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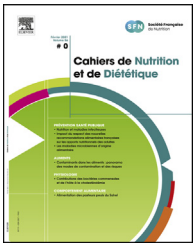

PREVENTION — PUBLIC HEALTH

Mediterranean Diet and cardiovascular diseases: A 2024 update

Régime méditerranéen et maladies cardiovasculaires : une mise à jour en 2024

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Summary Between 1958 and 1964, Keys and co-workers carried out the Seven Countries Study, which enrolled men aged 40—59 years in one of 16 cohorts from seven countries (Finland, Greece, Italy, Yugoslavia, Japan, USA, and Italy). After 15, 25, and 50 years of follow-up, a strong negative relation was observed between adherence to Mediterranean Diet (MedDiet) and coronary heart disease (CHD) mortality. Since that study, very numerous prospective observational studies and 3 randomized clinical trials, as well as meta-analyses of cohorts and RCTs have demonstrated the primary and secondary preventive effect of MedDiet towards cardiovascular diseases and more specifically CHD. This review, which is an update of a review published by the same author in 2022, aims to present the more recent results from prospective cohorts, RCTs and meta-analyses. A protective effect of MedDiet towards CHD is clearly confirmed.

MOTS CLÉS
Maladie coronarienne ;
Prévention primaire et secondaire des maladies cardiovasculaires ;

Résumé Entre 1958 et 1964, Keys et ses collaborateurs ont mené l'étude la « Seven Countries Study », qui a recruté des hommes âgés de 40 à 59 ans dans l'une des 16 cohortes de sept pays (Finlande, Grèce, Italie, Yougoslavie, Japon, États-Unis, et Italie). Après un suivi de 15, 25, et 50 ans, une forte relation négative a été observée entre l'adhésion à l'alimentation méditerranéenne (MedDiet) et la mortalité coronarienne. Depuis lors, de très nombreuses études prospectives et 3 essais cliniques randomisés (ECRs), ainsi que des méta-analyses de cohortes et d'ECRs ont démontré l'effet préventif primaire et secondaire de la MedDiet sur

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les maladies cardiovasculaires et plus particulièrement vis-à-vis de la maladie coronarienne (MC). Cette revue, qui est une mise à jour d'une revue publiée par le même auteur en 2022, a pour but de présenter les résultats les plus récents de cohortes prospectives, d'ECRs et de méta-analyses. Un effet protecteur de la MedDiet vis-à-vis de la MC est clairement confirmé.

Introduction

The most recent world epidemiologic data about cardiovascular diseases (CVD) have been published in 2023 [1]. Global CVD mortality decreased by 34.9% from 1990 to 2022. Coronary heart disease (CHD) had the highest global age-standardized DALYs (Disability-Adjusted Life Year) of all diseases at 2275.9 per 100,000. Dietary risks were the leading contributor to age-standardized CVD DALYs among the behavioral risks.

According to the latest WHO data published in 2020, CHD deaths in France reached 63,181 or 13.22% of total deaths. The age-adjusted death rate is 30.17 per 100,000 of population ranks France #182 in the world. A French recent myocardial infarction (MI) prevalence projection [2] indicated an increase in the coming years, for men from 2.52 to 4.02%, and for women from 0.85 to 1.44%. Thus, even if France has a low prevalence of CHD mortality, it is the first cause of death with cancer.

Among the individual dietary risks, a diet low in whole grains accounted for the largest number of deaths (4.6%), followed by a diet low in fruits (4.3%) and a diet high in sodium (4.2%). Leading dietary risks for DALYs were low intakes of whole grains (2.6%), fruits (2.6%), and nuts and seeds (2.1%). The greatest increase in attributable deaths and DALYs between 1990 and 2016 occurred for a diet high in red meat, followed by a diet high in sugar-sweetened beverages and a diet low in milk, respectively [3]. The Mediterranean Diet (MedDiet) is at odds to this dietary pattern. Since the very well-known Seven Countries Study initiated by Ancel Keys in the 1970s, several prospective studies, RCTs and meta-analyses have concluded to a protective effect of MedDiet towards CHD, as well in primary as in secondary prevention. This has been reviewed by ourself in 2022 [4].

The present commissioned short paper updates our previous one [4] by incorporating the most recent results, in particular from prospective cohorts and meta-analyses. The reader is invited to refer to our previous review for more details on studies and meta-analyses prior to 2022.

Randomized clinical studies (RCTs)

There are very few RCTs about the preventive effect of MedDiet towards CVD. The results of the Lyon Diet Heart Study (secondary prevention) [5], the GlObal Secondary Prevention strategiEs to Limit event recurrence after myocardial infarction (GOSPEL study) (secondary prevention) [6], and of the PREvencion con DIeta MEDiterranea (PREDIMED) study (primary prevention in patients at high CV risk) [7] have been reported in detail previously [4].

The more recent RCT is the CORDIOPREV study [8] (single-center, secondary prevention study in 1002 Spanish patients aged 20—75 years). Patients were randomized to receive a MedDiet or a low-fat diet intervention, with a follow-up of 7 years. The primary outcome (assessed by intention to treat) was a composite of major cardiovascular events (MACE). After multivariable adjustment for all known predisposing factors to CHD, MedDiet reduced the risk by 18% ($P < 0.024$). The effect was significant only in men, but there was only 17.5% women included.

In summary, three RCTs have concluded to a protective effect in secondary prevention, one with a 70% decrease in CV events (Lyon Heart Study), the other with a 30% reduction (CARDIOPREV study). The third one (PREDIMED study) concluded to a 30% reduction in MACE in primary prevention in subjects at high CV risk, but secondary analysis concluded to a significant effect only towards stroke.

Published prospective cohorts since 2022

We have previously detailed the results of meta-analyses from 2013 to 2021 [4].

The ATTICA study [9] included participants living in the province of Attica (Greece); they were evaluated for CVD after 5, 10, and 20 years of follow-up (2002—2022) After 10 years of follow-up (2002—2012), 1988 participants were separated in 4 subgroups depending on the trajectory of their adherence to MedDiet (sustained low, low to high, high to low, sustained high). After 20 years of follow-up, the participants with a sustained high trajectory exhibited a 45% lower CVD risk than those with a sustained low trajectory.

The Seguimiento Universidad de Navarra (SUN) cohort (1999—2019) [10] enrolled university graduates from all over Spain (18,419 participants, mean follow-up: 11.5 years). The primary composite paperweight included MI, stroke, and CVD death according to the same criteria as PREDIMED study [7]. One standard deviation increase in the MedDiet Score was associated with a 29% reduction in CVD risk. In subgroup analysis, the results for the comparison between extreme categories of baseline adherence to the MedDiet were con-sistent across categories of age, sex, cardiovascular risk

Table 1 Description of named dietary program categories [15].

Named dietary program category	Description
Low fat	Total fat intake reduced to 20—30% of caloric intake; saturated fat intake reduced to < 10% of caloric intake
Very low fat	Total fat intake reduced to 10—20% of caloric intake
Combined low fat and low sodium	As in low-fat diet, plus sodium reduction (< 2.4 g/day)
Modified fat	No decrease in total fat intake, but increase in polyunsaturated to saturated fat ratio
Mediterranean	Decreased fish, fruit, and vegetable intake; increased intake of monounsaturated fats (e.g., olive oil)
Ornish	Total fat intake reduced to < 10% of caloric intake; primarily plant based
Pritikin	Total carbohydrate intake 70—75% of caloric intake; total protein intake 15—20% of caloric intake; total fat intake 5—10% of caloric intake; fibre intake 40—45 g/1000 kilocalories
Minimal intervention	Usual diet or no advice, referral to own physician, usual care, non-dietary programming, or minimal dietary advice

Table 2 Meta-analyses since 2022 of observational studies (cohorts) and RCTs reporting the effects of MedDiet towards CVD.

References	Type of studies	Outcomes	Number of studies	Comparison	Relative risk	Risk reduction (%)
Taylor et al. [14]	Cohorts	Total CVD incidence	17	Highest vs. lowest MedDietS	0.85 (0.83, 0.87)	15
Karam et al. [15]	RCTs	CV mortality	12	MedDiet vs. other diet	0.55 (0.39, 0.78)	45
Karam et al. [15]	RCTs	Stroke incidence	12	MedDiet vs. other diet	0.65 (0.46, 0.93)	35
Karam et al. [15]	RCTs	MI incidence	12	MedDiet vs. other diet	0.48 (0.36, 0.65)	52
Pant et al. [16]	Cohorts (women)	Total CVD incidence	14	Highest vs. lowest MedDietS	0.76 (0.72, 0.81)	24
Pant et al. [16]	Cohorts (women)	CHD incidence	4	Highest vs. lowest MedDietS	0.75 (0.65, 0.87)	25
Pant et al. [16]	Cohorts (women)	Stroke incidence	3	Highest vs. lowest MedDietS	0.87 (0.76, 1.01)	NS
Pant et al. [16]	Cohorts (European women)	Total CVD incidence	5	Highest vs. lowest MedDietS	0.76 (0.59, 0.98)	24
Pant et al. [16]	Cohorts (non-European women)	Total CVD incidence	5	Highest vs. lowest MedDietS	0.79 (0.72, 0.87)	21
Pant et al. [16]	Cohorts (men)	Total CVD incidence	5	Highest vs. lowest MedDietS	0.78 (0.72, 0.83)	22

RCTs: randomized controlled trials; CVD: cardiovascular diseases; CHD: coronary heart disease; MI: myocardial infarction; MedDietS: Mediterranean Diet Score.

factors, educational level, sociodemographic characteristics, and the index of health consciousness.

Liang et al. [11] used a prospective cohort study from NHANES 1999—2010 database to explore, by using the alternative MedDiet (aMed) index, the effect of MedDiet on CV mortality in people with previous CHD or stroke ($n = 2052$; 5.6 years of follow-up). Excluding patients who died within the first 2 years of entry in NHANES study, CV mortality was 49% lower in those with higher adherence to MedDiet.

The Endocrine Vascular disease Approach (EVA) project is an observational registry of female and male Italian individuals referred to the cardiac catheterization laboratory to undergo coronary angiography and/or percutaneous coronary intervention for suspected CHD [12]. It

can be considered as a secondary prevention study. The type of CHD was determined based on angiography, with coronary obstruction < 50% indicating non-obstructive CHD and coronary obstruction ≥ 50% obstructive CHD. A greater adherence to MedDiet was associated with a 51% reduction of MACE after adjusting for confounding factors.

Fan et al. [13] used a prospective cohort study from National Health and Nutrition Examination Survey (NHANES) 2007—2018 database to explore, by using the alternative MedDiet (aMed) index, the effect of MedDiet on CV mortality in people with metabolic syndrome (MetS) ($n = 8301$; 6.3 years of follow-up). They were categorized in 3 groups: below median aMed score (0—3), median (4), above median (5—9). The roles of sedentary behavior and depression on CV mortality were also assessed. In brief summary, in people with MetS (at high CV risk), high or median adherence to MedDiet can attenuate or even reverse the adverse effects of sedentary behavior and depression on CV mortality.

In summary, these 5 prospective observational studies confirm previous ones and show a 30 to 50% protective effect in primary [9,10,13], in patients with MetS [12], or secondary prevention [11] towards CVD.

Meta-analyses

We have previously reported meta-analyses from 2013 to 2021 [4]. All these meta-analyses concluded that there was a significant reduction of CV risk (CVD, CHD, MI, stroke).

Taylor et al. [14], in 2023, included 159 cohort studies from 4 databases evaluating diet quality and CV outcomes. Among these 159 cohorts' studies, only 17 assessed the effect of MedDiet. CVD incidence comparing the highest Mediterranean Diet Score to the lowest was reduced by 15%.

Karam et al. [15], in 2023, have performed a network meta-anlysis of RCTs comparing the effects of seven popular structured dietary programmes (Table 1) on CV mortality, and individual CV events (stroke, non-fatal MI, unplanned CV intervention) in patients at increased CV risk. As compared to minimal intervention, MedDiet reduced CV mortality by 45%, stroke by 35%, and non-fatal MI by 52%. The remaining dietary programmes had little or no benefit compared with minimal intervention.

Pant et al. [16], in 2023, have performed a random effect meta-analysis of 14 prospective cohorts (678,372 female participants; median follow-up of 12.5 years) about primary prevention of CVD in women. Higher adherence to a MedDiet decreased by 24% incident CVD.

All these meta-analyses are summarized in Table 2.

Conclusion and perspectives

Since the Seven Countries Study carried out by Ancel Keys et coworkers, the prospective cohorts, the more recent meta-analyses and the 3 RCTs (Lyon Heart, PREDIMED, CORDIOPREV studies) all agree in favor of the efficacy of MedDiet for primary and secondary prevention of CVD. For these reasons and other health benefits and sustainability of MedDiet, it is quite necessary to revitalize MedDiet especially in Mediterranean Countries. Not only MedDiet has proved its health and sustainable benefits, but it is also the very best alternative to ultra-processed foods whose accumulation of recent data strongly suggest if not prove their deleterious CV effects.

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Author's contribution

Jacques Delarue is the sole author and takes responsibility for the whole content of this paper.

Disclosure of interest

The author declares that he has no competing interest.

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