-Salvadó et al[19] confirmed the need for a negative energy balance in the treatment of MS, either by reducing calories or by increasing energy expenditure.

In this sense, we can understand the suggestions by Project Guidelines[4], who values the need to reduce the energy content of proposed treatments for MS, rather than changes in macronutrient composition. We therefore recommend that high-quality randomized controlled trials be conducted to safely detect the effects of dietary exposures and provide more objective approaches in measuring dietary intake and the outcomes of relevance to public health.

This systematic review had limitations such as a potential failure to identify all publications despite the attempt to minimize this possibility by applying broad terms, repeating the search in databases and references of selected articles. As strengths, we highlight the systematic approach, the extensive search in relevant databases, inclusion of publications in any language and methodological rigor.

Although the set of interventions with low-calorie diet combined with physical activity has shown results that stood out among other types of nutritional proposals, the joint analysis of the studies provided evidence of the benefits of individualized diets low in saturated fats, rich in fiber, monounsaturated oils, vitamins and minerals in metabolic syndrome remission.

## Conclusion

Even taking into account factors that limited this systematic review, it can be concluded that scientific literature supports the beneficial effects of low-calorie diet associated with physical exercise, reinforcing the importance of changing lifestyle in the management of MS.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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### Study Association

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