Education and acute coronary syndromes: results from the CARDIO2000 epidemiological study

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Objective As a measure of socioeconomic status, low educational level is positively associated with the risk of developing adverse health events. The aim of this study was to investigate the relationship between the level of education and the risk of developing non-fatal acute coronary syndromes.

Methods During 2000 and 2001, 1619 randomly selected subjects from several regions of Greece were entered into a case-control study. Of these, 750 were patients with their first acute coronary heart syndrome event, and 869 were hospitalized controls with no cardiovascular disease in their medical history. Trends in cardiovascular risk factors were then examined across patient and control educational level by years of schooling.

Findings In both patients and controls, education status was related to economic and occupation status, smoking habits, physical inactivity, alcohol consumption and non-compliance to treatment. After adjusting for these and other conventional risk factors, as well as for the effects of age and sex, we found that coronary risk increases by 82% (odds ratio (OR) = 1.82, P <0.05) for individuals with a lower level of education, and by 65% (OR = 1.65, P <0.05) for individuals with an average education, compared to those with an academic education.

Conclusions Although the least-educated subjects adopted a more adverse lifestyle than the more-educated subjects, the inverse association between education and coronary risk was independent from such factors. The inverse association may be due to psychosocial differences, and prospective cohort studies are needed to confirm or refute these results.

Keywords Coronary disease/epidemiology; Acute disease/epidemiology; Education; Socioeconomic factors; Risk factors; Life style; Multicenter studies; Retrospective studies; Case-control studies; Developing countries; Greece (source: MeSH, NLM).

Introduction

Social conditions, and their relationship to human health, have long been studied as properties of societies or populations, rather than of individuals (1–3). However, it has also been shown that the socioeconomic and cultural status of adults in industrialized countries (constituted from occupation, educational level and income) are related to cardiovascular disease mortality and morbidity (4–10). These associations have been mostly explained by differences in known cardiovascular risk factors between social classes (11–24). Results from several epidemiological studies suggested that coronary heart disease and its risk factors were originally more common in the upper socioeconomic class (i.e. a “disease of affluence” (24), but throughout the middle of the 20th century this gradually changed in western populations, so that, currently, cardiovascular disease is more common in lower socioeconomic groups (7, 9, 10, 11). Sociodemographic factors also predict later morbidity in coronary heart disease (15–18). Thus, the differences in many preventable risk factors between the social classes seem to arise early in life.

The question of which components of socioeconomic status (i.e. education, economic level, occupation) are the most important risk factors in cardiovascular disease is debatable (20, 22). In health-related sociological studies, education (and therefore the ability to make an informed choice) has been used as a reliable measure of socioeconomic status because it has many advantages: it is stable and becomes established in early adulthood; it is not modified by chronic illness in later adulthood; and it is easy to measure (10, 11, 18–20, 22). The

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few studies that have investigated the role of education in the development of cardiovascular disease (25–27) have mainly shown that education affected the risk of developing cardiovascular disease via conventional cardiovascular risk factors (18, 24–28).

The aim of this work was to evaluate whether educational level was related to biological and lifestyle risk factors, and whether these associations influenced the risk of developing non-fatal, acute coronary syndromes.

Methods
CARDIO2000 was a multicentre, retrospective, case-control study that investigated the association between demographic, nutritional, lifestyle and medical risk factors, and the risk of developing acute coronary syndromes, in a population that grew up in a developing society. The study was retrospective and all participants recalled lifetime experiences from earlier decades, when Greece was a developing society. Between June 2000 and August 2001, a sample of 750 coronary patients and 869 individuals free of cardiovascular symptoms (controls) were entered into the study (selection criteria are described below). The number of study participants was determined by power analysis, and chosen to evaluate differences in coronary relative risk of greater than 7% (statistical power (P) >0.80, P<0.05).

All participants were informed about the aims of the study and agreed to participate. To eliminate recall bias, we tried to retrieve precise information about study participants' medical histories from hospital or insurance records. Information regarding the smoking status, physical activity, living and nutritional habits, and other sociodemographic factors were recorded in a questionnaire that included structured questions. To put study participants at ease, the confidential questionnaire was completed during a private interview held after the second day of hospitalization. All the collected information was retrieved by CARDIO2000 study investigators. Cases with missing values were not included in the study.

Study design and selection criteria
Our sampling was based on the population distribution provided by the Greek National Statistical Services census 2000. The sample was stratified into all the Greek regions, and included socioeconomic levels and cultural particularities. The number of patients and controls in each region were proportional to the regional populations, and were enrolled from the prefectural hospitals or from the major private hospitals of each county (7 cardiology clinics from Attica; 3 from Sterea Ellada; 3 from Thessalia; 2 from Hpeiros; 5 from Macedonia; 2 from Thrace; 5 from Peloponnese; 2 from Crete; 5 from Aegean; and 3 from Ionian islands). Study participants were drawn from approximately half of the available clinics in Athens and Thessalonika, and from nearly all the clinics of the other counties.

The coronary patients were randomly selected from the admission listings of the cardiology clinics by randomly assigning a “0” or “1” to the admission listings. Included in the study were patients who were assigned a “1” and who had experienced a first event of acute myocardial infarction (diagnosed by two or more of: typical electrocardiograph changes, compatible clinical symptoms, or elevated levels of specific diagnostic enzymes), or who were first diagnosed with unstable angina (corresponding to class III of the Braunwald classification).

Control subjects were also randomly selected by the same procedure from patients without any clinical symptoms or suspicions of cardiovascular disease in their medical history, and were matched to the coronary patients by age (± 3 years), sex and region. The control subjects were mainly patients in the surgical clinics (urology, ophthalmology or orthopaedic) of the same hospital, and were patients during the same period as the coronary patients. In a few cases (in county hospitals), where the number of hospitalized controls was insufficient for the matching procedure, we enrolled in the study friends or colleagues of the coronary patients. We used hospitalized controls to obtain more accurate medical information, to eliminate potentially adverse effects of unknown confounders, to increase the likelihood that cases and controls shared the same study base, and to reduce the problem of misclassification (29, 30). All controls were examined by a cardiologist who took precise medical histories and carried out physical examinations.

Patient sociodemographic variables
The study participants’ educational level was classified into three groups on the basis of self-administered questionnaires. Group I members had received education up to high school. These participants reported comprehensive school, trade school or technical institute/school as their basic education, but had not passed senior high school. Group II members had completed senior high school or college, but had not attained a university education. Group III members had studied at, or graduated from, university. The mean annual income of study participants during the past 5 years was defined as low (US$ <4750), moderate (US$ 4750–8500), good (US$ 8500–14 500), or very good (US$ >14 500), according to the Ministry of Economics classification. Finally, the occupation of study participants was classified into five categories: employed, professionals (self-employed), part-time employed, unemployed, and retired. Only participants who had been unemployed more than 6 months since 1999 were regarded as unemployed.

Assessment of medical, nutritional and lifestyle factors
Participants were defined as having hypertension if their mean systolic blood pressure was ≥140 mmHg and/or had a diastolic blood pressure ≥90 mmHg, or if they were under special treatment. Diabetic participants were defined as those with a mean fast blood glucose concentration >125 mg/dl (31), or who were under special treatment; and hypercholesterolemic participants were those with mean total cholesterol levels >220 mg/dl or who were under lipidemic treatment (32). According to the collected medical records, 75% of the control participants and 72% of the patients had had at least one laboratory measurement during the past 12 months. In addition, we took total cholesterol and blood glucose measurements during the first 12 hours of hospitalization. The subjects were classified as hypertensive, hypercholesterolemic or diabetic according to the mean values of the previous laboratory measurements, as well as any special treatment or information retrieved from their medical records. In addition, the onset of hypertension, diabetes mellitus and hypercholesterolemia were taken into account for the analysis.
Body mass index was calculated by dividing the participants’ weight by their height squared (kg/m²). Current smokers were defined as those who smoked at least one cigarette per day. Smoking status was quantified in pack-years, adjusted for a nicotine content of 0.8 mg/cigarette. Former smokers were defined as those who had stopped smoking more than one year previously. Physically active participants were those who reported engaging in non-occupational, physical activity more than once a week during the past year. All the others were considered to be physically inactive (3f).

Alcohol consumption was measured by daily ethanol intake, in units of wine glasses (100 ml, 12% ethanol content) (34, 35).

To account for the potentially confounding effect of patients who adopted a low-fat diet, a detailed nutritional questionnaire was applied. The Mediterranean type of diet is high in fruits, vegetables, bread and other cereals, potatoes, beans, nuts, poultry and fish, with little red meat and dairy products, moderate alcohol consumption, and olive oil as an important fat source (36). For each of the investigated food items, the frequency of consumption was approximately quantified in terms of the number of times a food item was consumed each month. Total diet was described by composite scores. Participants who adopted this special type of diet were categorized using the median values of the monthly food consumption score as cut-off points (37).

Statistical analysis
Continuous variables are presented as mean values ± one standard deviation, while qualitative variables are presented as absolute and relative frequencies. Estimates of the relative risks of developing acute coronary syndromes were calculated for several hypotheses, using the OR and corresponding confidence intervals through multiple conditional logistic regression analyses. The final risk model was developed through a stepwise elimination procedure (for the selection of variables), using 5% probability for entry and 10% probability for removal of a variable from the model, after controlling for the potential confounders and interactions between the investigated factors and education status. This method is widely used in logistic regression (e.g., 38). Deviance residuals were calculated to evaluate the model’s goodness-of-fit. All reported P-values are based on two-sided tests and compared to a significance level of 5%. STATA 6 software was used for all the statistical calculations (STATA Corp. College Station, Texas, USA).

Results
The age–sex distribution of the study participants is shown in Table 1, and the distribution of other demographic factors (educational level, lifestyle and coronary risk factors) is presented in Table 2. Based on crude comparisons, there was a significant inverse association between education and acute coronary events ($X^2 = 17.3, P <0.001$). When age and sex were accounted for, the acute coronary risk increased by 109% for Group I participants compared with those in Group III (OR = 2.09, 95% CI: 1.54–2.82, $P <0.001$), and 86% for Group II participants compared to those in Group III (OR = 1.86, 95% CI: 1.32–2.59, $P <0.001$).

However, the above findings represent crude estimations of the odds ratio, since several confounders related to cardiovascular disease, i.e. the presence of conventional risk factors, as well as compliance to treatment, or various lifestyle habits, were not taken into account. Thus, we applied an exploratory analysis that took into account the prevalence of smoking habits, hypertension, hypercholesterolemia, diabetes mellitus, family history of coronary heart disease, physical inactivity, body mass index, food and alcohol consumption, as well as financial and occupational status of patients and controls. We found a strong association between economic status and educational level for both study groups. In particular, compared to participants with lower education, those with an academic education were more likely to be in the upper economic class (good or very good income) (OR = 3.24, 95% CI: 2.45–4.17, $P <0.001$). In both patient and control group, education status was significantly related to the occupation level, ($P <0.001$), since unemployment or part-time employment were inversely associated with educational level, especially in the coronary group ($P <0.05$). Both in patients and controls, education status was not associated with the prevalence of hypertension ($P = 0.9, 0.3$, respectively), hypercholesterolemia ($P = 0.9, 0.2$, respectively) or diabetes mellitus ($P = 0.9, 0.4$, respectively).

On the other hand, the adoption of treatment for hypertension, for lowering lipids or for diabetes was directly related to the educational level of coronary patients ($P <0.05$); this association was even stronger for the control participants ($P <0.01$). Educational level was also positively related to the current smoking habit, in both groups of the study ($P <0.05$). However, when we investigated differences in the number of cigarettes smoked, we found that both patients and controls in education Group II smoked more cigarettes per day than those in Groups I and III ($46, 17, 43, 11, 42, 16$ pack-years respectively, for the patients and $27, 12, 23, 12, 21, 14$ pack-years, respectively, for the controls; $P <0.05$).

A positive association between physical activity and education was observed only for study participants in the control group ($P <0.001$), while a borderline association was found in the group of coronary patients ($P = 0.121$). A significant positive association was also found between daily alcohol consumption and educational level, both in patients and controls (Table 2). Finally, both in patients and controls the education status was not associated with the adoption of Mediterranean diet ($P = 0.7, 0.2$, respectively), or obesity ($P = 0.6, 0.5$, respectively).

After taking into account the previous associations the results from the multivariate analysis showed that educational

![Table 1. Age–sex distribution of the study population](image-url)
level was inversely and independently associated with the risk of developing non-fatal acute coronary syndromes (Table 3). In particular, the acute coronary risk increased by 82% in Group I, and by 65% in Group II, compared to Group III participants, after adjusting for age and sex, as well as for smoking, income, occupation, hypertension, hypercholesterolemia, family history of coronary heart disease, diabetes mellitus, body mass index and physical activity level. From the applied risk analysis, it can be seen that the effect of education on coronary risk remains significant, even after adjustment for conventional and emerging cardiovascular risk factors.

### Discussion

We investigated the association between educational level and the risk of developing non-fatal acute coronary syndromes, in a developing society. After accounting for the effects of conventional cardiovascular risk factors and other potential confounders, multivariate analysis showed that low education status was associated with an increased risk of developing non-fatal acute coronary syndromes. In addition, the analysis found significant associations between education status and smoking habit; physical inactivity; alcohol consumption; income; occupational status; and treatment for hypertension, lowering lipids or diabetes, both in coronary patients and controls. However, these factors had a moderate-to-insignificant effect on the relationship between education and acute coronary risk, in contrast to previous studies of “Westernized” societies, which found that this association was mainly explained by differences in the distribution of known risk factors among individuals (5–11, 17, 20, 39–41).

### Lifestyle and education

We found that patients and controls who had an academic education (Group III) were more likely to be current smokers than participants with a lower educational level, although Group III participants smoked fewer cigarettes compared to those in Groups I and II. This is consistent with other studies,

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**Table 2. Distribution of cardiovascular and lifestyle factors, by group of educational level**

<table>
<thead>
<tr>
<th>Educational level</th>
<th>ACS patients (n = 750)</th>
<th>Controls (n = 869)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (≤US$ 4750)</td>
<td>55 (12%)</td>
<td>19 (4%)</td>
</tr>
<tr>
<td>Moderate (US$ 4750–8500)</td>
<td>311 (68%)</td>
<td>287 (60%)</td>
</tr>
<tr>
<td>Good (US$ 8500–14 500)</td>
<td>87 (19%)</td>
<td>167 (35%)</td>
</tr>
<tr>
<td>Very good (US$ &gt;14 500)</td>
<td>5 (1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>60 (13%)</td>
<td>43 (9%)</td>
</tr>
<tr>
<td>Self-employed</td>
<td>92 (20%)</td>
<td>153 (32%)</td>
</tr>
<tr>
<td>Partially employed</td>
<td>27 (6%)</td>
<td>225 (47%)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>55 (12%)</td>
<td>48 (10%)</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>307 (67%)</td>
<td>325 (68%)</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>242 (53%)</td>
<td>296 (62%)</td>
</tr>
<tr>
<td>Alcohol consumption (wineglasses/day)</td>
<td>3.4 ± 1.9</td>
<td>3.4 ± 1.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti hypertensive treatment (diet or drugs)</td>
<td>243 (53%)</td>
<td>172 (36%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>279 (61%)</td>
<td>148 (31%)</td>
</tr>
<tr>
<td>Antilipidemic treatment (diet or drugs)</td>
<td>78 (28%)</td>
<td>81 (55%)</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 29.9 kg/m²)</td>
<td>92 (20%)</td>
<td>96 (20%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment (diet or disc or insulin)</td>
<td>119 (26%)</td>
<td>43 (9%)</td>
</tr>
</tbody>
</table>

* The %s for the Education Group are calculated from the total n, whereas the category percentages are calculated on the basis of the n for the education group.

* ACS = acute coronary syndrome.

NS = not significant.

### Table 3. Adjusted odds ratios for the effect of education on coronary risk

<table>
<thead>
<tr>
<th>Education group</th>
<th>ACS patients</th>
<th>Controls</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>458/750</td>
<td>478/869</td>
<td>1.82</td>
<td>1.24–2.67</td>
<td>0.002</td>
</tr>
<tr>
<td>Group II</td>
<td>188/750</td>
<td>200/869</td>
<td>1.65</td>
<td>1.11–2.45</td>
<td>0.012</td>
</tr>
<tr>
<td>Group III</td>
<td>104/750</td>
<td>191/869</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The adjusted odds ratios were controlled for age, sex, smoking, income, type of occupation, presence of hypertension, hypercholesterolemia, family history of coronary heart disease, diabetes mellitus, body mass index and physical activity level.

* ACS = Acute coronary syndrome.

* CI = Confidence interval.
which showed that the number of cigarettes smoked was inversely related to the educational level (18, 42–46). Previous studies have also shown that participants with a higher educational level, or a higher occupational status, are more physically active in their leisure time than those with a lower educational level or occupational status (18, 47–50). Our study showed that physical inactivity was significantly related to educational level in control participants. In particular, participants free of cardiovascular disease and with a higher educational level were more likely to be physically active, compared to other controls with lower education. Although this was also observed for the coronary patients, the significance was only borderline.

Based on the results from the Seven Countries study in the early 1970s (51), and the Lyon Heart Study of the late 1990s (52), the benefits of a Mediterranean type of diet have been recognized for cardiovascular diseases, metabolic disorders and several types of cancer, and studies have tried to associate the benefits of adopting a Mediterranean diet with social and cultural differences among populations (53, 54). In our study, the consumption of a Mediterranean or any other type of diet did not interfere with the link between education status and the risk of developing a non-fatal acute coronary syndrome.

Many studies have also shown that low-to-moderate alcohol consumption was associated with reduced mortality, primarily due to a reduction in coronary heart disease; in contrast, heavy drinking substantially increased coronary risk and mortality rates (34, 35, 55, 56). Additionally, many studies have shown that alcohol consumption is related to social class, with subjects in the lower social class consuming more alcohol than those in other classes (55). We also found that Group I participants consumed more alcoholic beverages than those in Group II or III. This may be related to lifestyle, economic, behavioural or emotional characteristics that were not investigated in this study. It is difficult to explain the poor compliance of the low education group to special treatment, since all subjects had the same access to the national health system services, and the same opportunities to receive treatment. Possibly, the poor compliance of participants with a low education status might be related to attitudes.

We observed significant associations between education and income, occupation and several lifestyle habits, both in coronary patients and controls. After accounting for the effect of these associations and several other covariates, the statistical analysis showed that a low level of education was independently associated with a higher risk of developing non-fatal acute coronary syndromes. However, it is hard to claim that our findings suggest a causal link. To explain the observed association, several other personal characteristics, such as psychosocial factors (job stress, depression, etc.) (57–59) that were not analysed in this study, may need to be taken into account, probably through a prospectively designed cohort. Despite the limitations and the undiscovered factors, a key conclusion of this study is that individuals with a low level of education are relatively unprotected against acute coronary risk. Consequently, public health policy-makers should focus their efforts on informing such people about the role an unhealthy lifestyle plays in enhancing the risk of developing acute coronary events.

**Limitations of the study**

Although we tried to eliminate bias in selecting study participants by setting objective criteria, insignificant misclassification may exist since a small percentage of asymptomatic coronary patients may have been wrongly assigned to controls, even though they were evaluated by a cardiologist. In addition, the enrolment of few population-based controls may influence our findings. Therefore we performed a sensitivity analysis (38) within the control group, without showing any significant alterations regarding the effect of education status on the coronary risk.

Coronary patients, who died at entry or the day after, were not included into the study. Although this bias could influence our results, the proportion of deaths during the first two days was estimated at only 2–4% by physicians in the study, and therefore excluding these patients probably did not significantly alter our findings. Also, even though we recovered detailed information, recall bias may still have existed, especially in measuring smoking, nutrition, alcohol consumption and the onset of other cardiovascular risk factors.

Finally, we also tried to reduce the effects of unknown and uncontrolled confounders by using multivariate analysis and by using the same study base for both patients and controls, but the unmeasured effect of psychosocial and other unknown factors could moderate our findings.

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**Conflicts of interest:** none declared.

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**Résumé**

**Niveau d’études et syndrome coronarien aigu : résultats de l’étude épidémiologique CARDIO2000**

**Objectif** En tant que mesure de la situation socio-économique, le faible niveau d’études est positivement associé au risque d’accidents de santé. La présente étude avait pour but d’examiner la relation entre le niveau d’études et le risque de syndrome coronarien aigu non mortel.

**Méthodes** En 2000 et 2001, 1619 personnes choisies par tirage au sort dans plusieurs régions de Grèce ont été recrutées dans une étude cas-témoins ; 750 d’entre elles étaient des patients ayant un premier épisode de syndrome coronarien aigu et 869 étaient des témoins hospitalisés sans antécédents de maladie cardio-
vasculaire. Les tendances des facteurs de risque cardio-vasculaire ont été examinées en fonction du nombre d’années d’études chez les cas et chez les témoins.

Résultats Chez les patients comme chez les témoins, on a observé une relation entre le niveau d’études et la situation économique et professionnelle, le tabagisme, la sédentarité, la consommation d’alcool et la non-observance du traitement. Après ajustement sur ces facteurs de risque et d’autres facteurs de risque classiques ainsi que sur l’âge et le sexe, nous avons trouvé que, par rapport aux sujets ayant fait des études supérieures, le risque coronarien était augmenté de 82 % (odds ratio (OR) = 1,82; p<0,05) chez les sujets ayant un faible niveau d’études et de 65 % (OR = 1,65; p<0,05) chez ceux ayant un niveau d’études standard.

Conclusion Bien que les personnes ayant le niveau d’études le plus faible adoptent un mode de vie moins favorable à la santé que les autres, l’association inverse entre le niveau d’études et le risque coronarien est indépendante de ces facteurs. Elle peut être due à des différences d’ordre psychosocial, et des études de cohorte prospectives devront être réalisées pour confirmer ou infirmer ces résultats.

Resumen

Educación y síndromes coronarios agudos: resultados del estudio epidemiológico CARDIO2000

Objetivo Como medida del estatus socioeconómico, un bajo nivel de instrucción es un factor positivamente asociado al riesgo de sufrir problemas de salud. Este estudio se propuso investigar la relación existente entre el nivel de educación y el riesgo de sufrir síndromes coronarios agudos no mortales.

Métodos Durante los años 2000 y 2001 se realizó un estudio de casos y testigos con 1619 personas seleccionadas al azar en varias regiones de Grecia. De ellas, 750 eran pacientes que habían sufrido su primer síndrome coronario agudo, y 869 eran controles.

Encontraron las tendencias de los factores de riesgo cardiovascular, controlando el nivel de instrucción de pacientes y testigos en función del número de años de escolarización.

Resultados Tanto en los pacientes como en los controles, el nivel de instrucción guardaba relación con el nivel económico y la profesión, el consumo de tabaco, la falta de ejercicio físico, el consumo de alcohol y la no observancia del tratamiento. Después de un ajuste en función de estos y otros factores de riesgo habituales, así como para tener en cuenta los efectos de la edad y el sexo, hallamos que el riesgo coronario aumenta en un 82% (razón de posibilidades (OR) = 1,82, P<0,05) en los individuos con bajo nivel de instrucción, y en un 65% (OR = 1,65, P<0,05) en los individuos que poseen estudios universitarios.

Conclusion Aunque los individuos con menor nivel de instrucción tenían estilos de vida menos sanos que los más instruidos, la relación inversa entre educación y riesgo coronario era independiente de esos factores. Esa relación inversa podría deberse a diferencias psicosociales, pero se necesitan estudios prospectivos de cohortes para confirmar o refutar los resultados.

References


