## JAMA Dermatology | Original Investigation

## Association Between Adult Acne and Dietary Behaviors Findings From the NutriNet-Santé Prospective Cohort Study

Laetitia Penso, MSc; Mathilde Touvier, PhD; Mélanie Deschasaux, PhD; Fabien Szabo de edelenyi, PhD; Serge Hercberg, MD, PhD; Khaled Ezzedine, MD, PhD; Emilie Sbidian, MD, PhD

**IMPORTANCE** Acne is a chronic, multifactorial inflammatory disease. The association between consumption of dairy products and fatty and sugary foods and occurrence and progression of acne remains unclear.

**OBJECTIVE** To assess the association between dietary behavior and current acne in adults.

**DESIGN, SETTING, AND PARTICIPANTS** A cross-sectional study was performed as part of the NutriNet-Santé study, which is an ongoing observational, web-based cohort study that was launched in France in May 2009. The present study was conducted from November 14, 2018, to July 8, 2019. A total of 24 452 participants completed an online self-questionnaire to categorize their acne status: never acne, past acne, or current acne. Associations between dietary behavior (food intake, nutrient intake, and the dietary pattern derived from a principal component analysis) and current or past acne were studied in multinomial logistic regression models adjusted for potential confounding variables (age, sex, physical activity, smoking status, educational level, daily energy intake, number of dietary records completed, and depressive symptoms).

**RESULTS** The 24 452 participants (mean [SD] age, 57 [14] years; 18 327 women [75%]) completed at least 3 dietary records. Of these, 11 324 individuals (46%) reported past or current acne. After adjustment, there was a significant association between current acne and the consumption of fatty and sugary products (adjusted odds ratio [aOR], 1.54; 95% CI, 1.09-2.16), sugary beverages (aOR, 1.18; 95% CI, 1.01-1.38), and milk (aOR, 1.12; 95% CI, 1.00-1.25). An energy-dense dietary pattern (high consumption of fatty and sugary products) was associated with current acne (aOR, 1.13; 95% CI, 1.05-1.18).

**CONCLUSIONS AND RELEVANCE** In this study, consumption of milk, sugary beverages, and fatty and sugary products appeared to be associated with current acne in adults. Further large-scale studies are warranted to investigate more closely the associations between diet and adult acne.

JAMA Dermatol. doi:10.1001/jamadermatol.2020.1602 Published online June 10, 2020. Editorial
Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Authors: Emilie Sbidian, MD, PhD, (emilie.sbidian@ aphp.fr), and Khaled Ezzedine, MD, PhD (khaled.ezzedine@aphp.fr), Department of Dermatology, Mondor Hospital (Assistance Publique, Hôpitaux de Paris), Paris Est Creteil University, 51 Ave du Maréchal de Lattre de Tassigny, F-94010 Créteil cedex, France.

cne has been reported to be the most common chronic inflammatory skin disease worldwide,<sup>1-3</sup> occurring mostly in the 15- to 17-year age group.<sup>4-6</sup> Epidemiologic data from Western countries suggest that the prevalence of acne in adults older than 25 years is approximately 50%, with female predominance.<sup>7-10</sup> In this so-called adult acne group, there are 2 distinct populations: patients who developed acne during adolescence and have persistent acne and those who developed de novo acne during adulthood.

Adult acne has various consequences; one of these is psychological harm associated with low self-esteem, poor perception of one's body, social isolation, and depressive symptoms.<sup>11,12</sup> Acne is reported to have the same emotional, social, and psychological consequences as chronic diseases, such as asthma, arthrosis, epilepsy, and diabetes.<sup>13</sup> Acne appears to be a multifactorial disease in which both genetic and environmental factors have pivotal roles. Endocrine disorders and genetic predispositions can lead to the development of acne; in addition, cosmetic products, tobacco use, stress, exposure to pollution, and dietary behavior may be associated with the development and severity of acne.<sup>14-19</sup>

People with acne have been reported to believe that consumption of foods affects their condition. Although chocolate, fatty foods, and milk are frequently thought to be responsible,<sup>20,21</sup> data on the role of nutrition in acne are scarce. It has been hypothesized that a glycemic diet<sup>22,23</sup> or the consumption of dairy products (particularly milk)<sup>24-28</sup> is associated with the pathophysiologic mechanism of acne via androgens and insulinlike growth factor-1 (IGF-1).<sup>29-32</sup> However, published studies presented several limitations. Randomized trials could not investigate multiple food exposition

jamadermatology.com

within the same time period and might be limited by a small population sample.<sup>22,33,34</sup> Observational studies frequently focus on teenage acne<sup>24,35</sup> and are based on frequency questionnaires<sup>17,24,35</sup> for previous food exposure, which lead to both a lack of precision in food records and a recall bias without taking into account various potential confounding factors, such as depression, energy intake (kilocalories per joule), and smoking.<sup>23,24,36</sup>

Thus, the objective of the present study was to assess the association between dietary behavior and current acne using a large cohort of French adults with accurate and timely dietary intake data.

## Methods

## **Study Population and Design**

The present study was performed as part of the NutriNet-Santé study. This ongoing, observational, web-based cohort study of adults was initiated in France in May 2009. Participants are extensively phenotyped via questionnaires on the dedicated NutriNet-Santé website (https://www.etudenutrinet-sante.fr/). Details of the NutriNet-Santé study's rationale, design, and procedures have been published elsewhere<sup>37</sup> (eMethods in the Supplement). The NutriNet-Santé study is conducted according to the tenets of the Declaration of Helsinki.<sup>38</sup> It was approved by the French Institute for Health and Medical Research's institutional review board; the present study is included in that approval. All participants provided electronic informed consent; data are deidentified. Participants do not receive financial compensation. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies.<sup>39</sup>

#### **Case Ascertainment and Data Collection**

A specific, optional questionnaire on acne was developed for the purposes of the present study and was distributed to NutriNet-Santé participants on November 14, 2018 (eTable 1 in the Supplement). The present study was conducted from November 14, 2018, to July 8, 2019. The questionnaire comprised 11 items related to the occurrence and diagnosis of acne and the participant's medical history; this information enabled us to determine whether the participant reportedly had acne at the present time and/or in the past. All participants who answered the questionnaire were eligible for the study. Each participant's acne status was classified as never acne, past acne (ie, acne at some time in their life but not at present), or current acne.

The participants' usual dietary intake was assessed at baseline and every 6 months after enrollment via a series of 3 nonconsecutive, validated, 24-hour dietary records<sup>40-42</sup> randomly assigned over a 2-week period (on 2 weekdays and 1 weekend day). In these records, participants were instructed to report all foods and beverages consumed from midnight to midnight. Participants estimated portion sizes from validated photographs,<sup>43</sup> using standard containers, or directly in grams or liters. Participants who provided at least

## **Key Points**

Question Is dietary behavior associated with acne in adults?

**Findings** In this cross-sectional study of 24 452 participants in the French NutriNet-Santé study, the consumption of fatty and sugary products, sugary beverages, and milk was associated with current acne in adults. This association was noted after adjustment for sociodemographic variables and confounding factors, including daily energy intake, the number of dietary records completed, and depressive symptoms.

**Meaning** These findings suggest that a Western diet (ie, rich in animal products and fatty and sugary foods) is associated with the presence of acne in adults.

3 dietary records were included in this study. More details about dietary records are shown in the eFigure in the Supplement.

For each participant, we calculated the mean intakes across all dietary records of each food group (in grams per day: fruit, vegetables, meat, fish, milk, dark chocolate, milk chocolate, refined cereals, snacks and fast foods, and fatty and sugary products) and each type of nutrient (in milligrams or grams per day: vitamins, zinc, fibers, carbohydrates, lipids, proteins, and saturated fatty acids) using the published NutriNet-Santé food composition database.<sup>37</sup> The latter database currently comprises nutritional values (eg, energy, alcohol, macronutrient, and micronutrient contents) for more than 3500 food items.

At baseline, participants were invited to complete questionnaires related to sociodemographic characteristics (eg, sex and educational level),<sup>44</sup> anthropometric data (eg, weight and height),<sup>45,46</sup> lifestyle (eg, smoking status and alcohol use), physical activity (assessed using the International Physical Activity Questionnaire),<sup>47</sup> health status (eg, any history and diagnosis of cardiovascular diseases, diabetes, and cancer), and, for women, reproductive health (age at menarche, pregnancy, and menopause). Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale; a score greater than or equal to 16 corresponds to the presence of depressive symptoms.

## **Statistical Analysis**

Qualitative variables are reported as the number (percentage) of participants. Food consumption and nutrient intakes were considered as continuous variables. In light of the literature results, we chose to assess 12 different food groups: fruit, vegetables, meats, fish, milk, sugary beverages, dark chocolate, milk chocolate, refined cereals, snacks and fast foods, fatty and sugary products, and delicatessen meats.<sup>17,20,24,48</sup> The following variables were considered in classes: age (in 4 classes); body mass index (BMI), calculated as weight in kilograms divided by height in meters squared (3 classes); educational status (3 classes); smoking status (3 classes); physical activity (3 classes); sex (male or female); and medical history (presence or absence).

The characteristics of participants in the current acne and past acne vs never acne groups were compared using an unadjusted  $\chi^2$  test for qualitative variables or the Kruskal-Wallis test

for quantitative variables. The strength of correlations between pairs of food intakes was determined by calculating Pearson coefficient *r* values; food intakes with *r*<0.80 were included in a multinomial analysis. Multinomial logistic regressions were performed to assess the association between food intakes and past (lifetime) acne or current adult acne; the results are expressed as the adjusted odds ratio (aOR) (95% CI) vs never acne. After using a backward selection, the regressions were adjusted for energy intake, the number of dietary records completed, sex, age, smoking status, physical activity, educational level, and depressive symptoms. Adjustments for BMI and a history of cardiovascular disease, cancer, type 1 diabetes, or type 2 diabetes were also tested. The same analyses (univariate analyses, Pearson test, and adjusted multinomial logistic regressions) were performed for the various types of nutrients.

Furthermore, because this was a post hoc analysis, dietary patterns were produced from principal components analysis based on 12 predefined food groups (fruit, vegetables, meat, fish, milk, sugary beverages, dark chocolate, milk chocolate, delicatessen meats, refined cereals, snacks and fast foods, and fatty and sugary products) using the SAS Proc Factor procedure (SAS Institute Inc). This factor analysis forms linear combinations of the original food groups, thereby grouping correlated variables. Coefficients defining these linear combinations are termed factor loadings. A positive factor loading means that the food group is positively associated with the factor, whereas a negative loading reflects an inverse association with the factor. For interpreting the data, we considered foods with a loading coefficient lower than -0.3 or higher than 0.3. We rotated factors by orthogonal transformation, using the SAS Varimax option to maximize the independence (orthogonality) of retained factors and obtain a simpler structure for easier interpretation. In determining the number of factors to retain, we considered eigenvalues greater than 1, the scree test (with values being retained at the break point between components with large eigenvalues and those with small eigenvalues on the scree plot), and the interpretability of the factors. For each participant, we calculated the factor score for each pattern by summing the reported consumption from all food groups weighted by the food group factor loadings. The factor score measures the conformity of an individual's diet to the given pattern. In addition, the dietary patterns noted in a principal component analysis were assessed in univariate and adjusted multinomial logistic analyses. Owing to a small number of missing values, we used complete-case analyses.

To limit the influence of hormonal factors linked to acne, we analyzed the subpopulation of women. In addition to the factors considered for the total population, multinomial analyses in women were adjusted for age at menarche, pregnancy, and menopause.

The threshold for statistical significance was set at P < .05. All analyses were performed with SAS Enterprise Guide software, version 7.1 (SAS Institute Inc).

## Results

## **Study Population**

Of the 31539 individuals who completed the questionnaire, 24 452 (78%) were included in the study because they had

(1) completed at least 3 dietary records, (2) reported a normal calorie intake, and (3) reported their acne status (items 1 and 8 from the acne questionnaire reported in eTable 1 in the **Supplement**). The study population included 18 327 women (75%), and the mean (SD) age was 57 (14) years. A total of 11 324 individuals (46%) indicated that they had acne at the time of the study or in the past; of these, 3576 individuals (32%) believed that diet was a factor in their acne, 3503 individuals (31%) believed that diet was not a factor in their acne, and 4195 individuals (37%) were unsure of whether diet was a factor. Data on comorbidities are summarized in **Table 1**, and data on the diagnosis of acne, age at onset, age at resolution, and treatments are summarized in eTable 2 in the Supplement.

There were 13128 participants (54%) in the never acne group, 9562 participants (39%) in the past acne group, and 1762 participants (7%) in the current acne group. Compared with the never acne and past acne groups, participants in the current acne group were younger (eg, 25-39 years: never, 9%; past, 17%; and current, 48%); had a higher educational level (never, 60%; past, 72%; and current, 78%); had a higher proportion of smokers (never, 12%; past, 12%; and current, 16%); had a lower level of physical activity (never, 20%; past, 23%; and current, 27%); had a lower BMI (<25: never, 66%; past, 70%; and current, 75%); had a lower frequency of cardiovascular disease (never, 18%; past, 14%; and current, 9%), type 2 diabetes (never, 2%; past, 1%; and current, 0.4%), and cancer (never, 7%; past, 6%; and current, 2%); and had a higher frequency of depressive symptoms (never, 16%; past, 17%; and current, 23%) (Table 1).

#### The Role of Diet

The results of the unadjusted and multiadjusted analyses of associations between food intakes and the presence of acne are summarized in **Table 2**. Unadjusted univariate analyses showed that, compared with participants in the never acne group, participants with current acne consumed significantly more milk (OR, 1.28; 95% CI, 1.18-1.39), sugary beverages (OR, 2.19; 95% CI, 1.94-2.48), milk chocolate (OR, 1.28; 95% CI, 1.19-1.38), snacks and fast foods (OR, 3.83; 95% CI, 3.34-4.40), and fatty and sugary products (OR, 4.35; 95% CI, 3.350-5.41) and significantly less meat (OR, 0.39; 95% CI, 0.31-0.48), fish (OR, 0.17; 95% CI, 0.13-0.23), vegetables (OR, 0.71; 95% CI, 0.66-0.76), fruit (OR, 0.71; 95% CI, 0.67-0.74), and dark chocolate (OR, 0.90; 95% CI, 0.84-0.96). After testing the correlation between the different pairs of foods, all food groups were included (*r*<0.4).

After adjustment, the consumption of milk (per glass, aOR, 1.12; 95% CI, 1.00-1.25; P = .04), sugary beverages (per glass, aOR, 1.18; 95% CI, 1.01-1.38; P = .04), and fatty and sugary products (per portion, aOR, 1.54; 95% CI, 1.09-2.16; P = .01) were found to be independently associated with current acne. Results were aOR, 1.76 (95% CI, 1.00-3.05) for 5 glasses of milk (1L); aOR, 2.29 (95% CI, 1.05-5.00) for 5 glasses of sugary beverages (1L), and aOR, 8.38 (95% CI, 1.54-47.02) for a complete meal of fatty and sugary products.

The results for nutrient levels were in agreement with the above findings. After adjustment, the carbohydrate intake (aOR, 1.43; 95% CI, 1.06-1.93; P = .02) and the saturated fatty

jamadermatology.com

Variable	No. (%)					
	Total	Acne status			Missina	
	population	Never	Past	Current	P value <sup>a</sup>	values
No. (%)	24 452	13 128 (54)	9562 (39)	1762 (7)		
Sex						0
Women	18 327 (75)	9426 (72)	7348 (77)	1553 (88)	< 001	
Men	6125 (25)	3702 (28)	2214 (23)	209 (12)	<.001	
Age, y						65 (0.3)
18-24	85 (0)	28 (0)	31 (0)	26 (1)		
25-39	3607 (15)	1192 (9)	1577 (17)	838 (48)	. 001	
40-54	6081 (25)	2484 (19)	2972 (31)	625 (36)	<.001	
≥55	14 614 (60)	9367 (72)	4975 (52)	272 (15)		
Educational level						158 (1)
Primary	4502 (18)	3111 (24)	1274 (13)	117 (7)	<.001	
Secondary	3590 (15)	1985 (15)	1337 (14)	268 (15)		
Higher	16 202 (66)	7935 (60)	6901 (72)	1366 (78)		
Smoking status						66 (0.3)
Smoker	2882 (12)	1506 (12)	1095 (12)	281 (16)		
Former smoker	8959 (37)	5268 (40)	3264 (34)	427 (24)	<.001	
Never smoker	12 545 (51)	6323 (48)	5175 (54)	1047 (59)		
Physical activity						36 (0.2)
High intensity	8623 (35)	5209 (40)	3004 (31)	410 (23)		
Moderate intensity	10 522 (43)	5340 (41)	4314 (45)	868 (49)	.001	
Low intensity	5271 (22)	2559 (20)	2232 (23)	480 (27)		
BMI <sup>b</sup>						29 (0.1)
<25	16 777 (69)	8722 (66)	6736 (70)	1319 (75)		
25-30	5662 (23)	3260 (25)	2092 (22)	310 (18)	<.001	
>30	1984 (8)	1129 (9)	723 (8)	132 (7)		
Medical history						
Depressive symptoms	4038 (17)	2036 (16)	1596 (17)	406 (23)	<.001	3786 (15
Cancer	1558 (6)	976 (7)	570 (6)	12 (0.7)	<.001	0
Cardiovascular disease	3823 (16)	2371 (18)	1286 (14)	166 (9)	<.001	0
Type 1 diabetes	48 (0)	30 (0.2)	15 (0.2)	3 (0.2)	.47	0
Type 2 diabetes	370 (2)	246 (2)	117 (1)	7 (0.4)	<.001	0

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

<sup>a</sup> *P* values were determined using a  $\chi^2$  test.

acid intake (aOR, 3.90; 95% CI, 1.02-15.00; P = .048) were found to be independently associated with current acne (**Table 3**).

#### **Principal Component Analysis**

Three principal components (interpreted as dietary patterns) accounted for 42% of the total variability. Labeling was descriptive based on foods with the greatest association with the dietary patterns. The healthy pattern (explaining 18% of the variance) was characterized by higher intakes of fruit, vegetables, and fish. The fatty and sugary pattern (explaining 13% of the variance) was characterized by higher intakes of fat and sugary products, including chocolate. The third pattern, which explained 11% of the variance, was referred to as animal products and refined cereals in view of the marked consumption of meat, milk, and refined cereals.

In an unadjusted analysis, the healthy and animal products and refined cereals dietary patterns were negatively associated with current acne (healthy: OR, 0.55; 95% CI, 0.52-0.57; P < .001; animal products and refined cereals: OR, 0.92; 95% CI, 0.88-0.97; P = .002), whereas the fatty and sugary dietary pattern was positively associated (OR, 1.25; 95% CI, 1.20-1.30; P < .001) (eTable 3 in the Supplement). After adjustment, adults with current acne were found to be less likely to have a healthy dietary pattern (aOR, 0.88; 95% CI, 0.83-0.94; P = .001) and more likely to have a fatty and sugary dietary pattern (aOR, 1.13; 95% CI, 1.05-1.18; P < .001) (Table 4).

<sup>b</sup> Not overweight, less than 25; overweight, 25 to 30; and obese, greater

## Further Analyses

than 30.

All 18 327 women in the study population were included in the subgroup analyses. The results appeared to support those of

#### Table 2. Univariate and Multivariate Analyses of Food Intake in the Study Population

	Univariate analysis vs never acne <sup>b</sup>				Multivariate analyses vs never acne <sup>c</sup>			
	Past acne		Current acne		Past acne		Current acne	
Food type <sup>a</sup>	OR (95% CI)	P value	OR (95% CI)	P value	aOR (95% CI)	P value <sup>d</sup>	aOR (95% CI)	P value <sup>d</sup>
No. of participants (%)	9562 (39)		1762 (7)		7983 (39)		1361 (7)	
Meat (portions/d)	0.74 (0.67-0.82)	<.001	0.39 (0.31-0.48)	<.001	0.93 (0.82-1.06)	.29	0.76 (0.58-1.00)	.05
Fish (portions/d)	0.65 (0.58-0.73)	<.001	0.17 (0.13-0.23)	<.001	0.94 (0.82-1.08)	.40	0.94 (0.68-1.29)	.69
Vegetables (portions/d)	0.98 (0.95-1.01)	.18	0.71 (0.66-0.76)	<.001	1.04 (1.00-1.08)	.048	0.94 (0.87-1.03)	.17
Fruit (portions/d)	0.94 (0.92-0.96)	<.001	0.71 (0.67-0.74)	<.001	0.98 (0.96-1.01)	.19	0.97 (0.91-1.03)	.32
Milk (glasses/d)	1.08 (1.03-1.14)	.001	1.28 (1.18-1.39)	<.001	1.02 (0.96-1.08)	.54	1.12 (1.00-1.25)	.04
Sugary beverages (glasses/d)	1.36 (1.23-1.49)	<.001	2.19 (1.94-2.48)	<.001	0.94 (0.84-1.05)	.24	1.18 (1.01-1.38)	.04
Dark chocolate (chunks/d)	1.02 (0.99-1.05)	.26	0.90 (0.84-0.96)	.002	1.01 (0.97-1.05)	.72	1.06 (0.99-1.15)	.11
Milk chocolate (chunks/d)	1.21 (1.15-1.27)	<.001	1.28 (1.19-1.38)	<.001	1.05 (0.99-1.12)	.09	0.99 (0.88-1.11)	.83
Snacks and fast foods (portions/d)	1.85 (1.69-2.03)	<.001	3.83 (3.34-4.40)	<.001	1.17 (1.04-1.33)	.01	1.16 (0.94-1.43)	.17
Fatty and sugary products (portions/d)	2.02 (1.75-2.34)	<.001	4.35 (3.50-5.41)	<.001	1.14 (0.93-1.39)	.20	1.54 (1.09-2.16)	.01
Refined cereals (portions/d)	1.05 (1.01-1.09)	.01	1.02 (0.95-1.10)	.62	1.02 (0.97-1.07)	.53	1.04 (0.93-1.16)	.52
Delicatessen meats (slices/d) <sup>e</sup>	0.96 (0.90-1.02)	.21	0.91 (0.80-1.03)	.13	NA		NA	

Abbreviations: aOR, adjusted odds ratio; NA, not applicable.

<sup>a</sup> One portion of meat, fish, fruit, vegetables, snacks and fast foods, fatty and sugary products, and refined cereals: 100 g; 1 glass of milk or sugary beverage: 200 mL; 1 chunk of chocolate: 7 g; and 1 slice of delicatessen meat: 40 g.

<sup>b</sup> Total of 13 128 never acne participants (54%).

<sup>c</sup> Total of 11 068 never acne participants (54%). Data are missing for some variables used in adjustment; therefore, the sample number (20 412) differed

from the overall population.

<sup>d</sup> P values were determined in a multinomial logistic regression after adjustment for total calorie intake, the number of dietary records completed, sex, age, smoking status, physical activity, educational level, body mass index, and history of cancer, diabetes, cardiovascular disease, or depressive symptoms.

<sup>e</sup> Delicatessen meat consumption showed no association in univariate analysis; therefore, we did not include it in the multivariate model.

## Table 3. Multivariate Analyses of Nutrient Intakes in the Study Population Using a Multinomial Logistic Regression

	Past acne		Current acne		
Nutrient type <sup>a</sup>	aOR (95% CI)	P value <sup>c</sup>	aOR (95% CI)	<i>P</i> value <sup>c</sup>	
Proteins	0.78 (0.58-1.06)	.12	0.68 (0.35-1.31)	.25	
Carbohydrates	1.09 (0.95-1.25)	.22	1.43 (1.06-1.93)	.02	
Saturated fatty acids	1.26 (0.67-2.35)	.47	3.90 (1.02-15.00)	.048	
Fibers	1.14 (0.60-2.17)	.68	0.31 (0.08-1.20)	.09	
Vitamin B <sub>12</sub> , µg	1.00 (0.99-1.01)	.79	1.00 (0.97-1.03)	.87	
Vitamin D, mg	1.01 (0.98-1.03)	.64	1.05 (0.99-1.10)	.08	

Abbreviation: aOR, adjusted odds ratio.

<sup>a</sup> Values based on intakes of 100 g/d.

<sup>b</sup> Analysis included 11 068 never acne participants (54%), 7983 past acne participants (39%), and 1361 current acne participants (7%). Data are missing for some variables used in adjustment; therefore, the sample number (20 412) differed from the overall population.

<sup>c</sup> P values were determined in a multivariate logistic regression after adjustment for total calorie intake, the number of dietary records completed, sex, age, smoking status, physical activity, educational level, body mass index, and history of cancer, diabetes, cardiovascular disease, or depressive symptoms.

the main analyses (eTable 4 in the Supplement). After adjustment, a regression analysis of the dietary patterns from the principal component analysis showed that the healthy pattern was negatively associated with current adult acne in women (aOR, 0.87; 95% CI, 0.80-0.94; P < .001), whereas the fatty and sugary pattern was positively associated (aOR, 1.12; 95% CI, 1.04-1.21; P = .003) (Table 5). The results of the primary and secondary analyses were the same after adjust-

ment for BMI and a history of cancer, types 1 and 2 diabetes, or cardiovascular disease.

## Discussion

The results of this study suggest an association between current acne and, after adjustment for confounding variables, the

# Table 4. Multivariate Analyses of Dietary Patterns From a Principal Component Analysis of the Study Population Using a Multinomial Logistic Regression

	Multivariate analyses vs never acne <sup>b</sup>					
	Past acne		Current acne			
Dietary pattern <sup>a</sup>	aOR (95% CI)	<i>P</i> value <sup>c</sup>	aOR (95% CI)	P value <sup>c</sup>		
Healthy	0.98 (0.94-1.01)	.17	0.88 (0.83-0.94)	.001		
Fatty and sugary	1.05 (1.01-1.08)	.006	1.13 (1.05-1.18)	<.001		
Animal products and refined cereals	0.98 (0.95-1.01)	.24	0.99 (0.92-1.07)	.87		

Abbreviation: aOR, adjusted odds ratio

<sup>a</sup> Healthy indicates frequent consumption of fruit, vegetables, and fish; fatty and sugary, frequent consumption of fatty and sugary products, including chocolate; and animal products and refined cereals, frequent consumption of animal products (eg, meat and milk) and refined cereals.

<sup>b</sup> Analysis included 11 068 never acne participants (54%), 7983 past acne participants (39%), and 1361 current acne participants (7%). Data are missing for some variables used in adjustment; therefore, the sample number (20 412) differed from the overall population.

<sup>c</sup> P values were determined in a multivariate logistic regression after adjustment for total calorie intake, the number of dietary records completed, sex, age, smoking status, physical activity, educational level, body mass index, and history of cancer, diabetes, cardiovascular disease, or depressive symptoms.

Table 5. Multivariate Analyses of Dietary Pattern From a Principal Component Analysis of the Subgroup of Women Using a Multinomial Logistic Regression

	Multivariate analyses vs never a	cne <sup>b</sup>						
	Past acne		Current acne					
Dietary pattern <sup>a</sup>	OR (95% CI)	<i>P</i> value <sup>c</sup>	OR (95% CI)	P value <sup>c</sup>				
Healthy	1.00 (0.96-1.04)	.98	0.87 (0.80-0.94)	<.001				
Fatty and sugary	1.04 (1.00-1.09)	.07	1.12 (1.04-1.21)	.003				
Animal products and refined cereals	1.00 (0.96-1.05)	.94	1.03 (0.94-1.12)	.59				

Abbreviation: OR, odds ratio.

<sup>a</sup> Healthy indicates frequent consumption of fruit, vegetables, and fish; fatty and sugary, frequent consumption of fatty and sugary products, including chocolate; and animal products and refined cereals, frequent consumption of animal products (eg, meat and milk) and refined cereals. for some variables used in adjustment; therefore, the sample number (20 412) differed from the overall population.

<sup>c</sup> P values were determined in a multivariate logistic regression after adjustment for total calorie intake, the number of dietary records completed, sex, age, smoking status, physical activity, educational level, body mass index, and history of cancer, diabetes, cardiovascular disease, or depressive symptoms.

<sup>b</sup> Analysis included 6998 never acne participants (52%), 5435 past acne participants (40%), and 1105 current acne participants (8%). Data are missing

consumption of fatty and sugary products, sugary beverages, and milk. In a principal component analysis, a fatty, energyrich diet (ie, high consumption of fatty and sugary products) was consistently found to be associated with the presence of adult acne. Similar results were noted in a subgroup analysis of the women in the study population.

The results of our study appear to support the hypothesis that the Western diet (rich in animal products and fatty and sugary foods) is associated with the presence of acne in adulthood. There are several possible explanations for this association. First, a high glycemic-load diet causes a rise in circulating levels of IGF-149 and insulin, which stimulates mammalian target of rapamycin 1 activity.<sup>50,51</sup> In turn, mechanistic target of rapamycin 1 stimulates cell proliferation and inhibits apoptosis, which increases levels of oxidative stress and inflammation, thus promoting the development of acne.<sup>50-52</sup> The elevation in IGF-1 levels also stimulates the production of androgens, which are associated with the production of sebum and thus the development of acne.<sup>29,31,32,53</sup> The consumption of milk also generates an increase in IGF-1 production by the liver and an increase in circulating insulin levels. Neither IGF-1 nor insulin is fully inactivated by pasteurization, homogenization, and digestion.54-57 Hence, milk consumption has similar consequences as a high glycemic-load meal. A role of IGF-1 in acne is also suggested by observations of patients with Laron syndrome, who do not produce IGF-1 and do not develop acne unless supplemented with this growth factor.  $^{55,58,59}$ 

The possible association between diet and development of acne has been investigated worldwide; conflicting results have been obtained (eTable 5 in the Supplement), perhaps because of interstudy differences in design, methods, case definitions, study populations (ie, eating habits and cultures), and end points. However, our present results appear to be in line with data on the glycemic load and exposure to dairy products. For example, a study of 44 acne cases and 44 controls by Ismail et al<sup>23</sup> noted that the glycemic load, according to 24-hour dietary records, was higher in the acne group than in the control group. Other studies have also reported an association between a high glycemic load (high carbohydrate consumption) and the presence of acne.<sup>22,31,60</sup> Our present results showed an apparent association between milk consumption and current acne, as also reported in the literature.<sup>24,27,31,61</sup> For example, Adebamowo et al<sup>24-26</sup> noted that the consumption of milk, particularly skimmed milk, was associated with the presence of acne in women after adjustment for age, age at menarche, BMI, and energy intake. Juhl et al<sup>27,28</sup> reported the same results for adolescent boys and all adults.

#### Strengths and Limitations

Our study's strengths included the large sample of adults in the NutriNet-Santé cohort, the large number of variables documented via self-questionnaires, and the accuracy of the food records. Food consumption was evaluated using at least three 24-hour dietary records linked to a large (3500-item) food composition database. The 24-hour dietary records linked to a large food composition database enabled us to take account of intraindividual variability and obtain what appeared to be precise, accurate estimates of usual dietary intakes. Furthermore, it has been reported that 24-hour dietary records obtained on several occasions, as used in the NutriNet-Santé cohort study, are more reliable than frequency questionnaires.<sup>62</sup>

One of the study's main limitations is that, relative to the French general population, the study population was younger, with a higher proportion of women, a higher educational level, and healthier dietary habits.<sup>63,64</sup> The low proportion of participants with current acne and the fact that the study population has healthier dietary habits than the French general population might have led us to underestimate the level of the associations.

Another limitation was the relatively high proportion (33%) of participants having self-diagnosed current acne; this subjective report may have introduced classification bias. None-theless, the fact that only the presence of acne was evaluated (ie, not the severity) minimized the risk of incorrect self-diagnosis.

The association between diet and current acne was consistent after adjustment for known and potential confounding factors, which thus minimized confounding bias. The sensitivity analysis of the subgroup of women enabled us to take hormone-related factors into account. The fact that the study

variables were collected, analyzed, and validated in the same way in each of the 3 acne groups is likely to have minimized any differential classification bias. Our database did not include information on polycystic ovary syndrome-a condition known to induce acne in women.<sup>65</sup> However, other hormonal factors (eg, age at menarche, pregnancy, and menopause) were taken into account and did not appear to change the results of the main analysis. Thus, temporality in the association found cannot be discussed. Rather, we can only note a possible association with current acne-not with the appearance or development of current acne (adult acne). In that context, we chose an adjusted multinomial regression design rather than a propensity score design. Our findings for participants in the past acne group must be interpreted with caution since these individuals may have changed their dietary habits since the time when they had acne. In addition, our study's crosssectional, observational design is not able to determine direct, causal associations between diet and the presence of acne in adulthood.

## Conclusions

The consumption of fatty and sugary products, sugary beverages, and milk appears to be associated with current acne. Our results may support the hypothesis that the Western diet (rich in animal products and fatty and sugary foods) is associated with the presence of acne in adulthood. Our findings provide data on the prevalence of adult acne; however, further largescale studies are needed to investigate more closely the association between diet and acne that might be of value in the prevention and management of acne.

#### ARTICLE INFORMATION

Accepted for Publication: April 18, 2020. Published Online: June 10, 2020. doi:10.1001/jamadermatol.2020.1602

Author Affiliations: Paris 13 University, Institut National de la Santé et de la Recherche Médicale. Institut National de la Recherche Agronomique, Conservatoire National Des Arts et Métiers, Nutritional Epidemiology Research Team, Epidemiology and Statistics Research Centre, University of Paris, F-93022 Bobigny, France (Penso, Touvier, Szabo de edelenyi, Hercberg); Epidemiology in Dermatology and Evaluation of Therapeutics, EA7379, Paris-Est University, Paris Est Créteil University, Département Infectieux/ Immuno/Vaccin, F-94000 Créteil, France (Deschasaux, Ezzedine, Sbidian); Department of Dermatology, Mondor Hospital (Assistance Publique, Hôpitaux de Paris), Paris Est Créteil University, F-94000 Créteil, France (Ezzedine, Sbidian); Clinical Investigation Center 1430. Institut National de la Santé et de la Recherche Médicale, F-94000 Créteil, France (Sbidian).

Author Contributions: Ms Penso had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Touvier, Ezzedine, Sbidian.

Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Penso, Sbidian. Critical revision of the manuscript for important intellectual content: Touvier, Deschasaux, Szabo de edelenyi, Hercberg, Ezzedine, Sbidian. Statistical analysis: Penso. Obtained funding: Touvier. Administrative, technical, or material support: Szabo de edelenyi, Hercberg. Supervision: Touvier, Hercberg, Ezzedine, Sbidian. **Conflict of Interest Disclosures:** None reported. **Additional Contributions:** Technical contributions to the NutriNet-Santé study were provided by

Younes Esseddik, MSc, Thi Hong Van Duong, MSc, Régis Gatibelza, MSc, Jagatjit Mohinder, MSc, and Aladi Timera, MSc (computer scientists); Cédric Agaesse, MSc (dietitian); Fabien Szabo de Edelenyi, PhD, Nathalie Arnault, MSc, Julien Allegre, MSc, and Laurent Bourhis, MSc (data manager/statisticians); Fatoumata Diallo, MD, and Roland Andrianasolo, MD; and Nathalie Druesne-Pecollo, MSc (operational coordinator). We thank all of the volunteers in the NutriNet-Santé cohort for their participation. David Fraser reviewed the manuscript.

#### REFERENCES

1. Degitz K, Placzek M, Borelli C, Plewig G. Pathophysiology of acne. *J Dtsch Dermatol Ges*.

2007;5(4):316-323. doi:10.1111/j.1610-0387.2007. 06274.x

2. Gollnick HP, Zouboulis CC. Not all acne is acne vulgaris. *Dtsch Arztebl Int*. 2014;111(17):301-312.

**3**. Hay RJ, Johns NE, Williams HC, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *J Invest Dermatol.* 2014;134(6):1527-1534. doi:10.1038/jid. 2013.446

4. Rademaker M, Garioch JJ, Simpson NB. Acne in schoolchildren: no longer a concern for dermatologists. *BMJ*. 1989;298(6682):1217-1219. doi:10.1136/bmj.298.6682.1217

 Kilkenny M, Merlin K, Plunkett A, Marks R. The prevalence of common skin conditions in Australian school students: 3; acne vulgaris. Br J Dermatol. 1998;139(5):840-845. doi:10.1046/j.1365-2133.1998.02510.x

**6**. Perkins AC, Cheng CE, Hillebrand GG, Miyamoto K, Kimball AB. Comparison of the epidemiology of acne vulgaris among Caucasian, Asian, Continental Indian and African American women. *J Eur Acad Dermatol Venereol*. 2011;25(9):1054-1060. doi:10. 1111/j.1468-3083.2010.03919.x

7. Cunliffe WJ, Gould DJ. Prevalence of facial acne vulgaris in late adolescence and in adults. *BMJ*. 1979;1(6171):1109-1110. doi:10.1136/bmj.1.6171.1109

jamadermatology.com

8. Goulden V, Stables GI, Cunliffe WJ. Prevalence of facial acne in adults. *J Am Acad Dermatol*. 1999;41 (4):577-580.

9. Collier CN, Harper JC, Cafardi JA, et al. The prevalence of acne in adults 20 years and older [published correction appears in J Am Acad Dermatol. 2008 May;58(5):874. Cafardi, Jennifer A [added]]. *J Am Acad Dermatol*. 2008;58 (1):56-59. doi:10.1016/j.jaad.2007.06.045

**10**. Semedo D, Ladeiro F, Ruivo M, et al. Adult acne: prevalence and portrayal in primary healthcare patients, in the Greater Porto Area, Portugal. *Acta Med Port*. 2016;29(9):507-513. doi:10.20344/amp. 6626

**11**. Tan JK. Psychosocial impact of acne vulgaris: evaluating the evidence. *Skin Therapy Lett*. 2004;9(7):1-3, 9.

12. Hull PR, D'Arcy C. Acne, depression, and suicide. Dermatol Clin. 2005;23(4):665-674. doi:10.1016/j. det.2005.05.008

**13.** Mallon E, Newton JN, Klassen A, Stewart-Brown SL, Ryan TJ, Finlay AY. The quality of life in acne: a comparison with general medical conditions using generic questionnaires. *Br J Dermatol.* 1999;140(4):672-676. doi:10.1046/j.1365-2133.1999.02768.x

**14**. Di Landro A, Cazzaniga S, Parazzini F, et al; GISED Acne Study Group. Family history, body mass index, selected dietary factors, menstrual history, and risk of moderate to severe acne in adolescents and young adults. *J Am Acad Dermatol*. 2012;67(6): 1129-1135. doi:10.1016/j.jaad.2012.02.018

**15.** Navarini AA, Simpson MA, Weale M, et al; Acne Genetic Study Group. Genome-wide association study identifies three novel susceptibility loci for severe acne vulgaris. *Nat Commun.* 2014;5:4020. doi:10.1038/ncomms5020

**16**. Lefebvre MA, Pham DM, Boussouira B, Bernard D, Camus C, Nguyen QL. Evaluation of the impact of urban pollution on the quality of skin: a multicentre study in Mexico. *Int J Cosmet Sci.* 2015;37(3):329-338. doi:10.1111/ics.12203

 Wolkenstein P, Misery L, Amici JM, et al. Smoking and dietary factors associated with moderate-to-severe acne in French adolescents and young adults: results of a survey using a representative sample. *Dermatology*. 2015;230(1): 34-39. doi:10.1159/000366195

**18**. Krutmann J, Moyal D, Liu W, et al. Pollution and acne: is there a link? *Clin Cosmet Investig Dermatol*. 2017;10:199-204. doi:10.2147/CCID.S131323

**19**. Stewart TJ, Bazergy C. Hormonal and dietary factors in acne vulgaris versus controls. *Dermatoendocrinol*. 2018;10(1):e1442160. doi:10. 1080/19381980.2018.1442160

20. Tan JKL, Vasey K, Fung KY. Beliefs and perceptions of patients with acne. J Am Acad Dermatol. 2001;44(3):439-445. doi:10.1067/mjd. 2001.111340

**21**. El-Akawi Z, Abdel-Latif Nemr N, Abdul-Razzak K, Al-Aboosi M. Factors believed by Jordanian acne patients to affect their acne condition. *East Mediterr Health J*. 2006;12(6): 840-846.

22. Smith RN, Mann NJ, Braue A, Mäkeläinen H, Varigos GA. A low-glycemic-load diet improves symptoms in acne vulgaris patients: a randomized controlled trial. *Am J Clin Nutr*. 2007;86(1):107-115. doi:10.1093/ajcn/86.1.107 23. Ismail NH, Manaf ZA, Azizan NZ. High glycemic load diet, milk and ice cream consumption are related to acne vulgaris in Malaysian young adults: a case control study. *BMC Dermatol*. 2012;12:13. doi:10.1186/1471-5945-12-13

24. Adebamowo CA, Spiegelman D, Danby FW, Frazier AL, Willett WC, Holmes MD. High school dietary dairy intake and teenage acne. *J Am Acad Dermatol*. 2005;52(2):207-214. doi:10.1016/j.jaad. 2004.08.007

**25**. Adebamowo CA, Spiegelman D, Berkey CS, et al. Milk consumption and acne in adolescent girls. *Dermatol Online J*. 2006;12(4):1.

**26**. Adebamowo CA, Spiegelman D, Berkey CS, et al. Milk consumption and acne in teenaged boys. *J Am Acad Dermatol*. 2008;58(5):787-793. doi:10. 1016/j.jaad.2007.08.049

27. Juhl CR, Bergholdt HKM, Miller IM, Jemec GBE, Kanters JK, Ellervik C. Dairy intake and acne vulgaris: a systematic review and meta-analysis of 78,529 children, adolescents, and young adults. *Nutrients*. 2018;10(8):E1049. doi:10.3390/ nu10081049

28. Juhl CR, Bergholdt HKM, Miller IM, Jemec GBE, Kanters JK, Ellervik C. Lactase persistence, milk intake, and adult acne: a mendelian randomization study of 20,416 Danish adults. *Nutrients*. 2018;10 (8):1041. doi:10.3390/nu10081041

**29**. Tasli L, Turgut S, Kacar N, et al. Insulin-like growth factor-I gene polymorphism in acne vulgaris. *J Eur Acad Dermatol Venereol*. 2013;27(2): 254-257. doi:10.1111/j.1468-3083.2011.04299.x

**30**. Mirdamadi Y, Thielitz A, Wiede A, et al. Insulin and insulin-like growth factor-1 can modulate the phosphoinositide-3-kinase/Akt/FoxO1 pathway in SZ95 sebocytes in vitro. *Mol Cell Endocrinol*. 2015; 415:32-44. doi:10.1016/j.mce.2015.08.001

**31**. Çerman AA, Aktaş E, Altunay İK, Arıcı JE, Tulunay A, Ozturk FY. Dietary glycemic factors, insulin resistance, and adiponectin levels in acne vulgaris. *J Am Acad Dermatol*. 2016;75(1):155-162. doi:10.1016/j.jaad.2016.02.1220

**32**. Rahaman SMA, De D, Handa S, et al. Association of insulin-like growth factor (IGF)-1 gene polymorphisms with plasma levels of IGF-1 and acne severity. *J Am Acad Dermatol*. 2016;75(4): 768-773. doi:10.1016/j.jaad.2016.05.019

**33.** Jung JY, Kwon HH, Hong JS, et al. Effect of dietary supplementation with omega-3 fatty acid and gamma-linolenic acid on acne vulgaris: a randomised, double-blind, controlled trial. *Acta Derm Venereol.* 2014;94(5):521-525. doi:10.2340/00015555-1802

**34**. Burris J, Rietkerk W, Woolf K. Relationships of self-reported dietary factors and perceived acne severity in a cohort of New York young adults. *J Acad Nutr Diet.* 2014;114(3):384-392. doi:10.1016/j.jand.2013.11.010

**35**. Ulvestad M, Bjertness E, Dalgard F, Halvorsen JA. Acne and dairy products in adolescence: results from a Norwegian longitudinal study. *J Eur Acad Dermatol Venereol*. 2017;31(3):530-535. doi:10.1111/ jdv.13835

**36**. LaRosa CL, Quach KA, Koons K, et al. Consumption of dairy in teenagers with and without acne. *J Am Acad Dermatol*. 2016;75(2):318-322. doi:10.1016/j.jaad.2016.04.030

**37**. Hercberg S, Castetbon K, Czernichow S, et al. The Nutrinet-Santé Study: a web-based prospective

study on the relationship between nutrition and health and determinants of dietary patterns and nutritional status. *BMC Public Health*. 2010;10:242. doi:10.1186/1471-2458-10-242

**38**. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194. doi:10. 1001/jama.2013.281053

**39**. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370(9596):1453-1457. doi:10.1016/S0140-6736 (07)61602-X

**40**. Touvier M, Kesse-Guyot E, Méjean C, et al. Comparison between an interactive web-based self-administered 24 h dietary record and an interview by a dietitian for large-scale epidemiological studies. *Br J Nutr.* 2011;105(7): 1055-1064. doi:10.1017/S0007114510004617

**41**. Lassale C, Castetbon K, Laporte F, et al. Validation of a Web-based, self-administered, non-consecutive-day dietary record tool against urinary biomarkers. *Br J Nutr*. 2015;113(6):953-962. doi:10.1017/S0007114515000057

**42**. Lassale C, Castetbon K, Laporte F, et al. Correlations between fruit, vegetables, fish, vitamins, and fatty acids estimated by web-based nonconsecutived dietary records and respective biomarkers of nutritional status. *J Acad Nutr Diet*. 2016;116(3):427-438.e5. doi:10.1016/j.jand.2015. 09.017

**43.** Le Moullec N, Deheeger M, Preziosi P, et al. Validation du manuel-photos utilisé pour l'enquête alimentaire de l'étude SU.VI.MAX. Validation of the photography manual of servings used in dietary collection in the SU.VI.MAX study. *Cah Nutr Diét*. 1996;31:158-164.

**44**. Vergnaud A-C, Touvier M, Méjean C, et al. Agreement between web-based and paper versions of a socio-demographic questionnaire in the NutriNet-Santé study. *Int J Public Health*. 2011;56 (4):407-417. doi:10.1007/s00038-011-0257-5

**45**. Touvier M, Méjean C, Kesse-Guyot E, et al. Comparison between web-based and paper versions of a self-administered anthropometric questionnaire. *Eur J Epidemiol*. 2010;25(5):287-296. doi:10.1007/s10654-010-9433-9

**46**. Lassale C, Péneau S, Touvier M, et al. Validity of web-based self-reported weight and height: results of the Nutrinet-Santé study. *J Med Internet Res.* 2013;15(8):e152. doi:10.2196/jmir.2575

**47**. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-1395. doi:10.1249/01.MSS. 0000078924.61453.FB

**48**. Spencer EH, Ferdowsian HR, Barnard ND. Diet and acne: a review of the evidence. *Int J Dermatol*. 2009;48(4):339-347. doi:10.1111/j.1365-4632.2009. 04002.x

**49**. Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J. Acne vulgaris: a disease of Western civilization. *Arch Dermatol*. 2002;138(12): 1584-1590. doi:10.1001/archderm.138.12.1584

**50**. Millward DJ, Layman DK, Tomé D, Schaafsma G. Protein quality assessment: impact of expanding

understanding of protein and amino acid needs for optimal health. *Am J Clin Nutr*. 2008;87(5):15765-1581S. doi:10.1093/ajcn/87.5.1576S

**51**. Nicklin P, Bergman P, Zhang B, et al. Bidirectional transport of amino acids regulates mTOR and autophagy. *Cell*. 2009;136(3):521-534. doi:10.1016/j.cell.2008.11.044

**52**. Zhenyukh O, Civantos E, Ruiz-Ortega M, et al. High concentration of branched-chain amino acids promotes oxidative stress, inflammation and migration of human peripheral blood mononuclear cells via mTORC1 activation. *Free Radic Biol Med*. 2017;104:165-177. doi:10.1016/j.freeradbiomed.2017. 01.009

**53.** Aizawa H, Niimura M. Elevated serum insulin-like growth factor-1 (IGF-1) levels in women with postadolescent acne. *J Dermatol.* 1995;22(4): 249-252. doi:10.1111/j.1346-8138.1995.tb03381.x

**54**. Francis GL, Upton FM, Ballard FJ, McNeil KA, Wallace JC. Insulin-like growth factors 1 and 2 in bovine colostrum: sequences and biological activities compared with those of a potent truncated form. *Biochem J*. 1988;251(1):95-103. doi:10.1042/bj2510095

**55**. Melnik B. Milk consumption: aggravating factor of acne and promoter of chronic diseases of Western societies. *J Dtsch Dermatol Ges*. 2009;7 (4):364-370. doi:10.1111/j.1610-0387.2009.07019.x

**56**. Costa A, Lage D, Moisés TA. Acne and diet: truth or myth? *An Bras Dermatol*. 2010;85(3):346-353. doi:10.1590/S0365-05962010000300008

**57**. Melnik BC. Evidence for acne-promoting effects of milk and other insulinotropic dairy products. In: Clemens RA, Hernell O, Michaelsen KF, eds. *Nestlé Nutrition Institute Workshop Series: Pediatric Program*. Vol 67. Karger; 2011:131-145. doi:10.1159/000325580

**58**. Ben-Amitai D, Laron Z. Effect of insulin-like growth factor-1 deficiency or administration on the occurrence of acne. *J Eur Acad Dermatol Venereol*. 2011;25(8):950-954. doi:10.1111/j.1468-3083.2010. 03896.x

**59**. Guevara-Aguirre J, Balasubramanian P, Guevara-Aguirre M, et al. Growth hormone receptor deficiency is associated with a major reduction in pro-aging signaling, cancer, and diabetes in humans. *Sci Transl Med.* 2011;3(70):70ra13. doi:10. 1126/scitranslmed.3001845

**60**. Berra B, Rizzo AM. Glycemic index, glycemic load: new evidence for a link with acne. *J Am Coll Nutr.* 2009;28(suppl):4505-4545. doi:10.1080/ 07315724.2009.10718111

**61**. Aghasi M, Golzarand M, Shab-Bidar S, Aminianfar A, Omidian M, Taheri F. Dairy intake

and acne development: a meta-analysis of observational studies. *Clin Nutr*. 2019;38(3):1067-1075. doi:10.1016/j.clnu.2018.04.015

**62**. Fassier P, Zelek L, Lécuyer L, et al. Modifications in dietary and alcohol intakes between before and after cancer diagnosis: results from the prospective population-based NutriNet-Santé cohort. *Int J Cancer*. 2017;141(3): 457-470. doi:10.1002/ijc.30704

**63.** Andreeva VA, Deschamps V, Salanave B, et al. Comparison of dietary intakes between a large online cohort study (Etude NutriNet-Santé) and a nationally representative cross-sectional study (Etude Nationale Nutrition Santé) in France: addressing the issue of generalizability in E-epidemiology. *Am J Epidemiol.* 2016;184(9):660-669. doi:10.1093/aje/kww016

**64**. Méjean C, Si Hassen W, Gojard S, et al. Social disparities in food preparation behaviours: a DEDIPAC study. *Nutr J*. 2017;16(1):62. doi:10.1186/ s12937-017-0281-2

**65**. Rosenfield RL. What every physician should know about polycystic ovary syndrome. *Dermatol Ther.* 2008;21(5):354-361. doi:10.1111/j.1529-8019. 2008.00217.x