Meat consumption and prospective weight change in participants of the EPIC-PANACEA study[1–3]

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The American Journal of Clinical Nutrition

ABSTRACT

Background: Meat intake may be related to weight gain because of its high energy and fat content. Some observational studies have shown that meat consumption is positively associated with weight gain, but intervention studies have shown mixed results.

Objective: Our objective was to assess the association between consumption of total meat, red meat, poultry, and processed meat and weight gain after 5 y of follow-up, on average, in the large European population who participated in the European Prospective Investigation into Cancer and Nutrition–Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating Out of Home and Obesity (EPIC-PANACEA) project.

Design: A total of 103,455 men and 270,348 women aged 25–70 y were recruited between 1992 and 2000 in 10 European countries. Diet was assessed at baseline with the use of country-specific validated questionnaires. A dietary calibration study was conducted in a representative subsample of the cohort. Weight and height were measured at baseline and self-reported at follow-up in most centers. Associations between energy from meat (kcal/d) and annual weight change (g/y) were assessed with the use of linear mixed models, controlled for age, sex, total energy intake, physical activity, dietary patterns, and other potential confounders.

Results: Total meat consumption was positively associated with weight gain in men and women, in normal-weight and overweight subjects, and in smokers and nonsmokers. With adjustment for estimated energy intake, an increase in meat intake of 250 g/d (eg, one steak at ≈450 kcal) would lead to a 2-kg higher weight gain after 5 y (95% CI: 1.5, 2.7 kg). Positive associations were observed for red meat, poultry, and processed meat.

Conclusion: Our results suggest that a decrease in meat consumption may improve weight management. *Am J Clin Nutr* 2010;92:398–407.

INTRODUCTION

Obesity is associated with an increased risk of several diseases, which include cardiovascular disease, diabetes, and some types of cancer (1). Because the prevention of weight gain through life is a major public health concern, the European Prospective Investigation into Cancer and Nutrition–Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating Out of Home and Obesity (EPIC-PANACEA) project aims to identify its predictors with the use of a large sample of European individuals with different dietary habits and lifestyles and large variation in obesity prevalence.[1234]

Mainly because of its high energy density and fat content, meat consumption has been considered a determinant of weight gain (2–8). On the other hand, it has been suggested that a high protein diet may have potential beneficial effects because of increased satiety and thermogenesis (9). Some intervention

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studies performed in overweight or obese subjects under energy restriction did observe a higher weight loss with a high-protein diet than with a high-carbohydrate diet (10–18). However, protein level targets were not reached by the increase of only meat intake, but also dairy products, nuts, and vegetables, which makes these results less appropriate to assess the relation between meat intake and weight gain. Indeed, some previous results suggested that weight gain may be inversely associated with dairy product and vegetable consumption (19, 20). Intervention studies on meat intake specifically showed mixed results (21–26), although in most of them no weight change difference was observed when energy from carbohydrates was partially substituted with meat (23–26).

Several prospective observational studies (2–8) reported a positive association between meat consumption and weight gain. However, it remains unclear whether the observed associations were fully attributable to meat intake itself. A dietary pattern closely associated with both the exposure and the outcome could have biased the results previously observed. The Western dietary pattern, characterized by high consumption of meat (especially processed meat), saturated fat, and refined carbohydrates and low consumption of fruit, vegetables, and fiber has often been positively associated with weight gain (27–30) and with some deleterious lifestyle habits, such as physical inactivity (31, 32).

To our knowledge, no previous observational study has investigated the relation between meat intake and weight gain, with underlying dietary patterns taken into account. In the present prospective study, we analyzed the relation of total meat consumption, red meat, poultry, and processed meat with long-term changes in body weight in a large sample of European men and women with heterogeneous dietary habits, with dietary pattern and other lifestyle confounders taken into account.

SUBJECTS AND METHODS

Study population

The EPIC is a multicenter, prospective cohort study that investigated the role of metabolic, dietary, lifestyle, and environmental factors in the development of cancer and other chronic diseases. Briefly, between 1992 and 2000, 521,448 volunteers aged between 25 and 70 y were recruited in 23 centers from 10 European countries (Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Spain, Sweden, and the United Kingdom). In France, Norway, Utrecht (Netherlands), and Naples (Italy), only women were included. In general, individuals were selected from the general population of a specific geographic area, a town or a province. Exceptions included the French cohort, based on members of the health insurance system for state-school employees, and the Utrecht cohort, based on women who underwent breast cancer screening. Participants were invited to participate either by mail or in person and those who agreed to participate signed an informed consent agreement. Approval for this study was obtained from the ethical review boards of the International Agency for Research on Cancer and from all local institutions. Details of the recruitment and study design have been published previously (33–35).

After the exclusion of individuals without dietary and nondietary questionnaires, individuals without data on weight and height at baseline or with extreme or implausible anthropometric values, pregnant women, and those in the top and bottom 1% of the ratio between energy intake to estimated energy requirement, 497,735 individuals were available for the analyses. We further excluded 123,932 subjects without weight data at follow-up or with extreme or implausible weight changes. Thus, 373,803 subjects (103,455 men and 270,348 women) were included in the present analysis (a flow chart can be found under "Supplemental data" in the online issue).

Assessment of anthropometric measures and weight change

Two weight measures were available for each participant: one measure at baseline and one at follow-up. In most centers, body weight and height were measured at baseline with the use of similar, standardized procedures. The exceptions were the centers of Oxford (United Kingdom), France, and Norway, where self-reported anthropometric values at baseline were collected (36). Self-reported weight was obtained at follow-up in all centers, except in Norfolk (United Kingdom) and Doetinchem (Netherlands), where weight was measured. The accuracy of self-reported anthropometric measures was improved with the use of

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[2] The project PANACEA received funding from the European Union, in the framework of the Public Health Programme (project no. 2005328). The work was further financially supported by the European Commission: Public Health and Consumer Protection Directorate 1993–2004; Research Directorate-General 2005; Ligue contre le Cancer, Société 3M, Mutuelle Générale de l'Education Nationale, Institut National de la Santé et de la Recherche Médicale (France); German Cancer Aid, German Cancer Research Center, Federal Ministry of Education and Research (Germany); Danish Cancer Society (Denmark); Health Research Fund of the Spanish Ministry of Health, the participating regional governments and institutions (Spain); Cancer Research UK, Medical Research Council, Stroke Association, British Heart Foundation, Department of Health, Food Standards Agency, the Wellcome Trust (United Kingdom); Greek Ministry of Health and Social Solidarity, Hellenic Health Foundation, Stavros Niarchos Foundation (Greece); Italian Association for Research on Cancer, National Research Council (Italy); Dutch Ministry of Public Health, Welfare and Sports, Dutch Ministry of Health, Dutch Prevention Funds, LK Research Funds, Dutch Zorg Onderzoek Nederland, World Cancer Research Fund (Netherlands); Swedish Cancer Society, Swedish Scientific Council, Regional Government of Skane (Sweden); and Norwegian Cancer Society (Norway).

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Received September 21, 2009. Accepted for publication May 11, 2010.
First published online June 30, 2010; doi: 10.3945/ajcn.2009.28713.

prediction equations derived from subjects with both measured and self-reported measures (35, 37). Body mass index (BMI; in kg/m^2) at baseline was calculated as weight in kilograms divided by height in meters squared. Because the follow-up times differed by center (from 2 y for Heidelberg to 11 y for Varese), our main outcome is the annual weight change (g/y; ie, weight at follow-up minus weight at baseline divided by time of follow-up (in y). Because the association of weight change with meat intake was similar with the use of self-reported or predicted weight, all the results presented here are based on predicted weight at follow-up.

Dietary assessment

Usual dietary intake at baseline was measured with the use of country-specific validated questionnaires. Most centers adopted a self-administered quantitative dietary questionnaire of 88–266 food items (35). Semiquantitative food-frequency questionnaires were used in Denmark, Norway, Naples, and Umeå (Sweden). Combined dietary methods were used in the United Kingdom and Malmö (35). Nutrient intakes were calculated with the use of the EPIC Nutrient DataBase, a standardized food-composition table (38, 39). To adjust for possible systematic under- or overestimation in dietary intake measure (40, 41), a dietary calibration study was conducted (42) with the use of a random sample of ≈36,900 men and women who completed an additional computerized 24-h dietary recall (EPIC-SOFT). In this study, total meat includes red meat (beef, veal, pork, and lamb), processed meat (ham, bacon, sausages, and other meat products mainly from beef and pork), and poultry (mainly chicken and in some cohorts, turkey and rabbit).

Assessment of other covariates

Lifestyle and health factors were collected by questionnaires at baseline (35). These included questions on tobacco smoking, educational attainment, physical activity (occupational and leisure-time activity), menstrual history, and history of previous illness. Smoking tobacco was also collected during follow-up, at the same time as the anthropometric measures. This permitted smoking status modification to be taken into account during follow-up in our analysis.

Statistical analyses

We first examined the distribution of the population's main characteristics according to sex-specific quintiles of meat consumption with the use of analysis of variance (ANOVA) or chi-square tests as appropriate. The association between meat consumption (in kcal/d or g/d) and annual weight change (g/y) was investigated with the use of a multilevel, mixed-effects, linear regression model, with meat consumption values on a continuous scale. We fit several multivariable-adjusted models that controlled for potential confounders (as fixed effects). The first model (M1) was adjusted for sex, age, and an indicator of meat consumption (consumer or nonconsumer). The second model (M2) was further adjusted for initial BMI, follow-up time (years), educational level (primary school, technical school, secondary school, or university degree), physical activity index (combination of occupational physical activity, cycling, and sport activities in 4 categories: inactive, moderately inactive, moderately active, and active (43)), smoking status (never, former, and current smoker), total energy intake (kcal/d), energy from alcohol (kcal/d), and a categorical variable that indicated plausibility of energy intake reporting. Participants were classified as underreporters [ratio of reported energy intake to predicted basal metabolic rate (EI:BMR) < 1.14], plausible reporters (EI:BMR = 1.14–2.1), or overreporters (EI:BMR > 2.1), with the use of cutoff points proposed by Goldberg (44). We also fitted a mutually adjusted model for the subtypes of meat and further adjusted it for menopausal status, but the results were unchanged and are thus not presented.

The third multivariable model was further adjusted for dietary patterns (M3). Three different methods were used to derive dietary patterns: maximum likelihood factor analysis (MLF), which maximizes the variance between all food groups; reduced rank regression, which explains as much variation in meat consumption as possible; and partial least-squares regression, which balances the 2 objectives of explaining variation in meat consumption and in other food groups. Food intakes were energy adjusted with the use of the residual method (45). The factors were rotated by an orthogonal transformation with the use of the Varimax option to increase interpretability. For each method, the 2 factors that explained the biggest part of total variance were retained. The results of the 3 methods were similar, and only those obtained with the MLF method are presented in this report. The foods that contributed to the first dietary pattern, labeled "prudent pattern" (distinguishes subjects with high intakes of vegetables, legumes, fruit, pasta and rice, and vegetable oils from those with high intakes of processed meat, potatoes, margarines, coffee and tea, and beer and cider) and the second dietary pattern labeled "fresh meat" (distinguishes subjects with high intakes of red meat, poultry, and vegetable oils from those with high intakes of cakes) are shown in the supplemental table under "Supplemental data" in the online issue. The second model was then further adjusted for the 2 dietary pattern scores (continuous) (M3).

We repeated the analyses with the use of calibrated dietary data for total meat obtained from country- and sex-specific calibration models. The 24-h total meat value was regressed on the total meat value obtained from the main dietary questionnaire, with adjustment for age, BMI at baseline, total energy, energy from alcohol, and study center (46). Data were weighted by the day of the week and the season of the year in which the 24-h dietary recall was collected. Nonconsumers in the main dietary questionnaires were excluded from the regression calibration models and zero was kept as the predicted value. The SE of the coefficient was estimated with the use of bootstrap sampling (10 loops) (40, 41).

We explored potential effect modification by sex, age, BMI, smoking status, physical activity, educational level, follow-up time, "prudent pattern" score, and center with the inclusion of interaction terms between each variable and meat intake in the models. Variables were selected a priori. P values for the interaction term were calculated with the use of the F test and group-specific coefficients are presented when significant interactions were detected.

Sensitivity analyses were performed with the exclusion of participants with chronic diseases at baseline (heart disease, stroke, diabetes mellitus, hypertension, hyperlipidemia, and/or cancer; n = 76,077), those likely to misreport energy intake (n = 121,425) (44), and those with incident cancer (n = 9,144) or change in smoking status during follow-up (n = 24,051). All statistical analyses were performed with SAS software, version 8.1.3 (SAS Institute Inc, Cary, NC) or STATA 9.0 (StataCorp, College Station, TX).

RESULTS

The highest averages of meat intake at baseline were observed in the cohorts from Denmark, Potsdam (Germany), Spain, Malmö (Sweden), Doetinchem (Netherlands), and Amsterdam/Maastricht (Netherlands), with >316 and 207 kcal/d in men and women, respectively. The lowest meat intakes were observed in Greece (193 and 142 kcal/d) and in the Oxford health-conscious cohort (United Kingdom), which included mostly vegetarian subjects (86 and 82 kcal/d). The majority of meat consumption was red meat for all centers except in Heidelberg, Potsdam (Germany), Malmö, Umeå (Sweden), and Norway, where the percentages of processed meat were higher (data not presented). On average, subjects had the highest BMI in Spain and Greece (>27.9) and the lowest in France and in the Oxford health-conscious cohort (<24.5) (**Table 1**). Overall, men reported higher meat consumption than women (296 ± 171 kcal/d compared with 195 ± 114 kcal/d, $P < 0.0001$) and higher weight gain (454 ± 1006 g/y compared with 416 ± 985 g/y).

The characteristics of the subjects according to sex-specific quintiles of energy from meat are summarized in **Table 2**. In crude analyses, participants in the lowest quintile of meat intake were slightly younger, had lower BMI at baseline, and reported a higher weight gain on average. They were more frequently highly educated, physically inactive, never smokers, and were more likely to have reported previous illness. After adjustment for total energy intake, they reported higher intake of vegetables, legumes, fruit, dairy products, cereals, and cakes and lower intake of potatoes, fish, eggs, nonalcoholic and alcoholic beverages. High meat consumers reported a higher proportion of processed meat and a lower proportion of poultry in men and a higher proportion of red meat in women, compared with low meat consumers.

The adjusted increase in annual weight gain (in g/y) per 100 kcal/d of meat consumption before and after calibration in the entire sample is presented in **Table 3**. Similar associations were obtained when meat was expressed in g/d instead of kcal/d, or when self-reported instead of predicted weights were used (results not presented). Annual weight gain was positively associated with total meat consumption in multivariable models [M2: β (95% CI) = 30 (24, 36), $P < 0.0001$]. Adjustment for dietary patterns (M3) only slightly attenuated the association [M3: β (95% CI) = 25 (19, 31), $P < 0.0001$]. The association was considerably strengthened when calibrated data were used [M3: β (95% CI) = 65 (39, 90), $P < 0.0001$].

Weight gain was also positively associated with poultry, red meat, and processed meat intakes. However, the strength of the association varied according to meat subtype. Weight gain was only weakly related to the intake of red meat [M3: β (95% CI) = 15 (1, 28), $P = 0.03$]. The association with processed meat was similar to that observed for total meat [M3: β (95% CI) = 25 (15, 34), $P < 0.0001$]. The strongest association was shown for poultry [M3: β (95% CI) = 45 (29, 62), $P < 0.0001$].

To explore whether the results were confounded by changes of diet before collection of dietary information or by potential misreporting of meat, we excluded from the analyses the participants with chronic diseases and those likely to misreport energy intake at baseline (n = 197,502). The association of weight gain with red meat was no longer significant [M3: β = 8 (−9, 25)]; it was attenuated and became similar to that observed for total meat for poultry [M3: β = 27 (1, 53)] and it was strengthened for processed meat [M3: β = 31 (17, 44)]. The exclusion of subjects with incident cancer or smoking status modification during follow-up did not change the results (data not shown).

TABLE 1
Characteristics of the population according to sex and center (n = 373,803)

Center	Men	Women	Meat consumption		BMI[1]		Annual weight gain[1]	
			Men	Women	Men	Women	Men	Women
	n	*n*	*kcal/d*		*kg/m²*		*g/y*	
France	—	66,929	—	225 ± 122[2]	—	23.5 ± 3.2	—	441 ± 1016
Spain	14,807	24,598	354 ± 177	221 ± 118	28.4 ± 3.3	28.1 ± 4.6	397 ± 1192	206 ± 1253
Italy	4700	16,184	256 ± 123	191 ± 91	26.3 ± 3.3	25.4 ± 4.1	320 ± 549	306 ± 529
Cambridge[3]	6377	8175	208 ± 109	188 ± 100	26.0 ± 3.1	25.5 ± 4.1	357 ± 1019	369 ± 1090
Oxford Health	6599	23,362	86 ± 113	82 ± 102	24.5 ± 3.3	23.6 ± 3.8	557 ± 930	560 ± 940
Oxford General	1481	3786	214 ± 106	201 ± 106	26.2 ± 3.4	25.3 ± 4.5	392 ± 919	457 ± 909
Doetinchem[3]	2190	2376	319 ± 129	224 ± 101	25.7 ± 3.0	25.1 ± 4.0	419 ± 841	442 ± 944
Amsterdam/Maastricht	4193	5366	316 ± 150	216 ± 117	25.4 ± 3.5	24.4 ± 4.0	568 ± 864	550 ± 884
Utrecht	—	12,572	—	201 ± 104	—	25.3 ± 3.9	—	855 ± 1002
Greece	10,008	14,572	193 ± 92	142 ± 66	27.9 ± 3.7	28.6 ± 5.1	499 ± 973	385 ± 875
Heidelberg	10,424	11,948	291 ± 179	178 ± 121	26.8 ± 3.5	25.1 ± 4.4	591 ± 1573	360 ± 1506
Potsdam	7059	11,229	357 ± 176	223 ± 117	26.8 ± 3.4	25.7 ± 4.5	364 ± 636	373 ± 659
Malmö	8414	13,169	326 ± 155	207 ± 99	25.9 ± 3.4	24.9 ± 4.0	545 ± 908	495 ± 922
Umeå	6437	7157	221 ± 122	154 ± 75	25.1 ± 3.2	24.0 ± 3.8	710 ± 616	642 ± 636
Denmark	20,766	23,472	398 ± 149	246 ± 98	26.5 ± 3.4	25.5 ± 4.3	331 ± 855	211 ± 863
Norway	—	25,453	—	178 ± 79	—	25.1 ± 3.8	—	397 ± 823
Total	103,455	270,348	296 ± 171	195 ± 114	26.6 ± 3.6	25.1 ± 4.3	454 ± 1006	416 ± 985

[1] Calculated with the use of the Oxford formula.
[2] Mean ± SD (all such values).
[3] Weight measured at both baseline and end of follow-up.

TABLE 2
Characteristics of the population according to sex-specific quintiles of energy from meat (n = 373,803)[1]

Characteristic	Quintiles of total meat consumption in men 1	3	5	Quintiles of total meat consumption in women 1	3	5
Median (quintile 1–quintile 3)	104 (50–133)	275 (256–295)	511 (459–600)	57 (15–83)	185 (172–198)	340 (306–396)
Age (y)	52.2 ± 11.9[2]	52.9 ± 9.4	52.6 ± 7.9	50.2 ± 11.3	51.7 ± 8.8	51.4 ± 8.0
BMI at inclusion (kg/m^2)	25.7 ± 3.5	26.6 ± 3.4	27.2 ± 3.7	24.1 ± 4.0	25.2 ± 4.2	25.6 ± 4.5
BMI ≥ 30 kg/m^2 at inclusion (%)	10.8	15	20.5	8.9	13	14.9
Weight change[3] (g/y)	487 ± 1004	429 ± 997	447 ± 1045	440 ± 987	396 ± 951	426 ± 1052
Educational level (%)						
None or primary school completed	23	32.1	40.2	19.2	28	27
Technical/professional school	20.2	24.3	26.1	18.1	22.2	19.9
Secondary school	15.7	14.2	9.8	24.8	26.1	27.6
University degree and longer	34.89	27.1	22.85	31.4	20.39	22
Physical activity (%)						
Inactive	21.2	16.4	14	20.7	20.4	20
Moderately inactive or active	48.9	53.3	52.6	53.5	51	59.2
Active	18.1	22.3	29.9	14.6	12.3	14.3
Smoking status (%)						
Never	40.8	32.7	27.5	60.4	56.9	56
Former	37.6	37.4	35.3	23.9	22.2	21.6
Smoker	19.4	28.8	36.9	13.3	18.6	20.1
Previous illness (%)	9.3	7.8	6.8	8.1	7.4	7.8
Total energy intake (kcal/d)	2019 ± 556	2381 ± 557	2919 ± 625	1706 ± 491	1892 ± 470	2318 ± 540
Follow-up time[4] (y)	5.2	5.1	5.1	5.1	5	3.9
Daily intakes[5]						
Total meat (%)	47.2 ± 0.2	123.3 ± 0.2	219.9 ± 0.2	26.4 ± 0.1	86.7 ± 0.1	160.7 ± 0.1
Red meat	43.6 ± 0.2	45.3 ± 0.2	44.0 ± 0.2	38.8 ± 0.1	42.3 ± 0.1	44.9 ± 0.1
Poultry	20.2 ± 0.1	17.2 ± 0.1	13.8 ± 0.1	17.8 ± 0.1	21.3 ± 0.1	18.5 ± 0.1
Processed meat	30.5 ± 0.2	32.1 ± 0.2	38.3 ± 0.2	37.5 ± 0.1	31.7 ± 0.1	32.2 ± 0.1
Potatoes and other tubers (g)	94.9 ± 0.6	121.9 ± 0.6	146.5 ± 0.6	68.4 ± 0.3	81.0 ± 0.3	91.0 ± 0.3
Vegetables (g)	268.4 ± 1.1	195.2 ± 1.1	156.0 ± 1.1	270.0 ± 0.6	217.9 ± 0.6	202.6 ± 0.6
Legumes (g)	23.3 ± 0.2	17.0 ± 0.2	17.3 ± 0.2	19.4 ± 0.1	12.5 ± 0.1	13.9 ± 0.1
Fruit (g)	286.4 ± 1.3	211.6 ± 1.2	143.5 ± 1.3	296.5 ± 0.7	251.2 ± 0.7	204.8 ± 0.8
Dairy products (g)	385.0 ± 1.8	338.4 ± 1.8	268.9 ± 1.9	356.1 ± 0.9	326.2 ± 0.9	281.7 ± 0.9
Cereals (g)	279.7 ± 0.7	249.9 ± 0.7	218.9 ± 0.7	224.2 ± 0.3	200.4 ± 0.3	174.3 ± 0.4
Fish and shellfish (g)	32.5 ± 0.3	39.0 ± 0.2	42.8 ± 0.3	31.3 ± 0.2	40.8 ± 0.2	38.0 ± 0.2
Eggs (g)	13.6 ± 0.1	19.0 ± 0.1	25.3 ± 0.1	15.3 ± 0.1	18.1 ± 0.1	21.1 ± 0.1
Added fat (g)	39.6 ± 0.1	37.1 ± 0.1	31.7 ± 0.1	24.4 ± 0.1	25.2 ± 0.1	22.0 ± 0.1
Sugar and confectionery (g)	50.3 ± 0.5	52.8 ± 0.5	53.4 ± 0.5	38.2 ± 0.1	38.1 ± 0.1	33.4 ± 0.2
Cakes (g)	56.4 ± 0.3	45.0 ± 0.3	26.1 ± 0.4	44.0 ± 0.2	40.9 ± 0.2	32.6 ± 0.2
Nonalcoholic beverages (g)	867.3 ± 5.4	1071.1 ± 5.2	1279.9 ± 5.6	1047.5 ± 3.3	1070.4 ± 3.3	1225.5 ± 3.4
Alcoholic beverages (g)	268.9 ± 2.8	342.4 ± 2.7	408.0 ± 2.9	96.6 ± 0.7	101.2 ± 0.6	119.4 ± 0.7

[1] P values for continuous variables (ANOVA) and chi-square tests for categoric variables are all <0.0001.
[2] Mean ± SD (all such values).
[3] Calculated with the use of the Oxford formula.
[4] Values are medians.
[5] Adjusted for total energy.

Significant interactions were observed for sex, age, BMI, smoking status, follow-up time, physical activity, and prudent pattern scores. When all interaction terms were simultaneously entered in the models, initial BMI was the most important modifier of the relation between weight gain, meat, and meat subtypes. The association of total meat with weight change was stronger in normal-weight subjects, former and current smokers, and participants who reported a higher prudent pattern score (characterized by high consumptions of vegetables, legumes, fruit, pasta/rice, and vegetable oils and low consumption of processed meat, potatoes, margarines, coffee/tea, and beer/cider) (P values for interaction < 0.01) (**Table 4**). The association was also more evident when weight at follow-up was assessed after ≤2 y (P for interaction = 0.003). Similar patterns were observed for red meat according to BMI and smoking status and for processed meat according to BMI, smoking status, follow-up time, and prudent pattern score. In addition, the relation between red meat and weight gain was also stronger in physically active subjects compared with moderately inactive or inactive subjects (P values for interaction = 0.02) and in subjects aged <35 y or >65 y compared with subjects aged between 35 and 64 y (P values for interaction < 0.0001). The relation between processed meat and weight gain was also stronger in men compared with women (P value for interaction = 0.03). Different effect modifications in the association of weight gain with poultry intake were observed. The relation was stronger in subjects >45 y (P for interaction < 0.0001), an inverse association was observed in obese subjects only [M3: $\beta = -44$ (-68, -19)], and

TABLE 3
Adjusted increase in annual weight change (in g/y) for a 100-kcal increase in meat consumption before and after calibration in the European Prospective Investigation into Cancer and Nutrition (n = 373,803)[1]

	β	95% CI	P value
Total meat			
Uncorrected data			
M1	14	(8, 19)	<0.00001
M2	30	(24, 36)	<0.00001
M3	25	(19, 31)	<0.00001
Calibrated data			
M1	13	(−5, 31)	0.15
M2	71	(47, 95)	<0.00001
M3	65	(39, 90)	<0.00001
Subtype of meat			
Red meat			
M1	18	(5, 31)	0.006
M2	36	(22, 50)	<0.00001
M3	15	(1, 28)	0.03
Poultry			
M1	46	(30, 62)	<0.00001
M2	74	(58, 91)	<0.00001
M3	45	(29, 62)	<0.00001
Processed meat			
M1	17	(9, 25)	<0.00001
M2	30	(20, 39)	<0.00001
M3	25	(15, 34)	<0.00001

[1] M1, model 1 (adjusted for sex, age, and an indicator of meat consumption); M2, model 2 (adjusted as in M1 + educational level, physical activity level, smoking status, initial BMI, follow-up time, total energy intake, energy from alcohol, and plausible total energy intake reporting); M3, model 3 (adjusted as in M2 + dietary factors 1 and 2 derived from maximum likelihood factor analysis).

the strongest relations according to smoking status were observed in former smokers and nonsmokers (P for interaction < 0.0001).

The adjusted (M3) increase in annual weight change (in g/y) per 100 kcal/d increase in total meat consumption (uncalibrated) in centers ranked by prudent pattern score average (P for interaction < 0.0001) is shown in **Figure 1**. Positive significant associations were observed in Denmark, Norway, France, Spain, Italy, and Greece. Nonsignificant associations were observed in all other cohorts. The heterogeneity of results seems to be explained by differences in dietary patterns across countries and by cohort size. The β coefficients according to center were positively associated with the average prudent pattern score (P = 0.03, data not shown). Meat intake was not significantly associated with weight gain in all centers with a negative average of the prudent pattern score (except Denmark and Norway)

DISCUSSION

In this large prospective study, total meat, red meat, poultry, and processed meat intakes were all positively associated with weight gain after an average of 5 y of follow-up. Results were statistically significant after adjustment for total energy intake, physical activity, dietary pattern scores, and other potential confounders. Total meat was significantly positively associated with weight gain in men and women, normal-weight and overweight subjects, and all smoking status subgroups. An intake of 250 g meat/d (eg, one steak at ≈450 kcal) would lead to an annual weight gain 422 g higher (95% CI: 303, 541) than the weight gain experienced with an isocaloric diet with lower meat content (with the use of calibrated data). After 5 y, the weight gain would be >2 kg higher. This absolute increase of weight may be considered low from a clinical point of view. Weight management through adult life cannot be achieved through control of meat intake only; a decrease in total energy intake and an increase in physical activity are mandatory (47). However, an average 2-kg weight gain in 5 y could have an important effect from a population perspective. More importantly, our results do not support that a high-protein diet prevents obesity or promotes long-term weight loss, contrary to what has been advocated (48).

Our results are in agreement with most previous observational studies that have shown a positive association between meat intake and weight gain (2–8). Only 2 studies did not report any significant association between meat consumption and weight gain or waist circumference (49, 50). In our study, we showed significant interactions with sex, age, BMI, smoking status, follow-up time, physical activity, and prudent pattern scores. Initial BMI was the most important modifier of the relation between weight gain, meat, and meat subtypes, with a stronger relation observed in leaner subjects. At least 2 explanations could account for this result. First, given that normal-weight subjects at baseline gained more weight during follow-up than did overweight and obese subjects, we cannot exclude the possibility that the higher coefficients in the normal-weight group were induced by a higher variability in weight change values in this category. Although the accuracy of self-reported weights at follow-up was improved with the use of a prediction equation, obese subjects are more likely to underestimate their weight than normal-weight subjects (51), and the assessment of weight change may be more prone to bias in overweight and obese individuals. Second, overweight and obese subjects tend to underreport their energy intake more than lean individuals (52), especially intake from "socially undesirable" food groups (53), which could have lead to an underestimation of the relation between meat intake and weight.

The strongest relation with annual weight change was observed for poultry. However, when subjects with previous illness and those likely to misreport their energy intake at baseline were excluded from the analyses, the association of weight gain with poultry was attenuated and the strongest association was observed for processed meat. This suggests that this result may be driven mainly by subjects with previous illness or weight-loss attempts that lead to diet intervention, as well as those who misreported their dietary intakes.

Our results appear to contradict experimental studies that provide evidence of short-term increases in satiety and thermogenesis and decreased energy intake with high-protein diets (54). It has also been shown that obese subjects on a low-carbohydrate/high-protein diet lost more weight after 3 mo than did those on a conventional diet (11). However, results were not confirmed after 1 y of follow-up (11, 55). Furthermore, most of the intervention studies specifically on meat intake (21–26) did not find any weight change difference when energy from carbohydrates was partially substituted with meat (23–26). These differences could be linked to differences in the food substitutions performed as well as differences in the population's initial dietary habits. With control of energy intake for 9 wk,

TABLE 4
Adjusted increase in annual weight change (in g/y) for a 100-kcal increase in meat consumption according to interaction variables[1]

	β	95% CI	P value	P for interaction[2]
Total meat				
BMI				<0.0001
<25 kg/m²	37	(30, 44)	<0.0001	
25–29 kg/m²	14	(7, 21)	<0.0001	
≥30 kg/m²	6	(−2, 15)	0.12	
Smoking status				<0.0001
Never	21	(20, 27)	<0.0001	
Former	27	(22, 34)	<0.0001	
Smoker	29	(22, 37)	<0.0001	
Follow-up time				0.003
≤2 y	44	(30, 57)	<0.0001	
3–5 y	28	(21, 34)	<0.0001	
6–7 y	23	(15, 31)	<0.0001	
>7 y	18	(7, 29)	0.0009	
Prudent pattern tertiles				0.009
First tertile	14	(7, 22)	<0.0001	
Second tertile	31	(24, 39)	<0.0001	
Third tertile	36	(28, 44)	<0.0001	
Red meat				
Age				<0.0001
<35 y	48	(23, 73)	0.0002	
35–44 y	18	(0, 35)	0.04	
45–54 y	13	(−2, 27)	0.08	
55–64 y	9	(−6, 24)	0.24	
≥65 y	39	(17, 61)	0.0006	
BMI				<0.0001
<25 kg/m²	28	(13, 42)	0.0002	
25–29 kg/m²	1	(−14, 16)	0.88	
≥30 kg/m²	4	(−13, 21)	0.63	
Smoking status				<0.0001
Never	5	(−9, 19)	0.47	
Former	19	(4, 34)	0.01	
Smoker	26	(10, 41)	0.0009	
Physical activity				0.02
Inactive	6	(−10, 22)	0.50	
Moderately inactive	11	(−4, 26)	0.14	
Moderately active	20	(5, 36)	0.01	
Active	25	(9, 41)	0.002	
Poultry				
Age				<0.0001
<35 y	18	(−39, 76)	0.53	
35–44 y	−14	(−40, 12)	0.30	
45–54 y	54	(33, 74)	<0.0001	
55–64 y	74	(52, 96)	<0.0001	
≥65 y	54	(13, 96)	0.01	
BMI				<0.0001
<25 kg/m²	67	(48, 87)	<0.0001	
25–29 kg/m²	62	(43, 81)	<0.0001	
≥30 kg/m²	−44	(−68, −19)	0.0004	
Smoking status				<0.0001
Never	47	(28, 65)	<0.0001	
Former	64	(42, 86)	<0.0001	
Smoker	11	(−12, 35)	0.35	
Processed meat				
Sex				0.03
Male	29	(19, 40)	<0.0001	
Female	20	(9, 31)	0.0002	
BMI				<0.0001
<25 kg/m²	44	(35, 53)	<0.0001	
25–29 kg/m²	9	(0, 18)	0.04	
≥30 kg/m²	7	(−4, 17)	0.22	
Smoking status				0.01
Never	20	(10, 30)	0.0001	
Former	23	(12, 34)	<0.0001	
Smoker	31	(20, 42)	<0.0001	
Follow-up time				<0.0001
≤2 y	67	(47, 87)	<0.0001	
3–5 y	22	(11, 33)	<0.0001	
6–7 y	26	(12, 40)	0.00	
>7 y	22	(3, 40)	0.02	
Prudent pattern tertiles				0.0087
First tertile	17	(6, 28)	0.004	
Second tertile	30	(18, 43)	<0.0001	
Third tertile	37	(23, 50)	<0.0001	

[1] Values were calculated with the use of uncalibrated data and adjusted for sex, age, indicator of meat consumption, educational level, physical activity level, smoking status, initial BMI, follow-up time, total energy intake, energy from alcohol, plausible total energy intake reporting, and dietary factors 1 and 2 derived from maximum likelihood factor analysis.

[2] *P* for interaction was tested by the insertion of an interaction term in the model with the use of continuous variables when available.

postmenopausal women who ate a diet supplemented with chicken ($n = 15$) lost significantly more body mass than did those supplemented with shortbread cookies and sugar-coated chocolates rich in carbohydrate and fat ($n = 14$) (21). All the other studies that substituted meat with healthier food such as soy products and legumes (23, 26), bread, pasta and rice (24), or fish, eggs, and cheese (25) did not find any significant weight-loss difference between the 2 interventions. In our study, the association between meat consumption and weight gain was weaker in subjects with a low prudent pattern score. Furthermore, meat intake was not significantly associated with weight gain in all centers with a negative average of the prudent pattern score (except Denmark and Norway), which indicates that the association could be diluted in populations with high consumptions of other high-energy-dense foods.

Several hypotheses have been made to explain the positive associations between meat intake and weight gain. First, an underlying detrimental dietary pattern closely associated with meat intake could confound the relation. However, the present study, which takes into account for the first time the dietary pattern as a potential confounder in this relation, does not support this hypothesis. A second explanation is linked to energy density, which may be a key element in body-weight regulation because it may alter appetite control signals (ie, hunger and satiety (56)). Although protein intake has been shown to increase satiety in intervention studies, the long-term effect of the consumption of a large amount of meat, which is an energy-dense food, remains unknown. Finally, beyond an underlying dietary pattern, an underlying lifestyle pattern could confound the relation. We adjusted for initial BMI, physical activity, educational level, smoking status, total energy intake, and plausible misreporting in the present study. However, if *1*) meat eaters tend to gather all

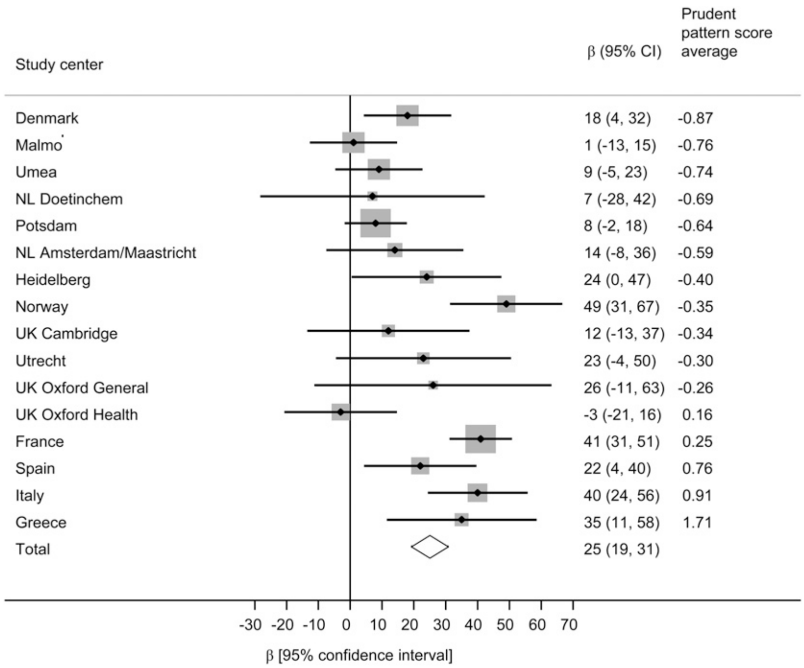

FIGURE 1. Adjusted increase in annual weight change (in g/y) per 100-kcal increase in total meat consumption in centers ranked by prudent pattern score average, with the use of uncalibrated data and adjusted for sex, age, indicator of meat consumption, educational level, physical activity level, smoking status, initial BMI, follow-up time, total energy intake, energy from alcohol, plausible total energy reporting, and dietary patterns scores. *P* for interaction with center < 0.0001. NL, Netherlands.

detrimental lifestyle components and *2*) the detrimental effect associated with the sum of all detrimental lifestyle components is superior to the sum of each individual effect, residual confounding could remain. All these hypotheses are only speculative and specific analyses need to be done to address these issues.

Some potential limitations of the present study should be mentioned. First, weight at follow-up was self-reported in most centers and was thus most likely underestimated (57). However, strong correlations have been observed between self-reported and measured weights (58). In addition, in our study the accuracy of self-reported weight was improved with the use of a prediction equation (37) and, overall, we observed similar mean annual weight gain in EPIC as in other European populations with measured weights at both baseline and follow-up (56). It is unlikely that the positive association with meat in this study is explained by inaccuracies in weight change. A second limitation is that we measured diet only at baseline and were not able to consider change in diet before or during follow-up. However, we conducted sensitivity analyses with the exclusion of those likely to have modified the diet because of previous illness, and the association persisted. We could not take into account weight change history in our analyses. Body weight tends to fluctuate (59, 60), which can lead to repeated cycles of weight loss and recovery (61–63). Weight cycling has been shown as the strongest predictor of subsequent large weight gain in men (64). Adjustment for self-reported weight at 20 y in a subsample of the study population (n = 169,100) did not change our results. Finally, even if overall response rate at follow-up was high in EPIC-PANACEA (80.6%), a selection bias could limit the generalization of our results.

The main strength of the present study is the very large sample size and the high heterogeneity of dietary patterns and obesity prevalence in the study population. Other strengths are the improvement of the estimates after partial correction for measurement error of diet (46, 65) and the adjustment for underlying dietary pattern scores. A study of the association between alcohol and type II diabetes mellitus has shown adjustment for dietary patterns to be more effective than adjustment for individual nutrients (66). In agreement with our results, MLF or partial least-squares regression provided the same results. Taken together, these results highlight the importance of taking dietary patterns into account in the analysis of individual food groups.

In conclusion, our results indicate that meat intake is positively associated with weight gain during adult life in European subjects. The association persisted after adjustment for total energy intake and underlying dietary patterns. Our results are therefore in favor of the public health recommendation to decrease meat consumption for health improvement.

The authors' responsibilities were as follows—A-CV (guarantor) and TN: statistical design, analysis of the data, and writing of the manuscript; DR, TM, AMM, NT, AA, MJS, BB-d-M, PO, AN, AT, SR, SH, HB, BB, MUJ, KO, AT, JH, TB, and DE: interpretation of data or writing of the manuscript; PP: principal investigator of the EPIC-PANACEA project; and ER: coordinator of the overall EPIC project. All authors directly participated in the planning, execution, or analysis of the study and reviewed the manuscript. None of the authors had a conflict of interest.

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