Are Dietary Indices Associated with Polycystic Ovary Syndrome and Its Phenotypes? A Preliminary Study

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Abstract: Polycystic ovary syndrome (PCOS) is a complex hormonal disorder which impairs ovarian function. The adherence to healthy dietary patterns and physical exercise are the first line of recommended treatment for PCOS patients, but it is yet unclear what type of diet is more adequate. In this case-control study, we explored associations between adherence to five dietary quality indices and the presence of PCOS. We enrolled 126 cases of PCOS and 159 controls living in Murcia (Spain). Diagnostic of PCOS and its phenotypes were established following the Rotterdam criteria (hyperandrogenism (H), oligoanovulation (O), polycystic ovaries morphology (POM)). We used a validated food frequency questionnaires to calculate the scores of five dietary indices: alternate Healthy Eating Index (AHEI), AHEI-2010, relative Mediterranean Dietary Score (rMED), alternate Mediterranean Diet Score (aMED) and Dietary Approaches to Stop Hypertension (DASH). We used multivariable logistic regression to estimate adjusted odds ratios and confidence intervals. In the multivariable analysis, AHEI-2010 index was inversely associated with Hyperandrogenism + Oligoanovulation (ORQ3 vs. Q1 = 0.1; 95% CI: [0.0; 0.9]; P for trend = 0.02). We did not find any statistical significant association between dietary indices and total anovulatory or ovulatory PCOS. However, further studies with higher sample sizes exploring these associations among the diverse phenotypes of PCOS are highly warranted.

Keywords: polycystic ovary syndrome (PCOS); PCOS phenotypes; Rotterdam criteria; hyperandrogenism; Mediterranean diet score (MDS); alternate healthy index (AHEI); alternate healthy index 2010 (AHEI-2010) and DASH index

1. Introduction

Polycystic ovary syndrome (PCOS) is a complex hormonal disorder which impairs ovarian function [1]. It could be considered a polygenic, polyfactorial, systemic and inflammatory disease [2]. Its reported overall prevalence according to the Rotterdam criteria is about 10% (95% CI: 8–13%) (Skiba et al., 2018). The impact of PCOS is considerable...
because it is linked to higher risk of obesity [3–6], insulin resistance and diabetes [7–9],
higher cardiovascular risk profile [10–12], poor thyroid function [13,14], infertility [15,16],
gestational diabetes [17–20], sleep disturbances [21] and even mental health problems [22].

Lifestyle modifications for PCOS, especially physical activity and diet, are of major
importance in the clinical management of women to improve most of the adverse outcomes
related to this condition. Diet is focused on weight loss in overweight PCOS women, the
subgroup with higher risk of metabolic deregulation and type 2 diabetes. However, it is
unclear what type of diet is better for this: hypocaloric or low in carbohydrates.

On the one hand, some case-control studies have shown that PCOS women consumed
higher quantity of monounsaturated fatty acids, and ω-3 polyunsaturated fatty acid and
simple carbohydrate (Barrea et al., 2019). Moreover, they presented higher fiber intake,
high glycemic index and glycemic load than controls [23,24]. All these key aspects are
considered in different dietary indices such as the alternate Mediterranean Diet Score
(aMED), relative Mediterranean Diet Score (rMED), Alternate Healthy Index (AHEI) and
Dietary Approaches to Stop Hypertension (DASH).

On the other hand, most interventional studies have employed low carbohydrates
and high protein diets for improving different PCOS manifestations [25–30]. A recent meta-
analysis of eight randomized controlled trials concluded that a low carbohydrate diet had
a stronger effect on increasing FSH level, rising SHBG levels and decreasing testosterone
levels comparing with a higher carbohydrate diet (diet composition carbohydrates: 40% vs. 50%) [25].
However long-term adherence may be difficult. Moreover, an unanswered
question is to what extent improvements will be maintained in association with a transition
to a less carbohydrate-restricted diet. Indeed, low carbohydrate diet interventions do not
often compare with other frequent healthy dietary patterns such as the Mediterranean
or DASH diet as the control group. In this way, DASH interventions for PCOS women
have had beneficial effects on body mass index (BMI), androstenedione, sex hormone-
binding globulin (SHBG), insulin metabolism, cardiovascular risk factors and oxidative
stress [31–34].

Because of that, our aim was to evaluate if there are differences in dietary indices in
women diagnosed with PCOS and its phenotypes compared to controls. To our knowledge,
this is the first study evaluating associations between Mediterranean Diet indices (aMED
and rMED) and different phenotypes of PCOS. Additionally, AHEI, Alternate Healthy
Index 2010 (AHEI-2010) and DASH were also assessed. This approach would allow us to
know if diet patterns may be related to PCOS, and not only specific macro or micronutrients.
Besides, we would be able to report more easily nutritional recommendations potentially
adapted to PCOS women.

2. Materials and Methods

This was a case-control study taken place in Southeast of Spain (Murcia Region) from
September 2014 to May 2016. All participants were between 18 and 40 years old (n = 300).
Exclusion criteria were pregnancy or lactating, oncological treatment, hormonal medication
during the three months prior to the study, genitourinary prolapse or endocrine disorders
(n = 5). Methods were explained in previous works [35–38]. Figure 1 shows the number of
participants and the exclusion criteria. Concisely, we finally enrolled, voluntarily, 126 cases
of PCOS and 159 women from the Department of Obstetrics and Gynecology, outpatient
clinics at the Virgen de la Arrixaca University Clinical Hospital. We excluded, because of
the objective of this paper, five subjects who did not complete the questionnaire about food
intake and four with an implausible total kcal per day. Thus, the analysed sample size were
276, being 121 PCOS cases and 155 control. In a second phase, we carried out sensitivity
tests excluding women:

- taking medication that interferes carbohydrate metabolism, not excluded previously
  (cases = 100; controls = 134)
- taking multivitamins 10–12 months (cases = 98; controls = 131)
- taking multivitamins 4–6 months or 10–12 months (cases = 90; controls = 123)
Energy-adjusted intakes were computed using the residual method [57]. After dietary assessment, we excluded five subjects who did not complete the FFQ and four did not have a plausible energy intake (≤ 500 or ≥ 4500 kcal) as shown in Figure 1. The study sample for statistical analyses was 276 women, being 121 cases and 155 controls.

2.2. Statistical Analyses

Data were checked for normal distributions using the Kolmogorov-Smirnov test. Continuous data with skewed distribution were described with median and interquartile ranges (IQR: 25th–75th) and comparisons were performed by the Kruskal-Wallis tests. We used the Chi-squared test for categorical variables and they were represented by frequency and percentage. The five dietary indices were recategorized in quartiles, the lowest quartile being the reference group.

We considered several variables as potential confounders and covariates (e.g., energy intake, nutrients intakes, physical activity, anthropometrics variables, age, gynaecological history). When inclusion of a potential covariate resulted in a change of the p-value corresponding to the dietary index variable less than 0.10, this covariate was kept in the final models. Hence, the covariates contained in the final models were total energy intake (kcal/day), body mass index (BMI) (Kg/m²), moderate-vigorous exercise (h/week), adjusted caffeine intake (mg/day) and adjusted carbohydrates intake (g/day). We used logistic regression to analyse the association between dietary indices (quartiles) and presence of PCOS, as well as PCOS phenotypes.

Additionally, we carried out a sensitivity analysis for evaluating if there was influence of medication interfering in the carbohydrate metabolism in our results. Concretely, we excluded from the analyses fifteen women taking corticosteroids (prednisone, betamethasone and gentamicin, deflazacort, budesonide, methylprednisolone), fourteen women taking hormonal contraceptives (drospirenone-estriadiol, emergency contraception, medroxyprogesterone) and eight women taking thyroid hormones (8).

Figure 1. Flow chart of inclusion and exclusion criteria of polycystic ovary syndrome (PCOS) case-control study of southeast of Spain from 2014 to 2016.

Diagnostic of PCOS were established following the Rotterdam criteria resulting from the consensus of European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine [39]. Thus, PCOS was diagnosed with two or more of the following criteria:

1. oligovulation/amenorrhea or anovulation (menstrual cycles > 35 days or amenorrhea > 3 months).
2. biochemical hyperandrogenism (total testosterone level ≥ 2.6 nmol or clinical (Ferriman-Galwey score ≥ 12) [40].
3. polycystic ovaries morphology (POM) using transvaginal ultrasound (TVUS) (≥12 follicles measuring 2–9 mm in diameter, mean of both ovaries) [41].

Moreover, the following phenotypes of PCOS were also assessed [42]:

- hyperandrogenism + oligo/amenorrhea + POM (H + O + POM) (n = 52).
- hyperandrogenism + oligo/amenorrhea (H + O) (n = 18).
- hyperandrogenism + POM (H + POM) (n = 33).
- oligo/amenorrhea + POM (O + POM) (n = 18).

Also, H + O + POM, H + O and O + POM phenotypes were reclassified, as anovulatory phenotype " (n = 88) and H + POM type as ovulatory phenotype (n = 33) and evaluated separately in the current study.

Controls were women without PCOS (or other major gynaecological conditions) attending the gynecological outpatient clinic for routine gynecological examinations. The same methods were performed in both cases and controls: anamnesis and questionnaires, physical examination, transvaginal ultrasound and blood draw, between days 2–5 of the menstrual cycle. Written informed consent was obtained from all women. This study was approved by the Ethics Research Committee of the University of Murcia and the Clinical University Hospital Virgen de la Arrixaca (no. 770/2013, approved 3 October 2013).
2.1. Dietary Assessment and Dietary Indices

We used a validated 117-food item semiquantitative food frequency questionnaire (FFQ) to assess the regular food intake which was previously validated for the Spanish population [43,44]. This questionnaire is based on a FFQ used by Willett and collaborators in the Nurse Health Study Cohort [45]. Subjects had to choose one of the nine options about how often, on average, they had consumed each food item (from never or less than once a month, to six or more times a day). Nutrient values for each food were obtained from the United States Department of Agriculture and supplemented with Spanish sources [46,47].

The FFQ dietary information was used to calculate the following five a priori-defined dietary indices:
1. AHEI
2. AHEI-2010
3. rMED
4. aMED
5. DASH.

All these represent healthy dietary patterns but use different range of scores, variations in food components and calculations. They are described in detail in a previous publication [48]. AHEI, AHEI-2010 and DASH were created in the United States to define a prudent dietary pattern high in vegetables, fruit, whole grains, legumes and lower in saturated fats and alcohol [49–51]. The AHEI was developed by Teresa Fung and coworkers to quantify adherence to the US federal dietary guidance of 1992, with a higher score reflecting better quality and adherence. The scores range from 0 to 87.5. The score evaluates nine components such as trans fats, protein sources, polyunsaturated/monounsaturated ratio and cereal fiber. Table 1 describes the dietary indices in detail. AHEI-2010 is the AHEI’s version for evaluating chronic diseases. AHEI and AHEI-2010 establish specific reference values of servings per day or grams per day for each food component and sum 10 if the subject reaches this amount. AHEI-2010 was designed in 2012 by Chiuve and colleagues based on updated literature to study the relation between food intake and chronic diseases. The AHEI-2010 scores 11 components for a total of 110 points, including whole grains intake (specific for women), legumes and nuts, red/processed meat ratio, sugar-sweetened beverages and fruit juices, sodium and polyunsaturated fats [52]. The overall scoring range is 0 to 80 for AHEI and 0 to 110 for AHEI-2010. However, DASH, rMED and aMED establish the scoring criteria using quintiles, terciles and the median intake of the study sample, respectively. DASH was developed for controlling blood pressure [53] but, nowadays, is useful for obesity, diabetes, metabolic syndrome and cardiovascular disease. The DASH dietary pattern is rich in fruit, vegetables and low-fat dairy products. rMED and aMED indices define the Mediterranean Diet and are versions of the original Mediterranean Diet score [54,55]. aMED considers red and processed meat and establishes the ratio of mono/polyunsaturated fats [49], while rMED evaluates dairy products, only uses olive oil as the primary fat source, evaluates in one item all types of meat and is more specific for the Spanish population [56]. The total score is 9 and 18, respectively. In all of these indices, higher intakes of healthy food items such as fruits, vegetables, whole grains, nuts and legumes add higher scores, whereas higher intake of trans fats, meat, saturated fats, sodium and alcohol are associated with lower scores.
| Category of Scoring Dietary Indices | AHEI^1 | AHEI-2010 | aMED | rMED | DASH |
|-----------------------------------|--------|-----------|------|------|------|
| | Min (0) | Max (10) | Min (0) | Max (10) | Min (0) | Max (1) | Min (0) | Max (2) | Min (0) | Max (5) |
| Vegetables | 0 | 5 servings/day | 0 | ≥5 servings/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Fruit | 0 | 4 servings/day | 0 | >4 servings/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Nuts | 0 | 1 servings/day | 0 | ≥1 servings/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Nuts and legumes | 0 | ≥1 servings/day | 0 | ≥1 servings/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Legumes | 0 | <median servings/day | ≥median servings/day | | | | | | | |
| Cereals | 0 | 15 g/day | 0 | 75 g/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Cereal fiber | 0 | 15 g/day | 0 | 75 g/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Whole grains | 0 | 15 g/day | 0 | 75 g/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Cereals | 0 | 15 g/day | 0 | 75 g/day | <median servings/day | >median servings/day | Lowest tertile | Greatest tertile | Lowest quintile | Greatest quintile |
| Meat | 0 | 4 | | | | | | | | |
| Ratio of white to red meat | 0 | 4 | | | | | | | | |
| Red and processed meat | | | ≥1.5 | 0 servings/day | >median servings/day | <median servings/day | Greatest tertile | Lowest tertile | | |
| Meat | | | | | | | | | | |
| Fats | | | | | | | | | | |
| Trans fat | ≥4 | ≤0.5% of energy | ≥4 | ≤0.5% of energy | | | | | | |
| Ratio of saturated to polyunsaturated | ≥4 | ≥1 | ≥4 | ≤0.5% of energy | | | | | | |
| Ratio of monounsaturated to saturated | | | | | | | | | | |
| Polyunsaturated | | | | | | | | | | |
| ω-3 fats (EPA + DHA)^4 | 0 | 250 mg/day | | | | | | | | |
| Olive oil | | | | | | | | | | |
| Fish | | | | | | | | | | |
| Dairy products | | | | | | | | | | |

Table 1. Description in detail of dietary indices.
Table 1. Cont.

| Category of Scoring Dietary Indices | AHEI<sup>1</sup> | AHEI-2010 | aMED | rMED | DASH  |
|-------------------------------------|-----------------|-----------|------|------|-------|
|                                     | Min<sup>2</sup> | Max<sup>3</sup> | Min | Max | Min | Max | Min | Max | Min | Max |
| Low-fat dairy                       |                 |            |      |      |      |      |      |      |      |      |
| Sodium                              |                 |            |      |      |      |      |      |      |      |      |
| Alcohol                             | 0 or >2.5 servings/day | 0.5–1.5 servings/day | 0.5–1.5 drinks/day | <5 or <25 d/day | 5–25 d/day |      |      |      |      |      |
| Sugar-sweetened beverages and fruit juices | ≥1              | 0         |      |      |      |      |      |      |      |      |
| Total maximum score                 | 87.5            | 110       | 9    | 18   | 40   |      |      |      |      |      |

<sup>1</sup> AHEI-2010, Alternate Healthy Index 2010; AHEI, Alternate Healthy Index; aMED, Alternate Mediterranean Diet Score; rMED, Relative Mediterranean Diet Score; DASH, Dietary Approaches to Stop Hypertension.  
<sup>2</sup> Criteria for minimum score.  
<sup>3</sup> Criteria for maximum score.  
<sup>4</sup> EPA, Eicosapentaenoic acid; DHA, Docosahexaenoic acid.
Energy-adjusted intakes were computed using the residual method [57]. After dietary assessment, we excluded five subjects who did not complete the FFQ and four did not have a plausible energy intake (≤500 or ≥4500 kcal) as shown in Figure 1. The study sample for statistical analyses was 276 women, being 121 cases and 155 controls.

2.2. Statistical Analyses

Data were checked for normal distributions using the Kolmogorov-Smirnov test. Continuous data with skewed distribution were described with median and interquartile ranges (IQR: 25th–75th) and comparisons were performed by the Kruskal-Wallis tests. We used the Chi-squared test for categorical variables and they were represented by frequency and percentage. The five dietary indices were recategorized in quartiles, the lowest quartile being the reference group.

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Additionally, we carried out a sensitivity analysis for evaluating if there was influence of medication interfering in the carbohydrate metabolism in our results. Concretely, we excluded from the analyses fifteen women taking corticosteroids (prednisone, betamethasone and gentamicin, deflazacort, budesonide, methylprednisolone), fourteen women taking hormonal contraceptives (emergency contraception, ethinyl drospirenone-estradiol, medroxyprogesterone acetate) and eight women taking thyroid hormones (n = 32). The final sample size was 232 subjects, 104 PCOS cases and 131 controls. In another sensitivity analysis we excluded women taking multivitamins and other s such us minerals, brewer’s yeast and probiotics. The prevalence was 9% (n = 21; total = 234) if we considered the use of vitamins during 4–6 months or 10–12 months in the previous year to the subject’s recruitment, and 2.1% (n = 5; total = 234) if we only considered use of vitamins during 10–12 months.

p-values ≤ 0.05 were considered statistically significant. All statistical analyses were performed in IBM SPSS 25.0 (IBM Corporation, Armonk, NY, USA).

3. Results

The average age was 29.1 (SD: 5.7) years. Table 2 shows demographic characteristics, metabolic parameters, hormonals determinations and nutrient intake across quartiles of adherence to healthful dietary scores for the study sample. AHEI, AHEI-2010, aMED indices presented a similar pattern. Women with higher adherence to any of these dietary scores had a higher age, physical activity and caffeine, carbohydrates and ω-3 fatty acids intake, but lower BMI. There was an increase of total energy intake across quartiles for AHEI, aMED and DASH scores, a decrease for rMED and no differences for AHEI-2010. In addition, greater adherence to any of these scores was associated with less intake of saturated fatty acids, except for the DASH score. Differences between median value scores across quartiles of rMED scores were different compared to the other dietary indices. Lastly, women with greatest adherences to rMED presented lower total energy and ω-3 fatty acids intake and were less physically active (Table 2). Differences in demographic characteristics, metabolic parameters and hormonal determinations among PCOS cases and controls have been published in a previous work [35].

In the multivariable analysis, we did not find any associations between the diet scores and total PCOS, neither in ovulatory nor anovulatory PCOS (Table 3). In the analyses by PCOS phenotypes, women with higher adherences to the AHEI-2010 pattern were less
likely to present PCOS, specifically “H + O” phenotype ($p$-value for trend $= 0.02$) (Table 4). This association was mainly driven by vegetables food items of the AHEI-2010 index, being marginally significant ($p$-value for trend $= 0.081$). In contrast, we observed an inverse lineal trend between DASH index and “O + POM” phenotype ($p$-value for trend $= 0.05$).

Results from the four sensitivity analyses showed similar findings to those already presented, not changing the observed results.
Table 2. Demographic characteristics and nutrient intake according to quintiles of adherence to dietary quality indices ($n = 275$).

| Median Value | AHEI | AHEI-2010 | αMED | rMED | DASH |
|--------------|------|-----------|------|------|------|
|              | Q1   | Q4        | Q1   | Q4   | Q1   | Q4   | Q1   | Q4   |
|              | (13–32) | (48–78) | (27–56) | (72–97) | (0–3) | (7–10) | (2–9) | (13–15) | (28–35) | (p-value) |
| Age (years)  |       |          |       |      |      |       |       |      |       | 1       |
| (23.0; 31.0) | (26.0; 32.0) | (23.5; 32.0) | (23.0; 29.0) | (0.00) | (23.0; 26.0) | (0.00) | (23.0; 34.0) | (26.0; 30.0) | (26.0; 31.0) | 0.01 |
| BMI (kg/m²)  |       |          |       |      |      |       |       |      |       | 2       |
| (21.4; 25.2) | (20.7; 23.2) | (21.5; 23.9) | (20.1; 20.5) | (0.00) | (20.1; 21.7) | (0.00) | (20.1; 27.5) | (21.7; 27.7) | (21.7; 24.0) | 0.00 |
| Calories     |       |          |       |      |      |       |       |      |       | 3       |
| intake (Kcal)|       |          |       |      |      |       |       |      |       | 0.01    |
| (1320.6; 1972.7) | (1723.1; 2847.6) | (1448.5; 2310.5) | (1420.7; 2358.6) | (0.00) | (1178.5; 1937.7) | (0.00) | (1605.1; 2384.6) | (1288.2; 1832.3) | (1086.8; 1576.0) | 0.00 |
| Physical     |       |          |       |      |      |       |       |      |       | 4       |
| activity     |       |          |       |      |      |       |       |      |       | 0.01    |
| (1.5; 2.2)   | (1.9; 5.5) | (14.2; 14.3) | (2.9; 14.3) | (0.00) | (2.0; 14.0) | (0.00) | (2.3; 13.7) | (2.0; 8.5) | (5.5; 13.8) | 0.00 |
| Alcohol      |       |          |       |      |      |       |       |      |       | 5       |
| (0.0; 0.5)   | (1.0; 1.5) | (1.1; 1.5) | (1.0; 1.4) | (0.00) | (1.1; 1.5) | (0.00) | (1.3; 1.4) | (0.0; 1.7) | (0.0; 1.7) | 0.00 |
| Carbohydrate |       |          |       |      |      |       |       |      |       | 6       |
| (13.5; 55.2) | (18.5; 33.4) | (18.5; 55.2) | (24.4; 55.2) | (0.02) | (22.4; 55.2) | (0.04) | (20.7; 68.4) | (20.4; 99.0) | (20.4; 99.0) | 0.05 |
| Saturated    |       |          |       |      |      |       |       |      |       | 7       |
| fats (g/day) |       |          |       |      |      |       |       |      |       | 0.01    |
| (13.7; 190.5) | (170.5; 190.5) | (197.3; 190.5) | (197.3; 190.5) | (0.00) | (197.3; 190.5) | (0.00) | (197.3; 190.5) | (167.2; 193.5) | (197.3; 193.5) | 0.00 |
| Omega-3      |       |          |       |      |      |       |       |      |       | 8       |
| (mg/day)     |       |          |       |      |      |       |       |      |       | 0.01    |
| (1.7; 1.7)   | (1.5; 5.2) | (1.5; 5.2) | (1.5; 1.4) | (0.00) | (1.5; 5.2) | (0.00) | (1.5; 1.4) | (1.5; 1.4) | (1.5; 1.4) | 0.00 |

1. Kruskal-Wallis tests were used to test for associations between the level of diet indexes.
Table 3. Multivariate adjusted 1 Odds Ratios (ORs) between dietary indices and total, anovulatory and ovulatory PCOS (total n = 276; cases = 121, controls n = 155).

| Range for Each Quartile of Index 2 | Cases = 121 | Anovulatory Cases = 88 | Ovulatory Cases = 33 |
|----------------------------------|------------|------------------------|-----------------------|
|                                  | OR 1       | 95% CI                 | p-Value               | OR 1       | 95% CI                 | p-Value               | OR 1       | 95% CI                 | p-Value               |
| AHEI2010                         |            |                        |                       |            |                        |                       |            |                        |                       |
| Q1 (27–56)                       | Ref.       | (0.5; 2.0)             | 0.93                  | Ref.       | (0.5; 2.3)             | 0.81                  | Ref.       | (0.3; 2.3)             | 0.69                  |
| Q2 (57–63)                       | 1.0        | (0.3; 1.2)             | 0.14                  | 1.1        | (0.2; 1.1)             | 0.09                  | 0.8        | (0.4; 2.9)             | 0.89                  |
| Q3 (64–71)                       | 0.6        | (0.3; 1.6)             | 0.44                  | 0.9        | (0.4; 2.0)             | 0.79                  | 0.7        | (0.2; 2.1)             | 0.50                  |
| Q4 (72–97)                       | 0.7        |                        |                       |            |                        |                       |            |                        |                       |
|                                  |            | 0.41                   |                        |            | 0.24                   |                        |            | 0.84                   |                       |
| p-value for trend                |            |                        |                       |            |                        |                       |            |                       |                       |
| AHEI                             |            |                        |                       |            |                        |                       |            |                       |                       |
| Q1 (13–32)                       | Ref.       | (0.8; 3.5)             | 0.22                  | Ref.       | (0.8; 3.9)             | 0.17                  | Ref.       | (0.4; 2.8)             | 1.00                  |
| Q2 (33–40)                       | 1.6        | (0.5; 2.3)             | 0.94                  | 1.8        | (0.5; 2.8)             | 0.66                  | 1.0        | (0.2; 2.4)             | 0.65                  |
| Q3 (41–47)                       | 1.0        | (0.5; 2.3)             | 1.2                   | (0.5; 2.8) | 0.66                  |                        | 0.8        | (0.2; 2.4)             | 0.65                  |
| Q4 (48–78)                       | 0.8        | (0.3; 2.0)             | 0.65                  | 1.0        | (0.4; 2.6)             | 0.97                  | 0.7        | (0.2; 2.2)             | 0.50                  |
| p-value for trend                |            | 0.31                   |                        | 0.41                   |                        |                       | 0.86                   |                       |
| aMED                             |            |                        |                       |            |                        |                       |            |                       |                       |
| Q1 (0–3)                         | Ref.       | (0.3; 1.2)             | 0.16                  | Ref.       | (0.4; 1.7)             | 0.58                  | Ref.       | (0.2; 1.5)             | 0.23                  |
| Q2 (4)                           | 0.6        | (0.4; 2.0)             | 0.86                  | 1.2        | (0.5; 2.6)             | 0.70                  | 0.7        | (0.2; 2.0)             | 0.50                  |
| Q3 (5–6)                         | 0.9        | (0.4; 2.0)             | 0.86                  | 1.2        | (0.5; 2.6)             | 0.70                  | 0.7        | (0.2; 2.0)             | 0.50                  |
| Q4 (7–10)                        | 0.8        | (0.4; 2.0)             | 0.68                  | 0.8        | (0.3; 2.1)             | 0.71                  | 1.0        | (0.3; 3.3)             | 0.97                  |
| p-value for trend                |            | 0.48                   |                        | 0.75                   |                        |                       | 0.55                   |                       |
| rMED                             |            |                        |                       |            |                        |                       |            |                       |                       |
| Q1 (2–9)                         | Ref.       | (0.4; 2.0)             | 0.62                  | Ref.       | (0.5; 2.5)             | 0.82                  | Ref.       | (0.2; 2.3)             | 0.59                  |
| Q2 (10)                          | 0.9        | (0.3; 1.3)             | 0.39                  | 0.9        | (0.4; 2.0)             | 0.74                  | 0.3        | (0.1; 1.5)             | 0.15                  |
| Q3 (11–12)                       | 0.6        | (0.7; 3.9)             | 0.31                  | 1.6        | (0.6; 4.1)             | 0.33                  | 1.1        | (0.3; 3.8)             | 0.85                  |
| Q4 (13–15)                       | 1.6        |                        |                       | 1.6        | (0.9; 3.3)             | 0.33                  | 1.1        | (0.3; 3.8)             | 0.85                  |
| p-value for trend                |            | 0.53                   |                        | 0.73                   |                        |                       | 0.48                   |                       |
| DASH                             |            |                        |                       |            |                        |                       |            |                       |                       |
| Q1 (11–19)                       | Ref.       | (0.4; 1.7)             | 0.58                  | Ref.       | (0.5; 2.3)             | 0.98                  | Ref.       | (0.2; 1.9)             | 0.44                  |
| Q2 (20–23)                       | 0.8        | (0.5; 2.5)             | 0.84                  | 0.9        | (0.4; 2.3)             | 0.90                  | 1.3        | (0.4, 3.9)             | 0.66                  |
| Q3 (24–27)                       | 1.1        | (0.5; 4.7)             | 0.39                  | 2.9        | (0.9; 9.3)             | 0.07                  | 0.4        | (0.1, 2.0)             | 0.26                  |
| Q4 (28–35)                       | 0.4        | (0.5; 4.7)             | 0.39                  | 0.9        | (0.9; 9.3)             | 0.07                  | 0.4        | (0.1, 2.0)             | 0.26                  |
| p-value for trend                |            | 0.59                   |                        | 0.26                   |                        |                       | 0.26                   |                       |

1,2 Adjusted for calories intake (kcal/day), BMI, moderate-vigorous physical activity (h/week), caffeine intake (mg/day) and carbohydrates intake (g/day). AHEI-2010, Alternate Healthy Index 2010; AHEI, Alternate Healthy Index; aMED, Alternate Mediterranean Diet Score; rMED, Relative Mediterranean Diet Score; DASH, Dietary Approaches to Stop Hypertension.
Table 4. Multivariate adjusted 1 ORs between dietary indices and phenotypes 3–5 of PCOS (n = 276).

| Index | H + O + POM $^2$ Cases = 52 | H + O $^3$ Cases = 18 | H + POM $^4$ Cases = 33 | O + POM $^5$ Cases = 18 |
|-------|-----------------------------|-----------------------|------------------------|------------------------|
|       | OR $^1$ 95%CI p-Value OR 95%CI p-Value OR 95%CI p-Value OR 95%CI p-Value | | |
| AHEI-2010 | | | | |
| Q1 (27-56) | Ref. | Ref. | Ref. | Ref. |
| Q2 (57-63) | 1.5 (0.7; 3.5) 0.34 | 0.2 (0.0; 0.7) 0.01 | 0.8 (0.3; 2.3) 0.69 | 4.9 (0.9; 25.6) 0.06 |
| Q3 (64-71) | 0.7 (0.3; 1.8) 0.43 | 0.1 (0.0; 0.9) 0.04 | 1.1 (0.4; 2.9) 0.89 | 2.5 (0.4; 16.7) 0.25 |
| Q4 (72-97) | 1.1 (0.4; 2.9) 0.85 | 0.2 (0.0; 1.2) 0.08 | 1.1 (0.3; 2.1) 0.50 | 4.9 (1.8; 30.4) 0.09 |
| p-value $^*$ | 0.42 | 0.02 | 0.84 |
| AHEI | | | | |
| Q1 (13-32) | Ref. | Ref. | Ref. | Ref. |
| Q2 (33-40) | 2.3 (0.9; 6.3) 0.09 | 0.4 (0.1; 1.5) 0.17 | 1.0 (0.4; 2.8) 1.00 | 2.9 (0.7; 12.9) 0.15 |
| Q3 (41-47) | 2.7 (1.0; 7.3) 0.06 | 0.0 (0.0; $\infty$) 0.00 | 0.8 (0.2; 2.4) 0.65 | 1.8 (0.4; 8.8) 0.48 |
| Q4 (48-78) | 1.7 (0.5; 5.5) 0.38 | 0.3 (0.0; 1.6) 0.15 | 0.7 (0.2; 2.2) 0.50 | 1.5 (0.2; 9.5) 0.69 |
| p-value $^*$ | 0.21 | 0.41 | 0.86 |
| aMED | | | | |
| Q1 (0-3) | Ref. | Ref. | Ref. | Ref. |
| Q2 (4) | 1.5 (0.6; 3.7) 0.38 | 0.2 (0.0; 0.9) 0.04 | 0.5 (0.2; 1.5) 0.23 | 1.1 (0.2; 5.8) 0.90 |
| Q3 (5-6) | 1.4 (0.6; 3.7) 0.46 | 0.3 (0.1; 1.4) 0.13 | 0.7 (0.2; 2.1) 0.50 | 3.6 (0.8; 16.8) 0.11 |
| Q4 (7-10) | 1.1 (0.4; 3.5) 0.96 | 0.2 (0.0; 1.0) 0.15 | 0.7 (0.2; 3.3) 0.97 | 3.2 (0.5; 18.7) 0.20 |
| p-value $^*$ | 0.78 | 0.12 | 0.55 |
| rMED | | | | |
| Q1 (2-9) | Ref. | Ref. | Ref. | Ref. |
| Q2 (10) | 1.1 (0.4; 2.9) 0.86 | 0.7 (0.1; 6.3) 0.77 | 0.7 (0.2; 2.3) 0.59 | 1.4 (0.4; 5.6) 0.63 |
| Q3 (11-12) | 0.8 (0.3; 2.1) 0.60 | 1.5 (0.4; 5.6) 0.57 | 0.3 (0.1; 1.5) 0.15 | 0.5 (0.1; 2.4) 0.35 |
| Q4 (13-15) | 1.9 (0.6; 5.4) 0.25 | 1.6 (0.3; 9.1) 0.88 | 1.4 (0.3; 3.8) 0.85 | 0.6 (0.1; 4.9) 0.60 |
| p-value $^*$ | 0.78 | 0.12 | 0.48 |
| Index | H + O + POM $^2$ Cases = 52 | H + O $^3$ Cases = 18 | H + POM $^4$ Cases = 33 | O + POM $^5$ Cases = 18 |
|-------|-----------------------------|-----------------------|------------------------|------------------------|
| DASH | OR 95%CI p-Value OR 95%CI p-Value OR 95%CI p-Value OR 95%CI p-Value | | |
| Q1 (11-19) | Ref. | Ref. | Ref. | Ref. |
| Q2 (20-23) | 1.0 (0.4; 2.6) 0.96 | 1.1 (0.3; 4.3) 0.84 | 0.6 (0.2; 1.9) 0.44 | 0.8 (0.1; 5.1) 0.79 |
| Q3 (24-27) | 0.8 (0.2; 2.4) 0.64 | 0.3 (0.1; 2.3) 0.27 | 1.3 (0.4; 3.9) 0.66 | 4.6 (0.9; 24.4) 0.08 |
| Q4 (28-35) | 3.2 (0.9; 11.9) 0.08 | 0.0 (0.0; $\infty$) 0.00 | 1.4 (0.2; 2.0) 0.26 | 9.2 (1.1; 74.7) 0.04 |
| p-value $^*$ | 0.07 | 0.05 |

$^1$ Adjusted for calories intake (kcal/day), BMI, moderate-vigorous physical activity (h/week), caffeine intake (mg/day) and carbohydrates intake (g/day). AHEI-2010, Alternate Healthy Index 2010; AHEI, Alternate Healthy Index; aMED, Alternate Mediterranean Diet Score; rMED, Relative Mediterranean Diet Score; DASH, Dietary Approaches to Stop Hypertension.

$^2$ H + O + POM “Hyperandrogenism + Oligo/amenorrhea + Polycystic ovaries morphology” phenotype.

$^3$ H + O “Hyperandrogenism + Oligo/amenorrhea” phenotype.

$^4$ H + POM “Hyperandrogenism + Polycystic Ovary Morphology” phenotype.

$^5$ O + POM “Oligo/amenorrhea + Polycystic Ovary Morphology” phenotype.
4. Discussion

We found no clear associations between dietary indices and the presence of PCOS or its phenotypes. Only suggestive associations between some a priori-defined dietary indices (AHEI-2010 and DASH) and some PCOS phenotypes (H + O and O + POM, respectively) were observed.

In detail, women with higher adherences to the AHEI-2010 score were less likely to present H + O PCOS phenotype. At this point in time, there are only two studies evaluating the association between AHEI and PCOS. In the first study, no differences were detected in diet quality (using the Alternate Healthy Index-2015) or dietary intake between PCOS women and controls in a sample of women from New York (USA) [58]. However, in the second study, the Brazilian Healthy Eating Index was negatively correlated with BMI and waist circumference among PCOS patients [59].

We found that the Mediterranean diet was a protective factor only for the H + O phenotype. However, we must be cautious with this result since we did not consider subgrouping by PCOS phenotypes for the calculation of the study sample size. Thus, it is important to bear in mind this potential underpower. Nonetheless, we thought it was worthwhile exploring association among the diverse phenotypes of PCOS because diet may be more beneficial for women with a particular phenotype than for others.

One possibility which may explain this association is that women with the H + O phenotype presented higher prevalence of overweight and obesity (52.9%) compared to controls (33.1%) and other PCOS phenotypes (33.9%), but we need further studies with higher sample size. Indeed, nutritional randomized controlled trials in PCOS women have shown more effectiveness in reducing symptoms in women with overweight or obesity. Other reason could be that these randomized controlled trials, through diet, accomplished a reduction in hyperinsulinemia and, as a consequence, diminished hyperandrogenism. In previous studies, PCOS with hyperandrogenism increased around two folds (OR = 2.2; 95% CI: 1.9–2.6) the incidence of metabolic syndrome and three times (OR = 3.1; 95% CI: 2.3–4.2) the incidence of insulin resistance compared to PCOS women without hyperandrogenism [60].

Regarding the findings of the AHEI-2010, this is the only one of the five indices which establishes the maximum score for whole grains at 75 g/day. This quantity much reduces glycemic load compared to the other indices. The other different item is sugar-sweetened beverages and fruit juice. AHEI-2010 scored 0 points if people drank one or more servings per day and the maximum score when subjects did not drink any sugar-sweetened beverages and fruit juice. The DASH score has an item for sweetened beverages as well, but it is based on quintiles intake. A subject drinking sweetened beverages would be more penalized in the AHEI-2010 than in the DASH index. We also explored if a higher consumption of any single food group of AHEI-2010 index could explain the inverse association. Only vegetables intake was close to statistical significance. Thus, the effect of the AHEI-2010 dietary pattern in the PCOS phenotype with hyperandrogenism and oligovulation may have a synergic effect of food groups and not be an isolated action of just one group. Moreover, compared to individual food items, dietary patterns measured a priori via dietary indices can incorporate complex interactions among foods/nutrients and can better reduce the risk of some diseases [61].

In our case, we did not find a clear explanation for the inverse relationship between DASH index and the O + POM phenotype, but the relatively low number of subjects in this phenotype may play a role in it. Therefore, we cannot rule out a chance finding may occur. Unexpectedly, the highest quartile of DASH index was positively associated with the O + POM phenotype, increasing the risk of having this phenotype with a higher DASH adherence. Contrarily, the DASH diet may improve BMI and other metabolic parameters which could reduce PCOS symptomatology. Three studies have shown that adherence to the DASH diet between eight and 12 weeks among PCOS women could have beneficial effects on BMI, androstenedione, anti-Müllerian hormone (AMH), insulin and lipid metabolism [31,32]. An interventional study with the DASH diet for eight weeks led
to a significant reduction in serum insulin, triglycerides and very-low-density lipoprotein cholesterol, and a significant increase in total antioxidant capacity, glutathione levels [34] and c-reactive protein [33]. The DASH diet is characterized by consumption of seafood, poultry, whole grains, fruits, and vegetables, which have been related to better fertility in women and better semen quality in men [62].

Another point to consider is the importance of fibre on PCOS because of its capacity in acting on gut microbiota as a prebiotic. An increment of gut permeability, the reduction of biodiversity and a growing endotoxemia by lipopolysaccharide of gram negative bacteria promote higher absorption of energy, activate the immune system and inflammation, and increase hyperandrogenism and insulin resistance [63]. The gut microbiota has been implicated to play a critical role in metabolic diseases such as PCOS, and may modulate the secretion of mediators of the brain–gut axis [64]. However, the research is still in its early stage [65–68]. Fibre and microbiome may be a confounding factor in the present study. However, fibre did not accomplish statistical criteria for inclusion in our analyses, whereas carbohydrates did. Fibre and carbohydrates intakes presented a high colinearity, for including both.

On the other hand, our study subjects were incident and prevalent PCOS cases. Therefore, some women could have recently changed their dietary patterns due to their symptoms. In fact, healthy dietary pattern adherence and physical exercise are the first line of treatment recommended for PCOS patients [69–73]. However, the monitoring of these changes in diet and physical activity is not integrated in the usual clinical practice [69,74]. Moreover, there are few studies that have explored diet changes after PCOS diagnosis, and their results are inconclusive [58,75–78].

Lastly, we have not found studies evaluating associations of diet among PCOS phenotypes. In fact, clinical manifestations of PCOS are notably different among PCOS phenotypes, such as those presenting androgenism or not, although all of them take part of the same syndrome [79].

To our knowledge, our study is the first one analyzing dietary indices among different PCOS phenotypes according to the Rotterdam criteria, instead of other classifications such as anovulatory and ovulatory PCOS. Our modest findings may reveal that it would be necessary to make dietary recommendations based on PCOS phenotypes according to physiological differences. Likewise, it has been reported that a phenotypic approach would be highly convenient for clinical practice and epidemiologic research [73,80].

Furthermore, the relation between diet and fertility in women has been studied in the last three decades [81]. Based on the Nurse Health Study cohort, a Fertility Diet was described, showing that its adherence was able to reduce the attributable risk of ovulatory disorder infertility in 66% of cases (95% CI: 29–86%) [82]. Relationships between AHEI and DASH indices and PCOS have been evaluated, but mostly in randomized controlled trials seeking to improve PCOS symptoms, mainly using low carbohydrate high proteins diets [83,84]. In women with PCOS, it would be worthwhile to carry out interventional studies with a mix approximation: firstly, to follow a high protein low carbohydrate diet, and secondly, a Mediterranean Diet. A high protein, low carbohydrate, diet may allow a quick reduction of body weight, hyperinsulinemia and inflammation. The Mediterranean Diet may be the second step for maintenance of the previous results with less secondary effects, and an increment of adherence to a long-term healthier diet. For example, the PREDIMED study was one of the most important nutritional interventions carried out in Spain. PREDIMED showed a 30% CVD risk reduction with the Mediterranean diet, which is of similar magnitude to that reported in statin trials [85].

The current study has some limitations. First, we used a FFQ as dietary assessment method that has limitations but was comparable to other tools for assessment of food intake in nutritional epidemiology studies. In addition, all self-reported dietary intakes are subject to misreporting, with different types of foods likely to be either over or under-reported [86]. However, we used a validated FFQ with a mean correlation coefficient for nutrient intakes equal to 0.40 for reproducibility and 0.47 for validity. Second, we applied dietary indices
which were not specifically created for the Spanish population, except the rMED index that was implemented for the Spanish cohort of European Prospective Investigation into Cancer (EPIC). This may limit external validity of this specific tool. However, all these dietary indices have already been used in multiple nutritional investigations worldwide. Third, case-control studies present a higher risk of selection and information bias than other study designs. Nevertheless, we selected both cases and controls from the same population of women who visited the same medical services in the same time period: a public hospital and outpatient clinics. Concerning information bias, if misclassification of PCOS status may have occurred, it would have contributed to underestimating the true magnitude of the relationship. Finally, we employed the Rotterdam criteria, which are widely used in gynecological studies and clinical practice.

In conclusion, we did not find any clear association between dietary indices (AHEI, AHEI 2010, AMED, RMED and DASH) and PCOS and its phenotypes. We only observed an inverse association between AHEI -2010 score and less probabilities of the H + O phenotype, but this finding must be taken cautiously. To our knowledge, our study is the first evaluating the association between dietary indices and four different phenotypes of PCOS, according to the Rotterdam criteria, and using Mediterranean Diet indices (aMED and rMED) to assess dietary patterns in women with PCOS. Further adequately powered studies are required to clarify if there are associations between dietary indices and PCOS phenotypes. In addition, prospective studies to monitor and evaluate the effect of changes in diet in PCOS women during regular clinical practice are necessary, which is one of the first treatment options for many women with PCOS according to the international practice guidelines.

**Author Contributions:** Conceptualization, J.M., M.L.S.-F. and A.M.T.-C.; data curation, J.V.; formal analysis, A.C.-T. and J.J.A.-G.; funding acquisition, J.M., M.L.S.-F. and A.M.T.-C.; methodology, J.M., M.L.S.-F. and A.M.T.-C.; resources, J.V.; software, J.V.; supervision, J.M.; writing—original draft, A.C.-T. and J.M.; writing—review & editing, A.C.-T., J.M., E.A., F.N.-L., M.T.P.-S., A.C.-B. and J.V. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by the Ministry of Economy and Competitiveness, Instituto de Salud Carlos III (ISCIII) (AES, Acción Estratégica en Salud), grant No. PI13/01237, and The Seneca Foundation, Murcia Regional Agency of Science and Technology, grant No. 19443/PI/14.

**Institutional Review Board Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Research Committee of the University of Murcia and the Clinical University Hospital Virgen de la Arrixaca (no. 770/2013, approved 3 October 2013)

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data that support the findings of this study are restricted for research use only. The data are not publicly available. Data are available from the authors upon reasonable request and with permission from the Departments of Preventive Medicine and Obstetrics and Gynecology, University Clinical Hospital Virgen de la Arrixaca, Spain.

**Acknowledgments:** The authors would also like to acknowledge Eva María Navarrete and EPINUT-BIBLIODIETA Group (Miguel Hernández University, Alicante, Spain) for their collaboration and the calculation of dietary indices.

**Conflicts of Interest:** The authors declare no conflict of interest.
Abbreviations

PCOS  Polycystic Ovarian Syndrome  
NIH  National Institute of Health  
European Society of Human Reproduction and Embryology  ASRM  American Society for Reproductive Medicine  
aMED  Alternate Mediterranean Diet Score  
BMI  Body Mass Index  
rMED  Relative Mediterranean Diet Score  
AHEI  Alternate Healthy Index  
AHEI-2010  Alternate Healthy Index 2010  
H  Hyperandrogenism  
DASH  Dietary Approaches to Stop Hypertension  
O  Oligo/amenorrhea  
POM  Polycystic ovaries morphology  
H + O  “Hyperandrogenism + Oligo/amenorrhea” phenotype  
H + O + POM  “Hyperandrogenism + Oligo/amenorrhea + Polycystic ovaries morphology” phenotype  
O + POM  “Oligo/amenorrhea + Polycystic ovaries morphology” phenotype  

References

1. Rothenberg, S.S.; Beverley, R.; Barnard, E.; Baradaran-Shoraka, M.; Sanfilippo, J.S. Polycystic ovary syndrome in adolescents. *Best Pract. Res. Clin. Obstet. Gynaecol.* 2018, 48, 103–114. [CrossRef] [PubMed]  
2. Patel, S. Polycystic ovary syndrome (PCOS), an inflammatory, systemic, lifestyle endocrinopathy. *J. Steroid Biochem. Mol. Biol.* 2018, 182, 27–36. [CrossRef] [PubMed]  
3. Kakoly, N.S.; Khomami, M.B.; Joham, A.E.; Cooray, S.D.; Misso, M.L.; Norman, R.J.; Harrison, C.L.; Ranasinha, S.; Teede, H.J.; Moran, L.J. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: A systematic review and meta-regression. *Hum. Reprod. Update* 2018, 24, 455–467. [CrossRef] [PubMed]  
4. Panidis, D.; Tziomalos, K.; Papadakis, E.; Vosnakis, C.; Chatzis, P.; Katsikis, I. Lifestyle intervention and anti-obesity therapies in the polycystic ovary syndrome: Impact on metabolism and fertility. *Endocrine* 2013, 48, 583–590. [CrossRef]  
5. Liu, A.L.; Xie, H.J.; Xie, H.Y.; Liu, J.; Yin, J.; Hu, J.S.; Peng, C.Y. Association between fat mass and obesity associated (FTO) gene rs9939609 A/T polymorphism and polycystic ovary syndrome: A systematic review and meta-analysis. *BMC Med. Genet.* 2017, 18, 89. [CrossRef]  
6. Orio, F.; Muscogiuri, G.; Nese, C.; Palomba, S.; Savastano, S.; Tafuri, D.; Colarieti, G.; La Sala, G.; Colao, A.; Yildiz, B.O. Obesity, type 2 diabetes mellitus and cardiovascular disease risk: An up-to-date in the management of polycystic ovary syndrome. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2016, 207, 214–219. [CrossRef]  
7. Mani, H.; Levy, M.J.; Davies, M.J.; Morris, D.H.; Gray, L.J.; Bankart, J.; Blackledge, H.; Khunti, K.; Howlett, T.A. Diabetes and cardiovascular events in women with polycystic ovary syndrome: A 20-year retrospective cohort study. *Clin. Endocrinol. Oxf.* 2013, 78, 926–934. [CrossRef]  
8. Albu, A.; Radian, S.; Fica, S.; Barbu, C.G. Biochemical hyperandrogenism is associated with metabolic syndrome independently of adiposity and insulin resistance in Romanian polycystic ovary syndrome patients. *Endocrine* 2015, 48, 696–704. [CrossRef]  
9. Lerchbaum, E.; Schwetz, V.; Giuliani, A.; Obermayer-Pietsch, B. Assessment of glucose metabolism in polycystic ovary syndrome: HbA1c or fasting glucose compared with the oral glucose tolerance test as a screening method. *Hum. Reprod.* 2013, 28, 2537–2544. [CrossRef]  
10. Daan, N.M.P.; Louwers, Y.V.; Koster, M.P.H.; Eijkemans, M.J.C.; de Rijke, Y.B.; Lentjes, E.W.G.; Fauser, B.C.J.M.; Laven, J.E. Cardiovascular and metabolic profiles amongst different polycystic ovary syndrome phenotypes: Who is really at risk? *Fertil. Steril.* 2014, 102, 1444–1451.e3. [CrossRef]  
11. Lo, J.C.; Feigenbaum, S.L.; Yang, J.; Pressman, A.R.; Selby, J.V.; Go, A.S. Epidemiology and adverse cardiovascular risk profile of diagnosed polycystic ovary syndrome. *J. Clin. Endocrinol. Metab.* 2006, 91, 1357–1363. [CrossRef]  
12. Chiu, W.-L.; Boyle, J.; Vincent, A.; Teede, H.; Moran, L.J. Cardiometabolic Risks in Polycystic Ovary Syndrome: Non-Traditional Risk Factors and the Impact of Obesity. *Neuroendocrinology* 2017, 104, 412–424. [CrossRef]  
13. Morgante, G.; Musacchio, M.C.; Orvieto, R.; Massaro, M.G.; De Leo, V. Alterations in thyroid function among the different polycystic ovary syndrome phenotypes. *Gynecol. Endocrinol.* 2013, 29, 967–969. [CrossRef]  
14. Garelli, S.; Masiero, S.; Plebani, M.; Chen, S.; Furmaniak, J.; Armanini, D.; Betterle, C. High prevalence of chronic thyroiditis in patients with polycystic ovary syndrome. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2013, 169, 248–251. [CrossRef]  
15. Joham, H.J.; Ranasinha, S.; Zoungas, S.; Boyle, J. Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: Data from a large community-based cohort study. *J. Women’s Health Larchmt* 2015, 24, 299–307. [CrossRef]
16. West, S.; Lashen, H.; Bloigu, A.; Franks, S.; Puukka, K.; Ruokonen, A.; Jarvelin, M.-R.; Tapanainen, J.S.; Morin-Papunen, L. Irregular menstruation and hyperandrogenaemia in adolescence are associated with polycystic ovary syndrome and infertility in later life: Northern Finland Birth Cohort 1986 study. *Hum. Reprod.* **2014**, *29*, 2339–2351. [CrossRef] [PubMed]

17. Helseth, R.; Vanky, E.; Salvesen, O.; Carlsem, S.M. Gestational diabetes mellitus among Norwegian women with polycystic ovary syndrome: Prevalence and risk factors according to the WHO and the modified IADPSG criteria. *Eur. J. Endocrinol.* **2013**, *169*, 65–72. [CrossRef]

18. Joham, A.E.; Ranasinha, S.; Zoungas, S.; Moran, L.; Teede, H.J. Gestational diabetes and type 2 diabetes in reproductive-aged women with polycystic ovary syndrome. *J. Clin. Endocrinol. Metab.* **2014**, *99*, E447–E452. [CrossRef]

19. Fux-Otta, C.; Maliqueo, M.; Echiburú, B.; Rosato, O.; Crisosto, N.; Iraci, G.S.; Fiol de Cuneo, M.; Szafryk de Mereshian, P.; Sir-Petermann, T. Pregnancy outcomes in women with polycystic ovary syndrome in two Latin American populations. *J. Obstet. Gynaecol. Res.* **2018**, *44*, 750–755. [CrossRef]

20. Lizneva, D.; Atabieiev, I.; Azziz, R. Polycystic Ovary Syndrome. In *Reference Module in Biomedical Sciences*; Elsevier: Oxford, UK, 2018; ISBN 9780128012383.

21. Lansdown, A.; Rees, D.A. The sympathetic nervous system in polycystic ovary syndrome: A novel therapeutic target? *Clin. Endocrinol. (Oxf.)* **2012**, *77*, 791–801. [CrossRef] [PubMed]

22. Cooney, L.G.; Lee, I.; Sammel, M.D.; Dokras, A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: A systematic review and meta-analysis. *Hum. Reprod.* **2017**, *32*, 1075–1091. [CrossRef] [PubMed]

23. Barrea, L.; Arnone, A.; Annunziata, G.; Muscogiuri, G.; Laudisio, D.; Salzano, C.; Pugliese, G.; Colao, A.; Savastano, S. Adherence to the Mediterranean diet, dietary patterns and body composition in women with polycystic ovary syndrome (PCOS). *Nutrients* **2019**, *11*, 2278. [CrossRef] [PubMed]

24. Eslamian, G.; Baghestani, A.-R.; Eghtesad, S.; Hekmatdoost, A. Dietary carbohydrate composition is associated with polycystic ovary syndrome: A case-control study. *J. Hum. Nutr. Diet.* **2017**, *30*, 90–97. [CrossRef] [PubMed]

25. Zhang, X.; Zheng, Y.; Guo, Y.; Lai, Z. The Effect of Low Carbohydrate Diet on Polycystic Ovary Syndrome: A Meta-Analysis of Randomized Controlled Trials. *Int. J. Endocrinol.* **2019**, *2019*, 4386401. [CrossRef] [PubMed]

26. McGrice, M.; Porter, J. The effect of low carbohydrate diets on fertility hormones and outcomes in overweight and obese women: A systematic review. *Nutrients* **2017**, *9*, 204. [CrossRef]

27. Phy, J.L.; Pohlmeier, A.M.; Cooper, J.A.; Watkins, P.; Spallholz, J.; Harris, K.S.; Berenson, A.B.; Boylan, M. Low Starch/Low Dairy Diet Results in Successful Treatment of Obesity and Co-Morbidities Linked to Polycystic Ovary Syndrome (PCOS). *J. Obes. Weight Loss Ther.* **2015**, *5*, 259. [CrossRef]

28. Pohlmeier, A.M.; Phy, J.L.; Watkins, P.; Spallholz, J.; Harris, K.S.; Cooper, J.A. Effect of a low-starch/low-dairy diet on fat oxidation in overweight and obese women with polycystic ovary syndrome. *Appl. Physiol. Nutr. Metab.* **2014**, *39*, 1237–1244. [CrossRef]

29. Barrea, L.; Marzullo, P.; Muscogiuri, G.; Di Somma, C.; Scacchi, M.; Oriol, F.; Aimaretti, G.; Colao, A.; Savastano, S. Source and amount of carbohydrate in the diet and inflammation in women with polycystic ovary syndrome. *Nutr. Res. Rev.* **2018**, *31*, 291–301. [CrossRef]

30. Perelman, D.; Coghlan, N.; Lamendola, C.; Carter, S.; Abbasi, F.; McLaughlin, T. Substituting poly- and mono-unsaturated fat for dietary carbohydrate reduces hyperinsulinaemia in women with polycystic ovary syndrome. *Gynecol. Endocrinol.* **2017**, *33*, 324–327. [CrossRef]

31. Azadi-Yazdi, M.; Karimi-Zarchi, M.; Salehi-Abargouei, A.; Fallahazadeh, H.; Nadjarzadeh, A. Effects of Dietary Approach to Stop Hypertension diet on androgens, antioxidant status and body composition in overweight and obese women with polycystic ovary syndrome: A randomised controlled trial. *J. Hum. Nutr. Diet.* **2017**, *30*, 275–283. [CrossRef]

32. Foroozanfard, F.; Rafiei, H.; Samimi, M.; Gilasi, H.R.; Gorjizadeh, R.; Heidar, Z.; Asemi, Z. The effects of dietary approaches to stop hypertension diet on weight loss, anti-Müllerian hormone and metabolic profiles in women with polycystic ovary syndrome: A randomized clinical trial. *Clin. Endocrinol. Oxf.* **2017**, *87*, 51–58. [CrossRef] [PubMed]

33. Asemi, Z.; Esmaillzadeh, A. DASH diet, insulin resistance, and serum hs-CRP in polycystic ovary syndrome: A randomized controlled clinical trial. *Horm. Metab. Res.* **2015**, *47*, 232–238. [CrossRef] [PubMed]

34. Asemi, Z.; Samimi, M.; Tabassi, Z.; Shakeri, H.; Sabihi, S.-S.; Esmaillzadeh, A. Effects of DASH diet on lipid profiles and biomarkers of oxidative stress in overweight and obese women with polycystic ovary syndrome: A randomized clinical trial. *Nutrition* **2014**, *30*, 1287–1293. [CrossRef] [PubMed]

35. Sánchez-Ferrer, M.L.; Mendiola, J.; Hernández-Peñalver, A.I.; Corbalán-Biyang, S.; Carmona-Barnosi, A.; Prieto-Sánchez, M.T.; Nieto, A.; Torres-Cantero, A.M. Presence of polycystic ovary syndrome is associated with longer anogenital distance in adult Mediterranean women. *Hum. Reprod.* **2017**, *32*, 2315–2323. [CrossRef]

36. Hernández-Peñalver, A.I.; Sánchez-Ferrer, M.L.; Mendiola, J.; Adoamnei, E.; Prieto-Sánchez, M.T.; Corbalán-Biyang, S.; Carmona-Barnosi, A.; Nieto, A.; Torres-Cantero, A.M. Assessment of anogenital distance as a diagnostic tool in polycystic ovary syndrome. *Reprod. Biomed. Online* **2018**, *37*, 741–749. [CrossRef]

37. Sánchez-Ferrer, M.L.; Prieto-Sánchez, M.T.; Corbalán-Biyang, S.; Mendiola, J.; Adoamnei, E.; Hernández-Peñalver, A.I.; Carmona-Barnosi, A.; Salido-Fiérez, E.J.; Torres-Cantero, A.M. Are there differences in basal thrombophilias and C-reactive protein between women with or without PCOS? *Reprod. Biomed. Online* **2019**, *38*, 1018–1026. [CrossRef]
38. Sánchez-Ferrer, M.L.; Adoamnei, E.; Prieto-Sánchez, M.T.; Mendiola, J.; Corbalán-Biyang, S.; Moñino-García, M.; Palomar-Rodríguez, J.A.; Torres-Cantero, A.M. Health-related quality of life in women with polycystic ovary syndrome attending to a tertiary hospital in Southeastern Spain: A case-control study. *Health Qual. Life Outcomes* **2020**, *18*, 232. [CrossRef]

39. Fauser, B.C.J.M. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil. Steril.* **2004**, *81*, 19–25. [CrossRef]

40. Afifi, L.; Saeed, L.; Pasch, L.A.; Huddleston, H.G.; Cedars, M.I.; Zane, L.T.; Shinkai, K. Association of ethnicity, Fitzpatrick skin type, and hirsutism: A retrospective cross-sectional study of women with polycystic ovarian syndrome. *Int. J. Women’s Dermatol.* **2017**, *3*, 37–43. [CrossRef]

41. Conway, G.; Dewailly, D.; Diamanti-Kandarakis, E.; Escobar-Morreale, H.F.; Franks, S.; Gamberini, A.; Kelestimur, F.; Macut, D.; Micic, D.; Pasquali, R.; et al. The polycystic ovary syndrome: A position statement from the European Society of Endocrinology. *Eur. J. Endocrinol.* **2014**, *171*, P1–P29. [CrossRef]

42. National Institutes of Health. *Evidence-Based Methodological Workshop on Polycystic Ovary Syndrome*; National Institutes of Health: Bethesda, MD, USA, 2012; pp. 1–14.

43. García-Arenzana, N.; Navarrete-Muñoz, E.M.; Vázquez-Carrete, J.A.; Moreno, P.; Vidal, C.; Salas, D.; Ederra, M.; Pedraz, C.; Collado-García, F.; Sánchez-Contador, C.; et al. Compliance with current dietary recommendations and geographical variability of diet in women participating in 7 screening programs for breast cancer in Spain. *Nutr. Hosp.* **2011**, *26*, 863–873. [CrossRef] [PubMed]

44. Garcia-Arenzana, N.; Navarrete-Muñoz, E.M.; Peris, M.; Salas, D.; Ascunce, N.; Gonzalez, I.; Sánchez-Contador, C.; Santamariña, C.; Moreo, P.; Moreno, M.P.; et al. Diet quality and related factors among Spanish female participants in breast cancer screening programs. *Menopause J. N. Am. Menopause Soc.* **2012**, *19*, 1121–1129. [CrossRef] [PubMed]

45. Willett, W.C.; Sampson, L.; Stampfer, M.J.; Rosner, B.; Bain, C.; Witschi, J.; Hennekens, C.H.; Speizer, F.E. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am. J. Epidemiol.* **1985**, *122*, 51–65. [CrossRef] [PubMed]

46. Palma, I.; Farran, A.; Cantós, D. *Tablas de Composición de Alimentos del CESNID* McGraw-Hill/Interamericana de España: Madrid, Spain, 2008; ISBN 9788448169060.

47. US Department of Health and Human Sciences. 2015–2020 Dietary Guidelines. Available online: https://health.gov/our-work/food-nutrition/2015-2020-dietary-guidelines/guidelines/#subnav-4 (accessed on 23 November 2020).

48. Cutillas-Tolivia, A.; Adoamnei, E.; Navarrete-Muñoz, E.M.; Vioque, J.; Moñino-García, M.; Jørgensen, N.; Chavarro, J.E.; Mendiola, J.; Torres-Cantero, A.M. Adherence to diet quality indices in relation to semen quality and reproductive hormones in young men. *Hum. Reprod.* **2019**, *34*, 1866–1875. [CrossRef] [PubMed]

49. Fung, T.T.; McCullough, M.L.; Newby, P.K.; Manson, J.A.E.; Meigs, J.B.; Rifai, N.; Willett, W.C.; Hu, F.B. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. *Am. J. Clin. Nutr.* **2005**, *82*, 163–173. [CrossRef]

50. US Department of Agriculture. *Dietary Guidelines for Americans*; US Department of Health and Human Services, US Department of Agriculture: Washington, DC, USA, 1995.

51. Fung, T.T.; Chiuze, S.E.; McCullough, M.L.; Rexrode, K.M.; Logroscino, G.; Hu, F.B. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. *Arch. Intern. Med.* **2008**, *168*, 713–720. [CrossRef]

52. Chiuze, S.E.; Fung, T.T.; Rimm, E.B.; Hu, F.B.; McCullough, M.L.; Wang, M.; Stamper, M.J.; Willett, W.C. Alternative dietary indices both strongly predict risk of chronic disease. *J. Nutr. Diet.* **2012**, *72*, 1009–1018. [CrossRef]

53. Sacks, F.M.; Obarzanek, E.; Windhauser, M.M.; Svetkey, L.P.; Vollmer, W.M.; McCullough, M.; Katan, N.; Din, P.H.; Steele, P.; Proschans, M.A.; et al. Rationale and design of the Dietary Approaches to Stop Hypertension trial (DASH). A multicenter controlled-feeding study of dietary patterns to lower blood pressure. *Ann. Epidemiol.* **1995**, *5*, 108–118. [CrossRef]

54. Trichopoulou, A.; Kouris-Blazos, A.; Wahlqvist, M.L.; Gainardis, C.; Lagiou, P.; Polychronopoulou, E.; Vassilakou, T.; Lipworth, L.; Trichopoulou, D. Diet and overall survival in elderly people. *BMJ* **1995**, *311*, 1457. [CrossRef]

55. Trichopoulou, A.; Costacou, T.; Bamia, C.; Trichopoulou, D. Adherence to a Mediterranean Diet and Survival in a Greek Population. *N. Engl. J. Med.* **2003**, *348*, 2599–2608. [CrossRef]

56. Buckland, G.; González, C.A.; Agudo, A.; Villardell, M.; Berenguer, A.; Amiano, P.; Ardanaz, E.; Arriola, L.; Barricarte, A.; Basterretxea, M.; et al. Adherence to the mediterranean diet and risk of coronary heart disease in the Spanish EPIC cohort study. *Am. J. Epidemiol.* **2009**, *170*, 1518–1529. [CrossRef] [PubMed]

57. Willett, W. *Nutritional Epidemiology*, 14th ed.; Oxford University Press: Oxford, UK, 2013; ISBN 9780199979448.

58. Lin, A.W.; Kazemi, M.; Jarrett, B.Y.; Vanden Brink, H.; Hoeger, K.M.; Spandorfer, S.D.; Lujan, M.E. Dietary and physical activity behaviors in women with polycystic ovary syndrome per the new international evidence-based-guideline. *Nutrients* **2019**, *11*, 2711. [CrossRef] [PubMed]

59. Dos Santos Rodrigues, A.M.; Martins, L.B.; Franklin, A.M.T.; Candido, A.L.; dos Santos, L.C.; Ferreira, A.V.M. Poor quality diet is associated with overweight status and obesity in patients with polycystic ovary syndrome. *Nutrients* **2018**, *10*, 28 (Suppl. 2), 94–101. [CrossRef] [PubMed]

60. Yang, R.; Yang, S.; Li, R.; Liu, P.; Qiao, J.; Zhang, Y. Effects of hyperandrogenism on metabolic abnormalities in patients with polycystic ovary syndrome: A meta-analysis. *Reprod. Biol. Endocrinol.* **2016**, *14*, 67. [CrossRef] [PubMed]

61. Hu, F.B. Dietary pattern analysis: A new direction in nutritional epidemiology. *Curr. Opin. Lipidol.* **2002**, *13*, 3–9. [CrossRef] [PubMed]

62. Gaskins, A.J.; Chavarro, J.E. Diet and fertility: A review. *Am. J. Obstet. Gynecol.* **2018**, *218*, 379–389. [CrossRef]
63. He, F.F.; Li, Y.M. Role of gut microbiota in the development of insulin resistance and the mechanism underlying polycystic ovary syndrome: A review. J. Ovarian Res. 2020, 13, 1–13. [CrossRef]

64. Liu, R.; Zhang, C.; Shi, Y.; Zhang, F.; Li, L.; Wang, X.; Ling, Y.; Fu, H.; Dong, W.; Shen, J.; et al. Dysbiosis of Gut Microbiota Associated with Clinical Parameters of Polycystic Ovary Syndrome. Front. Microbiol. 2017, 8, 324. [CrossRef]

65. Sanchez, H.N.; Moroney, J.B.; Gan, H.; Shen, T.; Im, J.L.; Li, T.; Taylor, J.R.; Zan, H.; Casali, P. B cell-intrinsic epigenetic modulation of antibody responses by dietary fiber-derived short-chain fatty acids. Nat. Commun. 2020, 11, 1–19. [CrossRef]

66. Torres, P.J.; Siakowska, M.; Banaszewska, B.; Pawelczyk, L.; Duleba, A.J.; Kelley, S.T.; Thackray, V.G. Gut Microbial Diversity in Women with Polycystic Ovary Syndrome Correlates with Hyperandrogenism. J. Clin. Endocrinol. Metab. 2018, 103, 1502–1511. [CrossRef]

67. Lindheim, L.; Bashir, M.; Münzker, J.; Trummer, C.; Zachhuber, V.; Leber, B.; Horvath, A.; Pieber, T.R.; Gorkiewicz, G.; Stadlbauer, V.; et al. Alterations in gut microbiome composition and barrier function are associated with reproductive and metabolic defects in women with polycystic ovary syndrome (PCOS): A pilot study. PLoS ONE 2017, 12, e0168390. [CrossRef] [PubMed]

68. Zhao, X.; Jiang, Y.; Xi, H.; Chen, L.; Feng, X. Exploration of the Relationship Between Gut Microbiota and Polycystic Ovary Syndrome (PCOS): A Review. Geburtshilfe Frauenheilkd. 2020, 80, 161–171. [CrossRef] [PubMed]

69. Teede, H.J.; Misso, M.L.; Costello, M.F.; Dokras, A.; Laven, J.; Moran, L.; Piltonen, T.; Norman, R.J.; Anderssen, M.; Azziz, R.; et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil. Steril. 2018, 110, 364–379. [CrossRef] [PubMed]

70. Bates, G.W.; Legro, R.S. Longterm management of Polycystic Ovarian Syndrome (PCOS). Mol. Cell. Endocrinol. 2013, 373, 91–97. [CrossRef] [PubMed]

71. Lim, S.S.; Hutchison, S.K.; Van Ryswyk, E.; Norman, R.J.; Teede, H.J.; Moran, L.J. Lifestyle changes in women with polycystic ovary syndrome. Cochrane Database Syst. Rev. 2019, 11, 1–90. [CrossRef]

72. Kite, C.; Lahart, I.M.; Afzal, I.; Broom, D.R.; Randeva, H.; Kyrou, I.; Brown, J.E. Exercise, or exercise and diet for the management of polycystic ovary syndrome: A systematic review and meta-analysis. Syst. Rev. 2019, 8, 1–28. [CrossRef] [PubMed]

73. Moran, L.J.; Noakes, M.; Clifton, P.; Buckley, J.; Brinkworth, G.; Thomson, R.; Norman, R.J. Predictors of lifestyle intervention attrition or weight loss success in women with polycystic ovary syndrome who are overweight or obese. Nutrients 2019, 11, 492. [CrossRef] [PubMed]

74. Garad, R.M.; Teede, H.J. Polycystic ovary syndrome: Improving policies, awareness, and clinical care. Curr. Opin. Endocr. Metab. Res. 2020, 12, 112–118. [CrossRef] [PubMed]

75. Lie Fong, S.; Douma, A.; Verhaeghe, J. Implementing the international evidence-based guideline of assessment and management of polycystic ovary syndrome (PCOS): How to achieve weight loss in overweight and obese women with PCOS? J. Gynecol. Obstet. Hum. Reprod. 2020, in press. [CrossRef]

76. Amirjani, S.; Asemi, Z.; Bazarganipour, F.; Aramesh, S.; Allan, H.; Sayadi, M.; Tabatabaei, M.-S.; Mohamadian, Z.; Zabti, F.; Iranpak, N.; et al. Dietary intake and lifestyle behaviour in different phenotypes of polycystic ovarian syndrome: A case–control study. J. Hum. Nutr. Diet. 2019, 32, 413–421. [CrossRef]

77. Moran, L.J.; Brown, W.J.; McNaughton, S.A.; Joham, A.E.; Teede, H.J. Weight management practices associated with PCOS and their relationships with diet and physical activity. Hum. Reprod. 2017, 32, 669–978. [CrossRef]

78. Kulkarni, S.D.; Patil, A.N.; Gudi, A.; Homburg, R.; Conway, G.S. Changes in diet composition with urbanization and its associated with clinical parameters in polycystic ovary syndrome. J. Clin. Endocrinol. Metab. 2017, 102, 758–763. [CrossRef] [PubMed]

79. Wang, J.; Wu, D.; Guo, H.; Li, M. Hyperandrogenemia and insulin resistance: The chief culprit of polycystic ovary syndrome. Life Sci. 2019, 236, 116940. [CrossRef] [PubMed]

80. Lizzneva, D.; Suturina, L.; Walker, W.; Brakta, S.; Gavrilova-Jordan, L.; Azziz, R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil. Steril. 2016, 106, 16–5. [CrossRef]

81. Chiu, Y.H.; Chavarro, J.E.; Souter, I. Diet and female fertility: Doctor, what should I eat? Fertil. Steril. 2018, 110, 560–569. [CrossRef] [PubMed]

82. Chavarro, J.E.; Rich-Edwards, J.W.; Rosner, B.A.; Willett, W.C. Diet and Lifestyle in the Prevention of Ovulatory Disorder Infertility. Obstet. Gynecol. 2007, 110, 1050–1058. [CrossRef]

83. Kazemi, M.; McBrearty, L.E.; Chizen, D.R.; Pierson, R.A.; Chilibeck, P.D.; Zello, G.A. A comparison of a pulse-based diet and the therapeutic lifestyle changes diet with exercise and health counselling on the cardio-metabolic risk profile in women with polycystic ovary syndrome: A randomized controlled trial. Nutrients 2018, 10, 1387. [CrossRef]

84. Moran, L.J.; Ko, H.; Misso, M.; Marsh, K.; Noakes, M.; Talbot, M.; Fearson, M.; Thondan, M.; Stepto, N.; Teede, H.J. Dietary Composition in the Treatment of Polycystic Ovary Syndrome: A Systematic Review to Inform Evidence-Based Guidelines. J. Acad. Nutr. Diet. 2013, 113, 520–545. [CrossRef]

85. Ros, E.; Martinez-González, M.A.; Estruch, R.; Salas-Salvadó, J.; Fito, M.; Martinez, J.A.; Corella, D. Mediterranean diet and cardiovascular health: Teachings of the PREDIMED Study. Adv. Nutr. 2014, 5, 330S–336S. [CrossRef]

86. Macdiarmid, J.; Blundell, J. Assessing dietary intake: Who, what and why of under-reporting. Nutr. Res. Rev. 1998, 11, 231–253. [CrossRef]