

**Diet or exercise: what is more effective in preventing or reducing metabolic alterations?**

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**Short running title:** preventive measures for metabolic abnormalities

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**Word count:** abstract 249; text 2679

## Abstract

**Objective/design:** The influence of diet and exercise on metabolic syndrome is controversial since fit individuals might also eat healthier foods. We evaluated the association of diet/exercise variation with reductions in metabolic variables and C-reactive protein (CRP) values in the experimental and control arms of a 1-year randomized lifestyle intervention trial performed in patients with multiple metabolic abnormalities. **Methods:** A prospective study of 169 cases and 166 controls after a lifestyle intervention was performed.

**Results:** In the intervention group, 15/169 (8.9%), 63/169 (37.3%), 70/169 (41.4%) reached only dietary, only exercise, dietary/exercise targets, respectively. Reductions in weight, BMI, and waist were significant only in patients who increased exercise.

Most controls did not reach any target (131/166, 78.9%), while only few patients reached only dietary (13/166, 7.8%), only exercise (5/166, 3.0%), and dietary/exercise targets (17/166, 10.2%).

Weight, BMI, and waist reduction was more pronounced in those reaching the exercise target.

In the whole cohort, increased exercise was inversely associated with weight, BMI, waist, and CRP, increased saturated fat was directly associated with weight, BMI, waist, and diastolic pressure variations, while increased fiber intake was inversely associated with glucose values in a multiple regression model. After adjusting for waist changes, the associations between exercise and CRP ( $\beta=-0.023$ ; 95% CI  $-0.028$   $-0.017$ ;  $p<0.001$ ) and the associations between fiber and glucose ( $\beta=-0.022$ ;  $-0.031$   $-0.013$ ;  $p<0.001$ ) remained significant.

**Conclusions:** Independent of weight reduction, exercise level and fiber intake are inversely associated with CRP, and fasting glucose values, respectively. Change in lifestyle may lower inflammation and prevent metabolic deterioration.

## **Introduction**

Intensive programs of lifestyle interventions have significantly reduced or delayed the progression to diabetes in subjects at high metabolic risk [1-3]. The metabolic syndrome, a constellation of risk factors associated with a high diabetes and cardiovascular risk [4-5], is increasing to an epidemic prevalence. There is great interest in identifying the best lifestyle approach for these patients to reduce the clinical and economical impact of metabolic disorders.

In randomized trials, lifestyle interventions reduced the prevalence of the metabolic syndrome by 40-80% in the intervention groups [6-12]. However, the respective influence of nutrient intake and exercise on the metabolic syndrome prevalence is difficult to disentangle since more fit individuals might also eat a healthier diet.

We have recently evaluated the prevalence of the metabolic syndrome in a cohort of adults representative of the general population [13], and have demonstrated with a randomized trial that a lifestyle intervention based on general recommendations effectively reduced metabolic/inflammatory abnormalities within a subgroup of patients taken from this cohort and affected by multiple metabolic/inflammatory abnormalities [11]. In particular, the intervention group significantly reduced the intake of total and saturated fat, and increased the intake of polyunsaturated fat, fiber, and the level of physical activity after the intervention, while no significant variation was reported in the controls [11]. Furthermore, weight, waist circumference, body mass index (BMI), diastolic blood pressure, fasting glucose, triglyceride, and C-reactive protein (CRP) values significantly decreased in cases, while most variables worsened in the controls [11]. The prevalence of the metabolic syndrome declined from 70.4% to 34.9% after the intervention.

The aim of the present paper was to evaluate the relative contribution of diet and exercise on metabolic and inflammatory alterations within the experimental and control arms of the randomized lifestyle intervention trial [11].

### **Subjects and methods**

The prevalence of the metabolic syndrome was evaluated in a representative sample of adults from Asti (Northwestern Italy) between 2001-2003 [13]. Briefly, all subjects aged 45-64 ( $n=1877$ ) from six family physicians, representative of the local Health Districts were contacted. For the 1658 subjects who agreed to participate by written informed consent (88.3%), we carried out a metabolic screening, including an interview on personal data, weight, waist circumference, and blood pressure measurement, as well as blood determination of fasting glucose, HDL-cholesterol, triglyceride, insulin, and CRP values.

The participants and the non-participants were both similar to the total resident population of the corresponding age-group in the same area with respect to the percentage of males, level of education, prevalence of known diabetes, and percentage living in a rural area [13].

#### *Lifestyle intervention*

Three hundred eighty-three subjects of the total cohort (23.1%) had metabolic syndrome, according to the National Cholesterol Education Program -Adult Treatment Panel III- (NCEP-ATPIII) [14]. After excluding patients with diabetes, cardiovascular diseases, chronic liver or kidney disease, and advanced cancer, 335 patients from this cohort showed either the metabolic syndrome or two components of the syndrome plus CRP serum values  $\geq 3\text{mg/l}$ , the cut-off point that differentiates high-risk groups for future cardiovascular events. They were randomized to a lifestyle intervention program [11].

From December 2004 to December 2005, these 335 patients were randomized to receive either a lifestyle intervention program according to recommendations carried out by trained professionals (intervention group,  $n=169$ ), or standard counseling given by the family physician (control group,  $n=166$ ) [11]. This randomized, prospective open trial was approved by the local Ethical Committee,

all patients gave their written informed consent, and procedures conformed to the Helsinki Declaration principles.

All subjects received verbal information about diet and exercise from their family physicians, emphasizing the importance of a healthy lifestyle according to their usual clinical practice. No further specific individualized programs were offered to the controls and they were re-evaluated only at the end of the follow-up period [11]. The intervention group received both the previously stated information and detailed verbal and written individualized dietary and exercise recommendations from trained professionals during dedicated sessions. Five sessions of at least 60-minutes, covering diet, exercise and behavior modifications, were held; the first of these was on a one-to-one basis, followed by group sessions. An individually prescribed diet was given, in line with existing guidelines [11]. Recommended daily caloric distribution was as follows: 50-60% carbohydrates, 15-20% proteins, <30% fat, <10% saturated fat, up to 10% polyunsaturated fat, and 20-30 g fiber. Similarly, advice on exercise was individualized, mainly by suggesting moderate-intensity activity, such as brisk walking for at least 150-minutes/week [15]. The group sessions were based on behavioral counseling to implement lifestyle recommendations.

Before and after the study, patients completed a validated semi-quantitative food-frequency questionnaire [16] and the Minnesota-Leisure-Time-Physical-Activity questionnaire [17].

A dietician blindly checked all questionnaires for completeness, internal coherence, and plausibility. Both in December 2004 and one year later, weight, waist circumference (measured by a plastic tape meter at the level of the umbilicus), blood pressure and blood glucose, HDL-cholesterol, triglyceride, insulin, and CRP values were measured in all patients of both groups, after an overnight fast.

Systolic and diastolic blood pressures were measured twice with a standard mercury sphygmomanometer in a sitting position, after at least 10 min of rest. The reported values are the mean of the two determinations.

Laboratory methods have been previously described [13, 18].

### *Definition*

The metabolic syndrome was defined by the presence of at least three of the following five criteria: fasting serum glucose  $\geq 6.1$  mmol/l; arterial blood pressure  $\geq 130/85$  mmHg; plasma triglycerides  $\geq 1.69$  mmol/l; HDL-cholesterol  $< 1.29$  mmol/l (females),  $< 1.04$  mmol/l (males); waist  $> 88$  cm (females),  $> 102$  cm (males)] [14].

Insulin resistance was calculated from the Homeostasis Model Assessment-Insulin Resistance model (HOMA-IR) according to the published algorithm [19].

The physical activity level was calculated as the product of duration and frequency of each activity (in hours/week), weighted by an estimate of the metabolic equivalent of the activity, and summed for the activities performed.

### *Statistical analyses*

Since the frequency distributions of CRP, HOMA-IR score, and triglyceride values were positively skewed, their values were log-transformed, thus approximating a normal distribution. In all analyses, the log-transformed values of these variables were then used.

A multiple regression model was fitted, using changes in metabolic endpoints as dependent variables, and changes in values in exercise and dietary components, as independent variables. To reduce the risk of type I statistical error, due to multiplicity of comparisons, only associations with  $p < 0.01$  were considered as statistically significant.

A logistic regression analysis was used to evaluate the association between the prevalence of metabolic syndrome at the end of the follow-up and changes in lifestyle components, after adjustments for age, sex and actual BMI.

### **Results**

The characteristics of patients who participated in the lifestyle trial are reported in Table 1, as previously reported [11].

Polyunsaturated fat up to 10%, total fat  $< 30\%$ , saturated fat  $< 10\%$ , fiber  $\geq 20$ g/day, and exercise  $\geq 20$ METS h/week (i.e., about the mean value in the whole cohort) were identified as lifestyle

targets. In the intervention group, at least one target was reached by 148/169 (87.6%) of the patients; 63/169 (37.3%) reached only dietary targets (at least one), 15/169 (8.9%) reached only exercise target, and 70/169 (41.4%) reached both dietary and exercise targets. Weight, BMI, and waist circumference reductions (absolute difference of the variable: end-of-study minus baseline values) were statistically significant both in patients who reached only the exercise objective and in those reaching both diet and exercise targets. Corresponding variations in subjects achieving only dietary targets were negligible (Table 2).

In the control group, most patients did not reach any target (131/166, 78.9%), while only few individuals reached only dietary (13/166, 7.8%), only exercise (5/166, 3.0%), and dietary/exercise targets (17/166, 10.2%). Weight, BMI, and waist reduction was more pronounced in those reaching the exercise target (Table 2).

In both groups, positive changes in exercise levels (expressed in METS) were inversely associated ( $p < 0.01$ ) with weight, BMI, waist circumference, and CRP variations, increased saturated fat intake was significantly associated with increase in BMI, waist circumference, and diastolic pressure, while increased fiber intake was inversely associated with glucose values at multiple regression analyses. Therefore, the analyses were performed in the whole cohort (intervention and control groups,  $n = 335$ ) (Table 3). After adjusting for waist changes, the associations between METS and CRP ( $\beta = -0.023$ ; 95% CI  $-0.028$   $-0.017$ ;  $p < 0.001$ ), and fiber and glucose ( $\beta = -0.022$ ;  $-0.031$   $-0.013$ ;  $p < 0.001$ ) remained statistically significant.

Neither changes in exercise and nutrient intake showed statistically significant relationships with the prevalence of metabolic syndrome (Table 3), nor other (not reported) nutrient changes with the metabolic variables. Finally, no significant interaction between diet and exercise was found ( $p > 0.20$ ).

## **Discussion**

In the intervention and control groups of a lifestyle intervention trial, statistically significant reductions in weight and waist circumference occurred in patients who increased their exercise

level. In these subjects, inverse associations between exercise and CRP values and between fiber intake and fasting glucose concentrations were also found.

The impact of physical inactivity was suggested by the metabolic deterioration in the so-called control groups of some intervention studies [11-12, 20]. Accordingly, in the STRRIDE study, which investigated the effects of different amounts of exercise on metabolic risk factors, the inactive group gained approximately 1% body weight after 6 months, whereas all the exercise groups lost weight in a dose-responsive manner in the absence of reduced caloric intake [20]. Thus, a very modest amount of exercise may prevent weight gain, even with no decrease in calorie intake [20]. Exercise determined in obese men a more important reduction in fat mass than diet [21], and, even without weight loss, proved useful for reducing abdominal fat and preventing further increase in obesity [21].

Data on the associations between exercise and metabolic abnormalities are conflicting. In post-hoc analyses of the Finnish Diabetes Prevention Study, individuals who increased their leisure time physical activity were about 70% less likely to develop diabetes [22] and metabolic syndrome [23]. When adjusted for changes in diet, the risk reduction was attenuated [22-23]. Exercise without weight loss was associated with an improvement in glucose uptake, but the association did not remain significant after controlling for the associated visceral fat reduction [21, 24]. An appreciable improvement in insulin sensitivity and hyperglycemia was determined only by a substantial increase in physical activity but not by exercise levels according to current recommendations [25], being in the latter case total and visceral fat more important contributors than exercise [26-28]. We did not find a significant relationship between exercise levels and the metabolic syndrome, in accordance with studies performed in patients with some metabolic abnormalities at baseline [21, 24-28], while strong relationships were found in healthier cohorts [29-30]. It could be hypothesized that in healthy subjects environmental factors play a more important role than in dysmetabolic patients. In the

latter, indeed, the reduction in abdominal fat might be the main determinant for insulin sensitivity improvement [21, 24-28].

One of the hypothesized mechanisms to explain the independent beneficial role of physical activity may be the anti-inflammatory effect of exercise. The association between low-grade systemic inflammation and the metabolic syndrome has been supported by many studies [13,18, 31].

Inflammatory cytokines might act by impairing insulin-mediated glucose uptake, inhibiting insulin signaling, and increasing the release of free fatty acids from adipose tissue [31]. Regular training suppressed the production of CRP and pro-inflammatory cytokines [31-33]. Accordingly, we found significant inverse relationships between exercise levels and CRP values. Weight loss reduces CRP levels [34]; thus, the exercise-induced changes in weight might explain the inverse association between physical activity and CRP concentrations. In our cohort, however, relationships remained significant even after adjusting for BMI or waist circumference variations. Thus, it might be hypothesized that exercise may have a direct effect on CRP, independent of any change in weight.

In our patients, total and saturated fat intake were associated with changes in weight, BMI, waist circumference and diastolic blood pressure, but not (or slightly) with metabolic variables. This differs from other studies that found a correlation with insulin resistance [35-36], but is in line with the results of many prospective or intervention trials [25, 27-28, 37]. Furthermore, beneficial effects were found for diets low in fats but also high in fiber, whole grain, and micronutrients [38-39], according to the reported protective effect for increased dietary fiber, particularly whole grains, on reducing diabetes and cardiovascular risk factors [40-42]. Fiber intake has shown to improve insulin sensitivity by a delayed rate of carbohydrate absorption, weight gain prevention, and decrease in inflammation and oxidative stress. Accordingly, fiber intake in our patients was inversely correlated with fasting glucose values, independent of weight change.

### *Limitations*

The intervention led to multiple changes in lifestyle patterns, and it is therefore difficult to attribute variations in a biomarker to a single component of the intervention. Participants were not randomized to receive different components of the intervention, and this could result in residual confounding. A randomized controlled trial with a two-per-two factorial design (diet-per-exercise) would be necessary. Nevertheless, though such trials are not available and few studies on this topic have been conducted so far, our data could contribute to the existing knowledge.

We acknowledge that the small number of participants in each group have underpowered the study, masking true differences within each group. The relationships observed were indeed robust and the significance limit was set at  $p < 0.01$  to avoid inflated type 1 error caused by multiple tests.

Lifestyle variables are difficult to measure since they are subject to recall and misclassification bias. However, data were consistent in the two groups, and there is also biological plausibility in our results. Nevertheless, our findings should be considered hypothesis-generating only and need to be confirmed in larger cohorts.

The metabolic syndrome represents a surrogate endpoint, whose clinical value has been extensively criticized [43]. However, metabolic abnormalities co-occur in an individual more often than might be expected by chance, and combinations of sub-clinical abnormalities confer a significant surplus of cardiovascular risk not predicted by the classical risk engines [44]. The NCEP-ATPIII definition for metabolic syndrome was used, and, while newer definitions have been proposed, it resulted in a better predictions for diabetes risk [45].

Finally, while the cut-off for exercise level ( $\geq 20$  METS h/week) is arbitrary, it is very similar to that used in the large Nurses' Health Study cohort to define the reference group of physically active individuals ( $\geq 21.8$  METS h/week) [26].

### *Conclusion*

Exercise levels are inversely associated with CRP concentrations, and fiber intake is negatively related to fasting glucose values independent of weight change. If confirmed in larger cohorts,

change in lifestyle may be an effective non-pharmacological strategy for lowering concentrations of inflammatory markers and for preventing metabolic deterioration.

### **Acknowledgments**

This study was supported by a grant from Regione Piemonte 2005.

### **Disclosure**

The authors declare that there is no conflict of interest that would prejudice their impartiality.

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**Table 1. Baseline characteristics of patients participating to the lifestyle intervention trial**

| Variables                                  | Patients enrolled in the trial |               |       |
|--|--------------------------------|---------------|-------|
|  | Intervention group             | Control group | P     |
| Number                                     | 169                            | 166           |       |
| Age (year)                                 | 55.7 ± 5.7                     | 55.7 ± 5.6    | .94** |
| Males (%)                                  | 41.4                           | 42.2          | .89§  |
| Primary school (%)                         | 78.7                           | 79.5          |       |
| Secondary school (%)                       | 14.2                           | 17.5          |       |
| University (%)                             | 7.1                            | 3.0           | .19§  |
| Non smokers (%)                            | 78.1                           | 78.3          | .96§  |
| Metabolic equivalent of activity (hr/week) | 18.9±13.3                      | 18.1 ± 16.0   | .59** |
| Total calories (kcal/day)                  | 1978.6±692.5                   | 1993.1±633.8  | .84** |
| Total fat (% energy)                       | 35.3±5.2                       | 35.0±5.8      | .67** |
| Saturated fat (% energy)                   | 12.3±2.6                       | 12.0±2.6      | .35** |
| Polyunsaturated fat (% energy)             | 4.3±1.3                        | 4.1±1.2       | .11** |
| Carbohydrate (% energy)                    | 48.2±7.1                       | 48.7±7.0      | .51** |
| Protein (% energy)                         | 16.5±2.3                       | 16.3±2.4      | .39** |
| Fiber (g/day)                              | 19.2±6.4                       | 19.4±7.8      | .82** |
| Weight (kg)                                | 81.7 ± 14.9                    | 81.3 ± 13.5   | .76** |
| Waist circumference (cm)                   | 99.6 ± 11.6                    | 99.8 ± 10.6   | .90** |
| BMI (kg/m <sup>2</sup> )                   | 29.7 ± 4.1                     | 29.8 ± 4.6    | .87** |
| Systolic pressure (mmHg)                   | 142.6 ± 14.1                   | 141.5 ± 15.2  | .46** |
| Diastolic pressure (mmHg)                  | 88.2 ± 8.8                     | 87.8 ± 9.5    | .71** |
| Fasting glucose (mmol/l)                   | 5.8 ± 0.8                      | 5.8 ± 0.7     | .86** |
| Total cholesterol (mmol/l)                 | 5.8 ± 1.1                      | 6.0 ± 1.1     | .10** |
| HDL-cholesterol (mmol/l)                   | 1.4 ± 0.3                      | 1.4 ± 0.3     | .47** |
| Triglycerides (mmol/l)*                    | 1.9 (0.9)                      | 1.9 (0.9)     | .54** |
| Fasting insulin (pmol/l)*                  | 20.4 (24.0)                    | 21.3 (31.2)   | .92** |
| HOMA-IR (mmol/l×μU/ml)*                    | 0.81 (1.11)                    | 0.84 (1.33)   | .95** |
| CRP (mg/l)*                                | 3.5 (4.6)                      | 3.1 (3.6)     | .43** |

Means±SD or percentage

\*median (inter-quartile range) for non-normally distributed values

\*\*p-values were determined by Student's *t*-test

§p-values were determined by chi-square test

Data previously published [see also ref. 11]

**Table 2. Clinical and laboratory characteristic changes according to dietary and exercise targets after the intervention.**

|                            | Intervention group          |                        |                         |                              |
|----------------------------|-----------------------------|------------------------|-------------------------|------------------------------|
|                            | No dietary/exercise targets | Only dietary<br>Target | Only exercise<br>target | Diet and exercise<br>targets |
| Number                     | 21                          | 63                     | 15                      | 70                           |
| Delta weight*              | 1.92 (0.05 3.79)            | -0.05 (-1.33 1.24)     | -2.00 (-3.26 -0.74)     | -1.91 (-3.11 -0.72)          |
| Delta BMI*                 | 0.70 (0.03 1.37)            | -0.02(-0.46 0.42)      | -0.77(-1.25 -0.29)      | -0.73(-1.16 -0.29)           |
| Delta waist circumference* | 0.69 (-0.65 2.03)           | -0.32(-1.61 0.98)      | -3.33(-4.33 -2.34)      | -5.36(-6.48 -4.23)           |
| Delta systolic pressure*   | 0.05 (-6.81 6.90)           | -3.13(-7.47 1.20)      | -1.13(-12.0 9.72)       | -1.76(-6.71 3.19)            |
| Delta diastolic pressure*  | 1.12 (-1.54 3.77)           | -3.30(-5.91 -0.69)     | -1.17(-3.87 1.54)       | -3.31(-5.58 -1.04)           |
| Delta fasting glucose*     | -0.03 (-0.25 0.19)          | -0.22(-0.41 -0.02)     | -0.16(-0.45 0.13)       | -0.39(-0.52 -0.26)           |
| Delta HDL-cholesterol*     | 0.03 (-0.06 0.11)           | 0.01(-0.02 0.04)       | 0.04(0.01 0.06)         | 0.01(-0.02 0.05)             |
| Delta log-triglycerides*   | -0.14 (-0.31 0.03)          | -0.15(-0.24 -0.06)     | -0.10(-0.20 0.005)      | -0.14(-0.23 -0.05)           |
| Delta log-HOMA-IR*         | 0.38 (0.005 0.75)           | -0.05(-0.30 0.20)      | -0.27(-0.82 0.29)       | -0.24(-0.48 0.00)            |
| Delta log-CRP*             | 0.02 (-0.27 0.31)           | -0.20(-0.38 -0.02)     | -0.64(-1.07 -0.22)      | -0.47(-0.66 -0.27)           |
|                            | Control group               |                        |                         |                              |
|                            | No dietary/exercise targets | Only dietary<br>Target | Only exercise<br>target | Diet and exercise<br>targets |
| Number                     | 131                         | 13                     | 5                       | 17                           |
| Delta weight*              | 2.76 (2.00 3.53)            | -1.28 (-3.72 1.16)     | -2.80 (-5.46 -0.14)     | -3.63 (-7.44 0.18)           |
| Delta BMI*                 | 1.03 (0.74 1.32)            | -0.54 (-1.55 0.46)     | -1.02 (-1.89 -0.14)     | -1.25 (-2.59 0.09)           |
| Delta waist circumference* | 3.55 (2.70 4.40)            | -2.77 (-7.09 1.55)     | -4.20 (-12.4 4.05)      | -4.82 (-10.2 0.52)           |
| Delta systolic pressure*   | 4.80 (1.95 7.65)            | -0.88 (-13.2 11.4)     | 19.0 (-2.7 40.7)        | 4.94 (-3.10 13.0)            |
| Delta diastolic pressure*  | 0.004 (-1.60 1.61)          | -6.46 (-14.0 1.11)     | -2.00 (-19.2 15.2)      | 2.79 (-2.55 8.14)            |
| Delta fasting glucose*     | 0.17 (0.07 0.27)            | -0.48 (-0.93 -0.02)    | 0.21 (-0.51 0.93)       | -0.30 (-0.55 -0.05)          |
| Delta HDL-cholesterol*     | -0.07 (-0.10 -0.04)         | -0.10 (-0.17 0.02)     | -0.13 (-0.30 0.04)      | -0.002 (-0.12 0.11)          |
| Delta log-triglycerides*   | 0.007 (-0.05 0.06)          | -0.30 (-0.42 -0.18)    | -0.11 (-0.53 0.31)      | -0.23 (-0.43 -0.04)          |
| Delta log-HOMA-IR*         | 1.00 (0.82 1.16)            | 1.00(-0.51 1.49)       | 1.33 (-0.61 2.06)       | 0.95 (-0.55 1.35)            |
| Delta log-CRP*             | 0.32 (0.22 0.43)            | 0.40 (-0.04 0.83)      | -0.61 (-1.57 0.36)      | -0.11(-0.49 0.26)            |

\*delta= absolute difference of the variable (end-of-study minus baseline values) with 95% confidence intervals.

**Table 3. Associations among variations in exercise/nutrient intake and metabolic/inflammatory endpoints in a multiple regression model in the whole cohort.**

| Dependent variables*            | Δ METS                  |          | Δ Total fat             |          | Δ Saturated fat        |          | Δ Fiber                |          |
|---------------------------------|-------------------------|----------|-------------------------|----------|------------------------|----------|------------------------|----------|
|                                 | β<br>95% CI             | P        | β<br>95% CI             | P        | β<br>95% CI            | P        | β<br>95% CI            | P        |
| Δ weight (kg)**                 | -0.12<br>-0.16 -0.08    | <.001    | 0.09<br>0.01 0.17       | .02      | 0.30<br>0.16 0.44      | <.001    | -0.04<br>-0.12 0.04    | .38      |
| Δ BMI (kg/m <sup>2</sup> )**    | -0.04<br>-0.06 -0.02    | <.001    | 0.04<br>0.007 0.07      | .01      | 0.12<br>0.07 0.17      | <.001    | -0.02<br>-0.05 0.01    | .24      |
| Δ Waist (cm)**                  | -0.14<br>-0.19 -0.09    | <.001    | 0.14<br>0.04 0.24       | .003     | 0.55<br>0.38 0.72      | <.001    | -0.06<br>-0.16 0.04    | .22      |
| Δ Systolic pressure (mmHg)§     | 0.07<br>-0.08 0.22      | .40      | 0.18<br>-0.03 0.45      | .20      | 0.07<br>-0.44 0.57     | .79      | -0.05<br>-0.32 0.22    | .72      |
| Δ Diastolic pressure (mmHg)§    | 0.03<br>-0.05 0.11      | .49      | 0.07<br>-0.08 0.21      | .39      | 0.47<br>0.20 0.74      | <.001    | -0.10<br>-0.25 0.05    | .18      |
| Δ Fasting glucose (mmol/l)§     | -0.004<br>-0.009 0.001  | .11      | 0.002<br>-0.008 0.01    | .67      | 0.02<br>0.002 0.04     | .03      | -0.02<br>-0.03 -0.01   | <.001    |
| Δ log-Triglycerides (mmol/l)§   | -0.0003<br>-0.003 0.002 | .84      | -0.001<br>-0.006 0.004  | .70      | 0.003<br>-0.007 0.01   | .54      | -0.004<br>-0.009 0.001 | .11      |
| Δ HDL cholesterol (mmol/l)§     | 0.002<br>0.001 0.003    | .01      | -0.0003<br>-0.002 0.002 | .79      | -0.002<br>-0.006 0.003 | .46      | 0.001<br>-0.001 0.003  | .45      |
| Δ log-HOMA-IR (μU/ml×mmol/l)§   | -0.0003<br>-0.009 0.009 | .94      | 0.017<br>0.0 0.34       | .05      | 0.03<br>0.003 0.06     | .04      | -0.008<br>-0.02 0.009  | .38      |
| Δ log-CPR (mg/l)§               | -0.024<br>-0.03 -0.02   | <.001    | 0.02<br>0.005 0.03      | .01      | 0.02<br>-0.001 0.04    | .10      | -0.01<br>-0.02 -0.002  | .03      |
|                                 | <b>OR\$<br/>95% CI</b>  | <b>P</b> | <b>OR<br/>95% CI</b>    | <b>P</b> | <b>OR<br/>95% CI</b>   | <b>P</b> | <b>OR<br/>95% CI</b>   | <b>P</b> |
| Metabolic syndrome <sup>o</sup> | 0.98<br>0.95 1.02       | .29      | 1.03<br>0.99 1.06       | .20      | 1.04<br>0.98 1.10      | .20      | 0.98<br>0.95 1.02      | .29      |

\* end of study – baseline values

\*\*multiple regression model after adjusting for age and sex

§multiple regression model after adjusting for age, sex, and actual BMI

<sup>o</sup> The metabolic syndrome was defined by the presence of ≥3 of the following five criteria: fasting glucose ≥6.1mmol/l; blood pressure ≥130/85mmHg; triglycerides ≥1.69mmol/l; HDL-cholesterol <1.29mmol/l (females) and <1.04mmol/l (males); waist circumference >88cm (females) and >102cm (males) [14]

\$logistic regression analysis evaluating the prevalence of the metabolic syndrome at the end of the follow-up, after adjustments for age, sex and actual BMI.