

Supplementary Online Content

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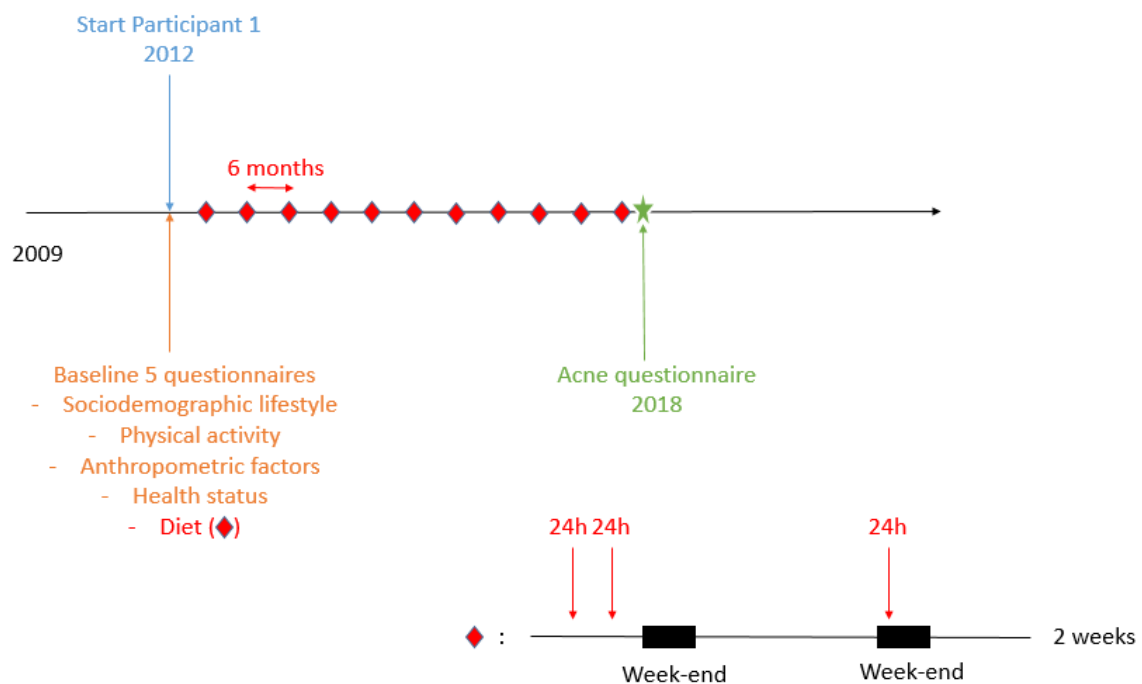
eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Methods Details

The Nutri-Net-Santé study is an ongoing, observational, web-based cohort, which aims to study the associations between nutrition and health. The cohort was launched in May 2009 by means of vast multimedia campaigns and recruited adults among the general population. Due to its design, participants are eligible if they have access to the internet where they can complete online self-questionnaires using a dedicated secure website (<https://www.etude-nutrinet-sante.fr/>). At baseline participants were asked to complete a set of 5 questionnaires regarding their diet, sociodemographic lifestyle (eg, sex, date of birth, educational level, smoking status), physical activity (7-day International Physical Activity Questionnaire [IPAQ]), anthropometric factors (eg, height, weight) and their health status. Inclusion in the cohort was completed at the end of the completion of this set of questionnaires. The same set of questionnaires was completed each year thereafter. In addition, participants were invited to fill each month complementary optional questionnaires related to determinants of dietary behavior and nutritional and health status. Finally, at inclusion and twice a year thereafter, participants were also invited to complete three nonconsecutive 24-h dietary records, which were randomly assigned over a 2-week period (two weekdays and one week-end day). Follow-up is insured by the online platform connected to their email address where they receive information about the study and questionnaire recalls. More details of the Nutri-Net-Santé study's rationale, design, and procedures have been previously published^{1, 2-4}

eFigure. Nutri-Net-Santé Design



To illustrate how the variables were collected, we will take the example of Participant 1 which started the Nutri-Net-Santé e-cohort in 2012. At baseline Participant 1 had to complete a set of 5 questionnaires about his/her diet, sociodemographic lifestyle (eg, sex, date of birth, educational level, smoking status), physical activity (7-day International Physical Activity Questionnaire [IPAQ]), anthropometric factors (eg, height, weight) and his/her health status. Therefore, all these questionnaires have been completed in 2012, at the index date. The package of dietary records was proposed every 6 months, and was composed by three 24-hour dietary records randomly assigned over a two-week period (two weekdays and 1 weekend day). Since the acne questionnaire was administrated in 2018, Participant 1 had at least 12 (depending on the month he started) dietary record completed between his first-inclusion and the acne questionnaire. To be included in our cross-sectional study, Participant had to complete the acne questionnaire and had at least 3 pack of dietary records available before the acne questionnaire to have a minimum time of exposure of 1 year. The food/nutrient exposure was collected for each participant as the mean daily intake for each food and each nutrient. The mean daily energy intake was calculated and the number of dietary records was collected for adjustment.

eTable 1. Optional acne questionnaire sent to the NutriNet cohort in November 2018

Questions	Response options
Do you (or did you) current acne?	Yes/No
Your acne was diagnosed by:	A dermatologist / Your general practitioner / Another physician or surgeon / Another healthcare professional (pharmacist, nurse, physiotherapist, midwife, naturopath, homeopathic practitioner, etc.) / Yourself (self-diagnosis) / Don't know
When did your acne appeared for the first time (approximately)?	Before the age of 10 / Between 10 and 15 / 16 or 17 / After 18 years old / Don't know
Did you consult for your acne?	Your general practitioner / A dermatologist in a consulting firm or in a private clinic / A health professional (pharmacist, nurse, physiotherapist, midwife, naturopath, homeopathic practitioner...) / Don't know
Have you been hospitalised for your acne?	Yes / No / Don't know
If so, how long after the appearance of acne were you hospitalized?	1 year later / 2 years later /3 years later / 4 years later / Don't know

What types of treatment (if any) did you receive? (tick all that apply):	A cream or balm / tablets / injections / phototherapy (UV therapy administered by a physician) / Acupuncture, homeopathy, mesotherapy or another type of alternative medicine / Don't know
Is your acne present at the moment?	Yes / No / Don't know
If it is no longer present, how old were you when your acne disappeared (approximately)?	Between 10 and 15 / 16 or 17 / 18 or over / Don't know
At the moment, how would you rate the severity of your acne?	Not at all severe / Mild / Moderate / Severe / Don't know
What impact does acne have on your daily life today	No impact / Slight impact / Moderate impact / Major or very major impact / Don't know
Do you think that your diet has or had an impact on your acne?	Yes / No / Don't know

eTable 2. Acne status of the study population

	Participants with past or current acne n=11,324 (46%)		Missing data	
	N	%	N	%
Diagnosed by a dermatologist	4,200	37	284	3
Diagnosed by a physician other than a dermatologist	1,830	16		
Diagnosed by another healthcare professional	79	1		
Self-diagnosis	4,931	44		
Age at onset			254	2
Before 10	90	1		
Between 10 and 15	7,087	63		
16 or 17	3,109	27		
18 or over	784	7		
Previous hospitalization for acne	18	0	20	0
Treatments with creams or balms	9,822	87	3800	34
Systemic treatments	3,491	31	3800	34

Other treatments: alternative medicine	606	5	3800	34
Acne present when the questionnaire was filled out	1762	16	130	1
Diet considered to have an impact on acne	3576	32	4195	37
Age at resolution (in the “past acne” group, n=9562)			465	5
Between 10 and 15	256	3		
16 or 17	2310	24		
18 or over	6531	68		
<i>Abbreviations: N = number of participants; % = percentage</i>				

eTable 3. Univariate analyses of dietary patterns from a PCA analysis of the study population, using a multinomial logistic regression

	Univariate analyses (vs. never acne)							
	n=13,128 (54%)							
	Past acne n=9,562 (39%)				Current acne n=1,762 (7%)			
	OR	95CI%		p-value	OR	95CI%		p-value
Factor 1: "Healthy"	0.86	0.83	0.88	<10⁻⁴	0.55	0.52	0.57	<10⁻⁴
Factor 2: "Fatty & sweet"	1.14	1.11	1.17	<10⁻⁴	1.25	1.20	1.30	<10⁻⁴
Factor 3: "Animal products and refined cereals "	0.98	0.95	1.01	0.125	0.92	0.88	0.97	0.002

OR: odds ratio; CI: confidence interval.

Statistically significant p-values (<0.05 in a chi-squared test) are given in bold type.

eTable 4. Multivariate analyses of food exposure in the subgroup of women, using a multinomial logistic regression								
	Multivariate analyses (vs. never acne) n=6,998 (52%)							
	Past acne n=5,435 (40%)				Current acne n=1,105 (8%)			
	OR	95CI%		p-value	OR	95CI%		p-value
Meat (portions/day)	0.88	0.74	1.05	0.161	0.71	0.51	0.99	0.042
Fish (portions/day)	1.05	0.87	1.26	0.642	1.09	0.75	1.59	0.666
Vegetables (portions/day)	1.03	0.98	1.08	0.313	0.92	0.83	1.01	0.078
Fruit (portions/day)	0.98	0.95	1.02	0.389	0.99	0.92	1.06	0.685
Milk (glasses/day)	1.02	0.95	1.10	0.551	1.16	1.02	1.31	0.028
Sweet beverages (glasses/day)	0.87	0.74	1.02	0.077	1.12	0.91	1.38	0.284
Dark chocolate (chunks/day)	1.02	0.97	1.07	0.427	1.06	0.97	1.17	0.204
Milk chocolate (chunks/day)	1.02	0.94	1.10	0.697	1.02	0.90	1.16	0.761
Snacks and fast foods (portions/day)	1.13	0.96	1.32	0.136	1.28	1.00	1.65	0.048
Fatty and sugary products (portions/day)	1.20	0.92	1.57	0.176	1.51	0.98	2.33	0.060
Refined cereals (portions/day)	1.07	0.99	1.15	0.071	1.08	0.94	1.24	0.280

Details:

One portion of meat, fish, fruit, vegetables, snacks & fast foods, fatty & sugary products, and refined cereals: 100 grams.

One glass of milk or sugary beverage: 200 millilitres.

One chunk of chocolate: 7 grams.

One slice of deli meat: 40 grams.

P-values were obtained 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, *BMI, medical history of cancer, diabetes or cardiovascular disease, age at menarche, pregnancy, menopause* and depressive symptoms).

Statistically significant p-values (<0.05) are given in bold type. OR: odds ratio; CI: confidence interval

eTable 5. Observational and interventional studies of the association between diet and acne since 2005									
<u>References</u>	<u>Year</u>	<u>Country</u>	<u>Study design</u>	<u>Population</u>	<u>Total N</u>	<u>Study length</u>	<u>Acne assessment</u>	<u>Exposition</u>	<u>Association found</u>
<u>Adebamowo et al.⁵</u>	<u>2005</u>	<u>USA</u>	<u>Cross-sectional</u>	<u>Female from "Nurses Health II" about their teenage years</u>	<u>45,355</u>	<u>NA</u>	<u>Physician</u>	<u>Dairy products</u>	<u>±</u>
<u>Adebamowo et al.⁶</u>	<u>2006</u>	<u>USA</u>	<u>Cohort</u>	<u>Female (9-15 yo)</u>	<u>6,094</u>	<u>∅</u>	<u>Self-reported</u>	<u>Dairy products</u>	<u>±</u>
<u>Kaymak et al.⁷</u>	<u>2007</u>	<u>Turkey</u>	<u>Case-control</u>	<u>Male, female (19 - 34 yo)</u>	<u>91 (49 cases)</u>	<u>NA</u>	<u>Clinical exam</u>	<u>Glycemic charge</u>	<u>=</u>
<u>Smith et al.⁸</u>	<u>2007</u>	<u>Australia</u>	<u>Interventional (randomised)</u>	<u>Male (15 - 25 yo)</u>	<u>54 (27 exposed)</u>	<u>12 weeks</u>	<u>Dermatologist</u>	<u>Low glycemic load diet</u>	<u>=</u>
<u>Adebamowo et al.⁹</u>	<u>2008</u>	<u>USA</u>	<u>Cohort</u>	<u>Male (9-15 yo)</u>	<u>4,273</u>	<u>∅</u>	<u>Self-reported</u>	<u>Dairy products</u>	<u>±</u>
<u>Ghodsi et al.¹⁰</u>	<u>2009</u>	<u>Iran</u>	<u>Cross-sectional</u>	<u>Male, female (12 - 20 yo)</u>	<u>1,002 (933 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Sweets</u> <u>Nuts</u> <u>Chocolate</u> <u>Oily food</u> <u>Spicy food</u>	<u>±</u> <u>±</u> <u>±</u> <u>±</u> <u>0</u>
<u>Kim et al.¹¹</u>	<u>2010</u>	<u>Korea</u>	<u>Interventional</u>	<u>Male, female (18 - 30 yo)</u>	<u>36 (18 exposed)</u>	<u>12 weeks</u>	<u>Dermatologist</u>	<u>Lactoferrin-enriched</u>	<u>=</u>

			(randomised)					fermented milk	
<u>Reynolds et al.</u> ¹²	<u>20</u> <u>10</u>	<u>Australia</u>	<u>Interventional</u>	<u>Male (mean age ± SD, 17 ± 1 yo)</u>	<u>43 (23 low GI; 20 high GI)</u>	<u>8 weeks</u>	<u>Dermatologist</u>	<u>Low glycemic index diet vs. High glycemic index diet</u>	<u>0</u>
<u>Aksu et al.</u> ¹³	<u>20</u> <u>11</u>	<u>Turkey</u>	<u>Cross-sectional</u>	<u>Male, female (13 - 18 yo)</u>	<u>2,300 (1,353 cases)</u>	<u>NA</u>	<u>Self-reported</u>	<u>Unhealthy fruits and vegetables intake</u> <u>Unhealthy sugar intake</u> <u>Unhealthy fat intake</u> <u>Frequent sausages, burgers intake</u> <u>Frequent pastries, cakes intake</u>	<u>0</u> <u>±</u> <u>±</u> <u>±</u> <u>±</u>
<u>Block et al.</u> ¹⁴	<u>20</u> <u>11</u>	<u>USA</u>	<u>Interventional</u>	<u>Male (18 - 35 yo)</u>	<u>10</u>	<u>7 days</u>	<u>Ø</u>	<u>Chocolate</u>	<u>±</u>

<u>Di Landro et al.</u> ¹⁵	<u>20</u> <u>12</u>	<u>Italy</u>	<u>Case-control</u>	<u>Male, female (10 - 24 yo)</u>	<u>563 (205 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Milk</u> <u>Cheese/Yogurt</u> <u>Bread/Pasta</u> <u>Cakes/Sweets</u> <u>Chocolate</u> <u>Fruits/Vegetables</u> <u>Fish</u> <u>Red meat</u> <u>Ham/Salami</u>	<u>+</u> <u>0</u> <u>0</u> <u>0</u> <u>0</u> <u>=</u> <u>0</u> <u>0</u>
<u>Ismail et al.</u> ¹⁶	<u>20</u> <u>12</u>	<u>Malaysia</u>	<u>Case-control</u>	<u>Male, female (18 - 30 yo)</u>	<u>88 (44 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Glycemic load</u> <u>Milk</u>	<u>+</u> <u>+</u>
<u>Kwon et al.</u> ¹⁷	<u>20</u> <u>12</u>	<u>Korea</u>	<u>Interventional (randomised)</u>	<u>Male, female (20 - 27 yo)</u>	<u>32 (17 exposed)</u>	<u>10 weeks</u>	<u>Dermatologist</u>	<u>Low glycemic load diet</u>	<u>=</u>
<u>Salomone et al.</u> ¹⁸	<u>20</u> <u>12</u>	<u>India</u>	<u>Case-control</u>	<u>Male, female (13 - 25 yo)</u>	<u>80 (40 cases)</u>	<u>NA</u>	<u>Ø</u>	<u>Ice cream ingestion</u> <u>Juices with sugar</u> <u>Carbonated drinks</u> <u>Milk</u> <u>Bread</u> <u>White rice</u> <u>Lower consumption</u>	<u>+</u> <u>+</u> <u>0</u> <u>+</u> <u>+</u> <u>0</u> <u>0</u> <u>=</u>

								<u>of fruits</u> <u>Lower</u> <u>consumption</u> <u>of vegetables</u>	
<u>Wolkenstein et al.</u> ¹⁹	<u>20</u> <u>14</u>	<u>France</u>	<u>Cross-sectional</u>	<u>Male, Female (15 - 24 yo)</u>	<u>2,266 (1,375 cases)</u>	<u>NA</u>	<u>Self-reported</u>	<u>Alcohol</u> <u>Sugary fizzy drink</u> <u>Fast food</u> <u>Dairy product</u> <u>Sweets and chocolate</u>	<u>0</u> <u>0</u> <u>0</u> <u>+</u> <u>-</u>
<u>Caperton et al.</u> ²⁰	<u>20</u> <u>14</u>	<u>USA</u>	<u>Interventional (randomised)</u>	<u>Male (18 - 35 yo)</u>	<u>13</u>	<u>7 days</u>	<u>Ø</u>	<u>Chocolate</u>	<u>+</u>
<u>Cao et al.</u> ²¹	<u>20</u> <u>15</u>	<u>Many</u>	<u>Meta-analysis</u>	<u>2 articles (15 - 27 yo)</u>	<u>75 (44 exposed)</u>	<u>12 weeks</u>	<u>Dermatologist</u>	<u>Low glycemic load diet</u>	<u>=</u>
<u>El Darouti et al.</u> ²²	<u>20</u> <u>15</u>	<u>Egypt</u>	<u>Case-control</u>	<u>Male, female (14 - 36 yo)</u>	<u>400 (200 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Salty food</u> <u>Spicy food</u>	<u>+</u> <u>0</u>
<u>Vongraviopap et al.</u> ²³	<u>20</u> <u>15</u>	<u>Thailand</u>	<u>Interventional</u>	<u>Male, (18 - 25 yo)</u>	<u>25</u>	<u>4 weeks</u>	<u>Dermatologist</u>	<u>Chocolate</u>	<u>+</u>

<u>Okoro et al.</u> ²⁴	<u>20</u> <u>16</u>	<u>Nigeria</u>	<u>Cross-sectional</u>	<u>Male, female</u> <u>(mean age ± SD,</u> <u>13 ± 4 yo)</u>	<u>464 (299 cases)</u>	<u>NA</u>	<u>Self-reported</u>	<u>Milk</u> <u>Banana</u> <u>Fried beef</u> <u>Corn</u> <u>Cakes</u> <u>Glycemic index</u> <u>Fried food</u> <u>Fatty food</u> <u>Snacks</u> <u>Fruits</u>	<u>+</u> <u>+</u> <u>+</u> <u>+</u> <u>+</u> <u>0</u> <u>0</u> <u>0</u> <u>0</u> <u>0</u>
<u>Di Landro et al.</u> ²⁵	<u>20</u> <u>16</u>	<u>Italy</u>	<u>Case-control</u>	<u>Female, (25+ yo)</u>	<u>518 (248 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Milk</u> <u>Dairy products</u> <u>Starchy foods</u> <u>Cakes and sweets</u> <u>Chocolate</u> <u>Vegetables and fruits</u> <u>Fish</u> <u>Beef</u>	<u>0</u> <u>0</u> <u>0</u> <u>0</u> <u>=</u> <u>=</u> <u>0</u>
<u>Larosa et al.</u> ²⁶	<u>20</u> <u>16</u>	<u>USA</u>	<u>Case-control</u>	<u>Male, female (14 - 19 yo)</u>	<u>225 (120 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Dairy products</u>	<u>+</u>
<u>Delost et al.</u> ²⁷	<u>20</u> <u>16</u>	<u>USA</u>	<u>Interventional (randomised)</u>	<u>Male, female (17 - 25 yo)</u>	<u>54 (26 exposed, 28 after swap)</u>	<u>∅</u>	<u>Dermatologist</u>	<u>Chocolate bar vs. Jelly beans</u>	<u>+</u>

<u>Ulvestad et al.</u> ²⁸	<u>20</u> <u>16</u>	<u>Norway</u>	<u>Cohort</u>	<u>Male, female (15 - 16, 18 - 19 yo)</u>	<u>2489</u>	<u>Ø</u>	<u>Self-reported</u>	<u>Dairy products</u>	<u>±</u>
<u>Grossi et al.</u> ²⁹	<u>20</u> <u>16</u>	<u>Italy</u>	<u>Semantic connectivity map approach</u>	<u>Male, female (10 - 24 yo)</u>	<u>563 (205 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Milk</u> <u>Cheese</u> <u>Sweets/cakes</u> <u>Chocolate</u>	<u>±</u>
<u>Cerman et al.</u> ³⁰	<u>20</u> <u>16</u>	<u>Turkey</u>	<u>Cross-sectional</u>	<u>Male, female (mean age ± SD, 19 ± 3 yo)</u>	<u>86 (50 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Dietary glycemic load</u> <u>Milk</u> <u>Glucose</u>	<u>±</u> <u>0</u> <u>0</u>
<u>Burris et al.</u> ³¹	<u>20</u> <u>17</u>	<u>USA</u>	<u>Cross-sectional</u>	<u>Male, female (18 - 40 yo)</u>	<u>64 (32 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Glycemic load / glycemic index</u>	<u>+/0</u>
<u>Aghasi et al.</u> ³²	<u>20</u> <u>18</u>	<u>Many</u>	<u>Meta-analysis</u>	<u>14 articles (9 - 30 yo)</u>	<u>Ø</u>	<u>Ø</u>	<u>Ø</u>	<u>Dairy products</u>	<u>±</u>
<u>Burris et al.</u> ³³	<u>20</u> <u>18</u>	<u>USA</u>	<u>Interventional (randomized)</u>	<u>Male, female (18 - 40 yo)</u>	<u>66 (34 exposed)</u>	<u>2 weeks</u>	<u>Dermatologist</u>	<u>Low glycemic load and glycemic index diet</u>	<u>=</u>
<u>Juhl et al.</u> ³⁴	<u>20</u> <u>18</u>	<u>Many</u>	<u>Meta-analysis</u>	<u>14 articles (7 - 30 yo)</u>	<u>78,529 (23,046 cases)</u>	<u>Ø</u>	<u>Ø</u>	<u>Dairy products</u>	<u>±</u>
<u>Juhl et al.</u> ³⁵	<u>20</u> <u>18</u>	<u>Danemark</u>	<u>Case-control</u>	<u>Male, female from GESUS (20 - 96 yo)</u>	<u>20,416 (303 cases)</u>	<u>NA</u>	<u>Self-reported</u>	<u>Dairy products</u>	<u>0</u>

<u>Suppiah et al.</u> ³⁶	<u>20</u> <u>18</u>	<u>Malays</u> <u>ia</u>	<u>Case-</u> <u>control</u>	<u>Male, Female</u> <u>(14+ yo)</u>	<u>114 (57 cases)</u>	<u>NA</u>	<u>Clinician</u>	<u>Chocolate</u> <u>Sweets</u> <u>Potato chips</u> <u>Nuts</u> <u>Yogurt</u> <u>Ice cream</u> <u>Carbonated</u> <u>drink</u> <u>Milk</u>	<u>+</u> <u>0</u> <u>0</u> <u>0</u> <u>0</u> <u>0</u> <u>0</u> <u>+</u>
<u>Stewart et al.</u> ³⁷	<u>20</u> <u>18</u>	<u>Austral</u> <u>ia</u>	<u>Case-</u> <u>control</u>	<u>Male, Female</u> <u>(16+ yo)</u>	<u>703 (453 cases)</u>	<u>NA</u>	<u>Clinician</u>	<u>Vegan diet</u> <u>Vitamin D</u> <u>deficiency</u>	<u>0</u> <u>+</u>
<u>Wolkenstein et al.</u> ³⁸	<u>20</u> <u>18</u>	<u>Many</u>	<u>Cross-</u> <u>sectional</u>	<u>Male, Female (15</u> <u>- 24 yo)</u>	<u>10,521 (6,063</u> <u>cases)</u>	<u>NA</u>	<u>Self-</u> <u>reported</u>	<u>Milk</u> <u>Dairy</u> <u>products</u> <u>Fruit juice</u> <u>Sweetened</u> <u>sodas</u> <u>Chocolate</u> <u>Sweets</u> <u>Ice</u> <u>cream/sorbet</u> <u>Pasta/Rice/Se</u> <u>molina</u>	<u>+</u> <u>+</u> <u>0</u> <u>0</u> <u>+</u> <u>+</u> <u>0</u> <u>+</u> <u>+</u> <u>0</u> <u>+</u>

<u>Huang et al.</u> ³⁹	<u>20</u> <u>19</u>	<u>China</u>	<u>Cross-sectional</u>	<u>Male, Female</u> <u>(mean age ± SD,</u> <u>18 ± 1 yo)</u>	<u>8,197 (833 cases)</u>	<u>NA</u>	<u>Dermatologist</u>	<u>Daily water intake except drinks</u> <u>Carbonated soda</u> <u>Sweetened tea drinks</u> <u>Fruit-flavored drinks</u> <u>Alcohol drinking</u>	<u>0</u> <u>+</u> <u>+</u> <u>+</u> <u>0</u>
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*Abbreviations; yo: years old; -: negative association; +: positive association; 0: no association; Ø lack of data; NA: not appropriate
Bibliographic research done between January 2019 – February 2019 for the periode 2005 – February 2019, using the following words combination: acne AND (diet OR nutrition OR dietary) ; acne AND chocolate; acne and (dairy OR milk), in Pubmed.*

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