Maturitas 178 (2023) 107841

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Review article

Mediterranean diet for cancer prevention and survivorship

Aitana Monllor-Tormos [a], Alicia García-Vigara [b], Orly Morgan [c], Miguel-Ángel García-Pérez [d], Nicolás Mendoza [e], Juan J. Tarín [f], Antonio Cano [a,g,*]

[a] Service of Obstetrics and Gynecology, Hospital Clínico Universitario – INCLIVA, Av. Blasco Ibáñez 17, 46010, Valencia, Spain
[b] Women's Health Research group, INCLIVA, Menéndez Pelayo, 4, acc., 46010, Valencia, Spain
[c] University of Miami Miller School of Medicine, Department of Medical Education, 1600 NW 10th Ave, FL 33101, United States
[d] Department of Genetics, Faculty of Biological Sciences, University of Valencia, INCLIVA, Burjassot 46100, Valencia, Spain
[e] Department of Obstetrics and Gynecology, University of Granada, Granada, Spain
[f] Department of Cellular Biology, Functional Biology and Physical Anthropology, Faculty of Biological Sciences, University of Valencia, Dr. Moliner 50, 46100 Burjassot, Valencia, Spain
[g] Department of Pediatrics, Obstetrics and Gynecology, University of Valencia, Av. Blasco Ibáñez 15, 46010, Valencia, Spain

ARTICLE INFO

Keywords:
Mediterranean diet
Cancer
Cancer risk
Cancer survivorship
Cancer mortality

ABSTRACT

Cancer is one of the main noncommunicable diseases in terms of health impact. Factors such as a progressively aging population point to future increases in the incidence of cancer on a global level. The elevated number of affected individuals, together with continuous improvements in cancer prevention and therapy, is creating a growing population of cancer survivors, with often inadequately met needs.

Lifestyle is a key modulator of cancer risk and of associated morbidity and mortality, and is included in all approaches to the long-term management of cancer. Diet is a principal component of lifestyle, and most of the available evidence is centered on the Mediterranean diet. Our objective was to provide a narrative review of the evidence on the effect of the Mediterranean diet on cancer risk and health threats related to cancer survivorship. For this purpose, we searched the PubMed database for articles published between January 1, 2000, and June 12, 2023.

Current data show that the Mediterranean diet is inversely associated with risk, or is risk neutral, for most types of cancer. Tumors of the digestive system have received preferential interest, but studies have also been published on tumors in other organs. The evidence, however, is meager due to the observational nature of most studies, although it is reassuring that benefit is reproduced in studies performed in different populations and environments. Evidence related to cancer survivors is limited by the paucity of studies, yet several findings regarding survival, recurrence, and short- and long-term morbidity suggest a potential role for the Mediterranean diet that warrants further research.

1. Introduction

Cancer is one of the main non-communicable diseases (NCD) and is the second leading cause of death on a global level [1,2]. The International Agency for Research on Cancer estimates that 19.3 million new cases were diagnosed in 2020, with mortality at around 10 million [3]. Moreover, greater life expectancy worldwide is a major contributor, since aging is a high-risk factor. Cancer treatment and early detection are improving dramatically, resulting in an already large and growing population of survivors. This population is estimated to reach 26 million in the US alone by 2040 [4,5]. People surviving cancer constitute a particularly vulnerable population due to their higher oncological risk (recurrent or secondary cancer), and the physical and psychological short- and long-term adverse effects associated with cancer treatment [6].

Lifestyle is a recognized risk factor for cancer, and unlike other factors such as genetics, can be controlled. Tobacco, alcohol, sedentarism and unhealthy diet increase the risk of cancer and influence cancer progression, with differences according to tumor type [7]. The Mediterranean diet (MedDiet) accounts for the lion's share of evidence concerning the effect of diet on NCD, including cancer.

The MedDiet does not have a strictly defined composition, partly

* Corresponding author at: Department of Pediatrics, Obstetrics and Gynecology, Facultad de Medicina, Av Blasco Ibáñez 15, 46010, Valencia, Spain.
E-mail addresses: monllortormosaitana@alumni.uv.es (A. Monllor-Tormos), agarvi4@alumni.uv.es (A. García-Vigara), oxm229@med.miami.edu (O. Morgan), Miguel.garcia@uv.es (M.-Á. García-Pérez), nicomendoza@ugr.es (N. Mendoza), Juan.J.Tarin@uv.es (J.J. Tarín), Antonio.cano@uv.es (A. Cano).

https://doi.org/10.1016/j.maturitas.2023.107841
Received 9 July 2023; Received in revised form 15 August 2023; Accepted 20 August 2023
Available online 24 August 2023

because of differences between the countries in the Mediterranean basin. A meticulous search for features common to the regions in the area culminated in the MedDiet pyramid, which was published in 1995 [8]. The layers in the pyramid reflect food groups by recommended intake (number of servings), from the more frequent foods recommended for each meal, to others with more sporadic, once or twice weekly recommended intake (Fig. 1). Interesting results were obtained from a group of Australian researchers who compiled information from food frequency questionnaires over a time span of 46 years in 15 different populations, in order to more precisely define the MedDiet [9]. Certain variability between studies was found although they all generally respected the main pyramid criteria. This highlights one of the strengths of the MedDiet, which by providing only general recommendations to follow (as per the food pyramid) can therefore accommodate features specific to each environment, thus favoring adherence.

Other characteristics supporting a key role for the MedDiet include its compliance with Paris agreement recommendations regarding climate change and sustainability, and also palatability, compatibility with most culinary cultures, and evidence-based support [10]. This latter point is of particular interest. From initial publications aimed at investigating the impact on cardiovascular disease (CVD), widely subjected to meta-analytic procedures [11], interest has extended progressively to other areas such as diabetes, neurological diseases, and cancer [12]. It is noteworthy that diets rich in red meat and low in fruit and vegetables, diametrically opposed to the MedDiet, have shown a positive correlation with risk of colorectal cancer (CRC) and other types of cancers [13].

Our objective was to provide an updated review of the evidence regarding the effect of MedDiet on cancer risk and on health threats related to cancer survivorship. In addition, we reviewed the data supporting the modulatory role of MedDiet on cancer pathways.

2. Methods

PubMed database was searched from January 1, 2000 until June 12, 2023 to identify literature that assessed the effect of MedDiet in people with cancer (any type) following the four elements, population, intervention, comparison, and outcome (PICO), of clinical evidence [14]. The risk of disease and the impact on health, as well as the short- and long-term undesirable effects of any form of cancer treatment, were considered. The search terms were “Mediterranean diet”, which was paired with (cancer OR tumor OR cancer risk OR cancer survivor* OR cancer treatment). Papers were considered only if published in English or Spanish and with adult human subjects.

The search generated 1424 references. Five researchers (AMT, OM, MAGP, NM and JJT) screened the identified papers by title, or title and abstract when required. Studies on special populations, such as pregnant women, transplant patients, children or adolescents were excluded. Discrepancies were resolved by the corresponding author (AC). Conclusions from meta-analyses and systematic reviews were prioritized, but clinical studies published subsequently, and therefore not included in the most recent meta-analyses, were also included. Of the 1424 records identified, 79 studies were selected, the full text of which was reviewed by at least one member of the review team and shared with the corresponding author. The flowchart of the literature search is shown in Fig. 2.

3. Mediterranean diet and disease pathways in cancer

The current state of knowledge supports a role for some basic mechanisms operative in the pathogenesis of disease that have been shown to be influenced by the MedDiet.

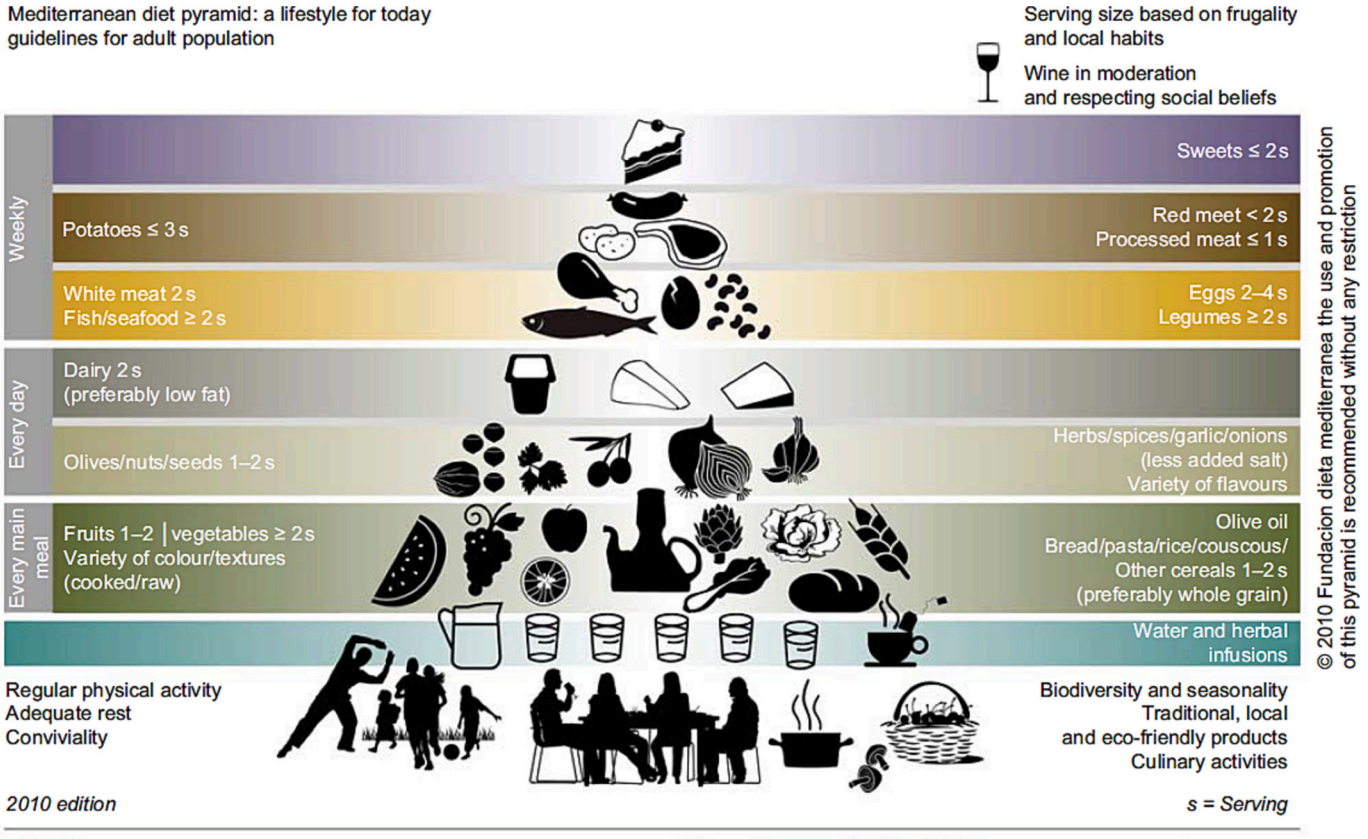

Fig. 1. The Mediterranean diet pyramid. The food groups are stratified according to their respective frequencies per meal, per day or per week. Reproduced with permission of Dr. L. *Serra*-Majem.

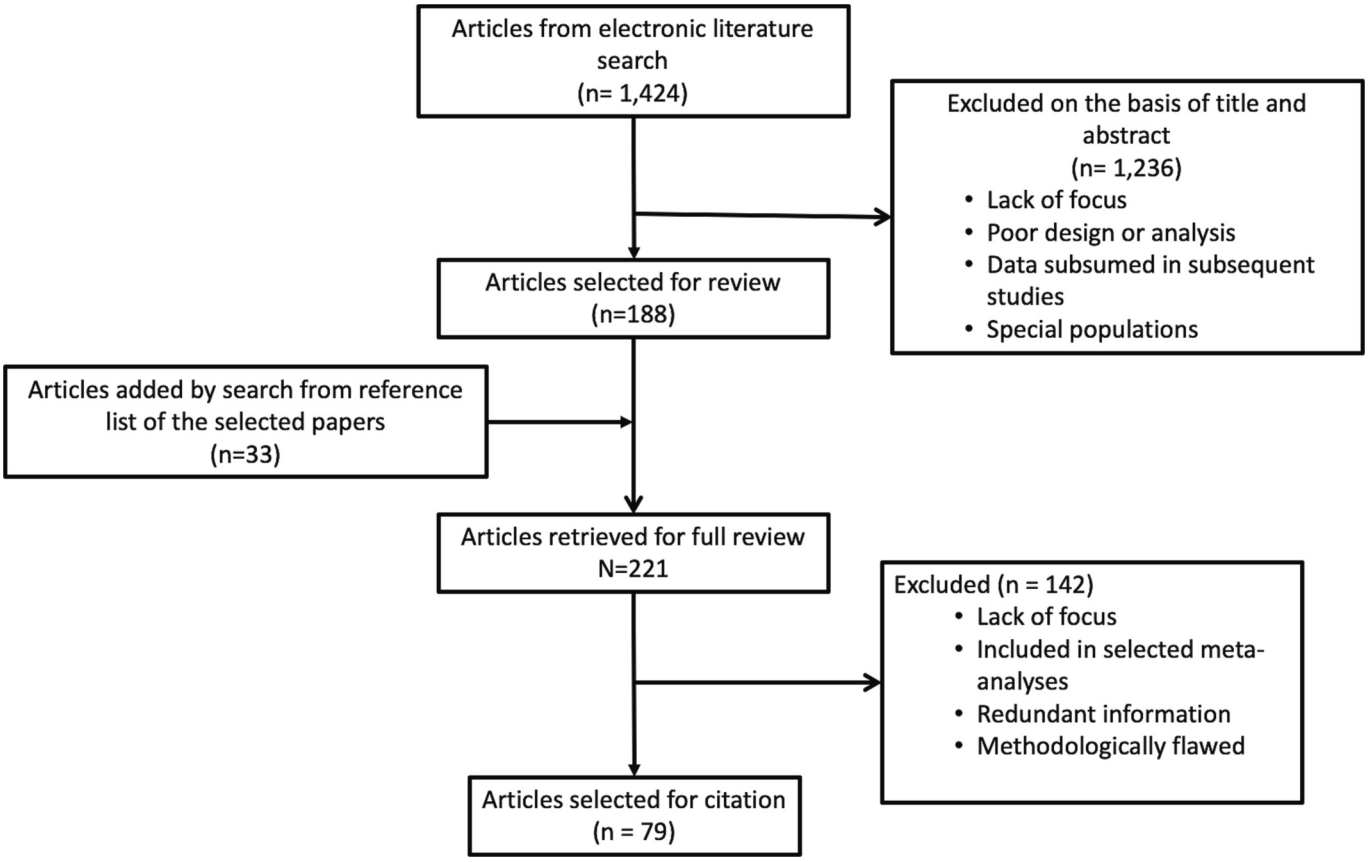

Fig. 2. Flowchart for article selection.

3.1. Oxidative stress and inflammation

Oxidative stress is intertwined with inflammation in the mechanisms of several NCD, including cancer [15,16]. The MedDiet is credited with the ability to protect against disease thanks to the action of phytochemicals present in several of its constituent foods. The most prominent components of these foods are unsaturated fats and polyphenols, highly concentrated in olive oil and nuts, and in the case of polyphenols, also in fruit [17,18].

Unsaturated fats are mainly composed of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA). Polyphenols are a large family of bioactive compounds containing phenol rings and include several sub-classes, such as flavonoids, phenolic acids, stilbenes and lignans. The most common polyphenol group is flavonoids, which includes important sub-groups such as isoflavones, together with anthocyanidins, flavanols, flavones, flavonols and flavanones [19] [Fig. S1].

Both unsaturated fatty acids and polyphenols have demonstrated anti-oxidant and anti-inflammatory properties, with an effect on cancer [20–22]. Among these are the anti-proliferative, pro-apoptotic, and anti-angiogenic activity exhibited by key components of the MedDiet such as olive oil [23], or more specifically some of its molecular components, like the polyphenol hydroxytyrosol [24].

3.2. Microbiota

Gut microbiota has been shown to be sensitive to diet and varies when comparing diets based on animal or plant-based ingredients [25–27]. Reducing visceral obesity through the MedDiet leads to protection against low-grade inflammation, which has been associated with several types of cancer, such as breast and others [28]. However, interest in the impact of the MedDiet on the microbiota has focused preferentially on reducing the risk of tumors of the gastrointestinal tract. Indeed, it has been suggested that the microbiota plays a modulatory role in the development of CRC, both in carcinogenesis and in the expansion phases of cancer, including growth and metastasis [29–32].

Changes in microbiota composition by MedDiet have been associated with microbe phyla like *Enterorhabdus*, *Lachnoclostridium,* and *Parabacteroides*, which have been linked with i) increased production of short-chain fatty acids (SCFA), the main nutrient for colonic cells and promoter of intestinal health [33], and ii) a reduction in pro-inflammatory cytokines [26,27,34,35]. The concept of an anti-inflammatory profile related to MedDiet-induced microbiota composition is supported by a recent meta-analysis [36].

Fig. 3 shows the general scheme proposed for integrating the direct and indirect modulatory action of MedDiet in cancer protection.

4. Epidemiological evidence on cancer risk

A considerable number of studies, mostly observational, have investigated the association of MedDiet with cancer incidence, either overall or for specific cancer types. The bulk of information comes from studies in Italy, Spain or Greece, where the MedDiet is more prevalent. Adherence to this diet has been assessed using various validated scales, predominantly the Mediterranean Diet Score (MDS) [37].

4.1. MedDiet and overall cancer risk

There is conflicting evidence as to the MedDiet's association with overall cancer incidence. A possible protective effect (60 % reduction, $p < 0.05$ after adjustments) was found in the Lyon Heart Study randomized controlled trial [38].

The prospective Netherlands Cohort Study followed 120,852 subjects for 20.3 years. No evidence of protection was found in men and

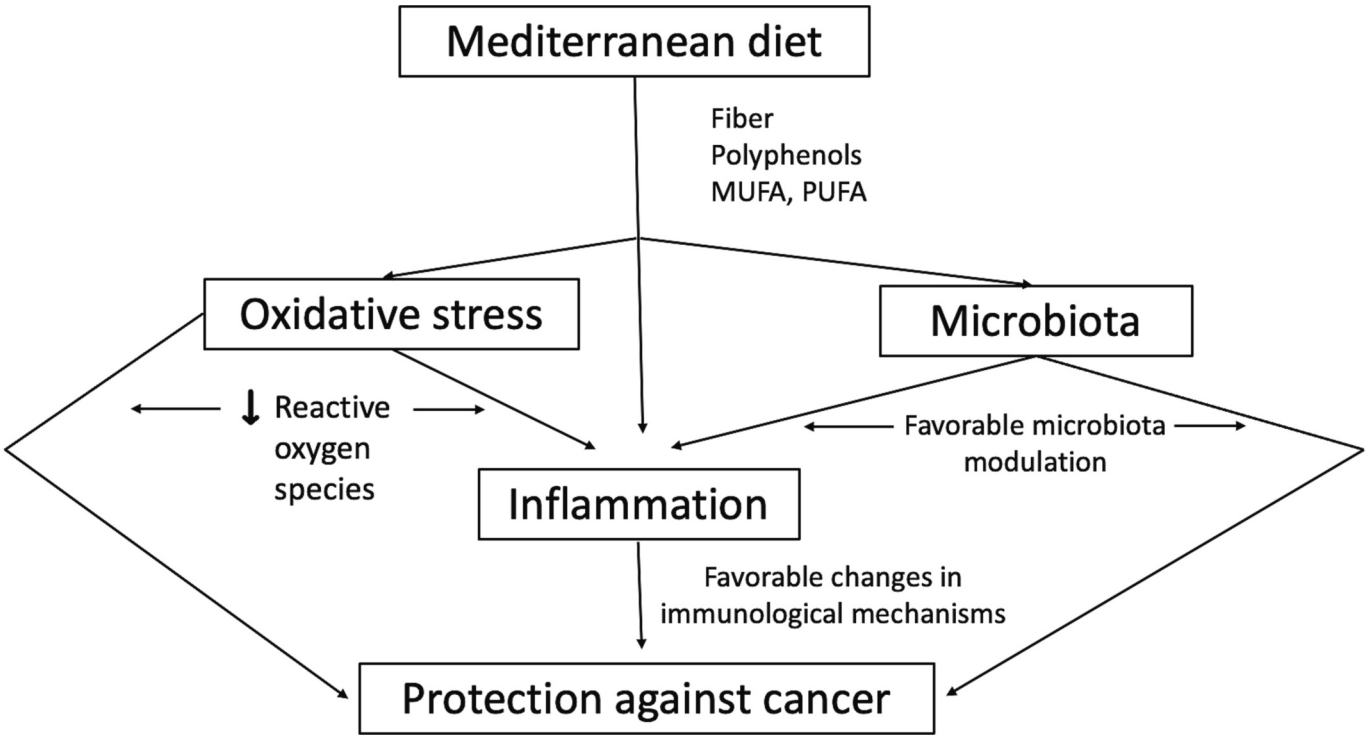

Fig. 3. The Mediterranean diet (MedDiet) provides several beneficial components at various steps related to carcinogenesis and cancer progression. Fiber, polyphenols and unsaturated fatty acids (monounsaturated fatty acids, MUFA, and polyunsaturated fatty acids, PUFA) have a protective effect against different pathways related to tumor pathophysiology, such as oxidative stress, microbiota imbalance (dysbiosis) and inflammation. The MedDiet has been shown to promote a reduction in the production of free radicals and a concomitant reduction in oxidative stress. From the reduction at this end, less direct carcinogenic effect and less inflammation are expected. The MedDiet also promotes changes in the microbiota, with an increase in microbial species that favorably modulate inflammatory mechanisms. Thus, the enterotoxigenic and genotoxic action of some bacteria, such as *Bacteroides fragilis* or *Escherichia coli*, are impaired, while protective microbial phyla, such as *Enterorhabdus*, *Lachnoclostridium* and *Parabacteroides*, are promoted. A direct anti-inflammatory action of MedDiet components, such as polyphenols and unsaturated fatty acids, has been demonstrated.

only a moderate risk reduction was observed in women, although much of the benefit was lost after multivariate analysis [39]. In contrast, the Framingham Offspring Study, which included 2966 participants followed for a median of 18 years, found that women with moderate or high adherence to MedDiet had a 29 % reduction [HR = 0.71, (0.52–0.97)] in overall cancer compared to women with lowest adherence. The reduction was weaker for men [40].

4.2. MedDiet and risk for specific types of cancer

There is an abundance of literature on the relationship between MedDiet adherence and specific cancer types. The findings for tumors of the digestive system are summarized in Table 1.

4.2.1. Digestive system tumors

4.2.1.1. Colorectal cancer. Diet is a widely recognized risk factor for CRC, the third most common cancer, representing an estimated 10 % of all new cases each year [2].

In the Italian research centers network analysis, MedDiet adherence reduced CRC risk by 48 % when considering case-control studies [41]. A small, but nonetheless significant level of protection was confirmed in two meta-analyses including nine prospective cohort studies up to September 2019 [42] and 17 observational studies updated to April 2020 [43], respectively. The European Prospective Investigation into Cancer and Nutrition (EPIC) study, not included in the previous meta-analyses, followed 41,437 subjects for a median of 17 years in Spain, observing a 16 % reduction in CRC [44]. It appears, therefore, that there is consistency suggesting a small level of protection in the various analyses of the available data, even though they are all observational.

4.2.1.2. Upper gastrointestinal tract. Cancers of the upper gastrointestinal (UGIC) tract, including nasopharynx, esophagus, and stomach, account for approximately 8 % of new cancer cases each year [2]. Pooling data from 11 studies, Dutch investigators found that the MedDiet was significantly associated with an average 28 % reduction in the incidence of UGIC [45].

Gastric cancer (ranked first among UGIC malignancies) has been the focus of specific research interest. A meta-analysis of seven observational studies found a 30 % reduction in risk [43]. A Spanish case-control study published soon after this meta-analysis using five different indexes to calculate adherence to the MedDiet concluded that high adherence reduced risk between 48 % and 75 %, depending on the index used [46].

It is possible that, as suggested by the published literature, the level of protection in UGIC is higher than in CCR. However, conclusions about the differences should be taken with caution given the limited quality of the data, already noted by some investigators [45].

4.2.1.3. Liver and pancreas. Evidence regarding other cancers of the digestive tract is scant. Liver cancer ranks fifth in cancer mortality among men and seventh among women in the US [2]. In a meta-analysis of four observational studies, the MedDiet was linked with an overall 36 % risk reduction in liver cancer [43].

Pancreatic cancer (PC) is fourth in mortality for both men and women [2]. No effect of the MedDiet on PC risk was found in a meta-analysis of four studies [43]. A more recent meta-analysis including eight observational (six cohort and two case-control) studies assessed the risk of PC as related to MedDiet adherence in 1,301,320 individuals followed for a mean of 15.6 years. Stricter adherence to the MedDiet was associated with a reduced risk (18 %) of PC [47].

Table 1
Results obtained by meta-analyses and clinical observational studies about adherence to the Mediterranean diet and risk for digestive cancer.

Type of cancer	Design	No. of studies/participants	Risk (95 % CI)	Author, year [ref]	Comments
CRC	Case-control studies in Network of Italian Research Centers.	3 case-control studies (3745 cases and around 6800 controls).	OR = 0.52 (0.43–0.62)	Serra-Majem, 2019 [41]	
	Meta-analysis (updated September 2019)	9 prospective cohort studies	RR = 0.90 (0.84–0.96)	Zhong, 2020 [42]	
	Meta-analysis (updated April 2020)	9 cohort, 1 case-cohort (36,006 incident cases) and 7 case-control studies (9683 prevalent cases).	RR = 0.83 (0.76–0.90)	Morze, 2021 [43]	
	Prospective, EPIC cohort	41,437 men and women for a median of 17.0 years	HR = 0.84 (0.73–0.98)	Castelló, 2022 [44]	
UGIC	Systematic review and meta-analysis (updated February 2020)	5 cohort studies (1,022,760 participants, mean follow up 13.3 years), and 6 case-control studies (10,447 subjects).	Pooled OR = 0.72 (0.61–0.88)	Moazzen, 2020 [45]	Pooled results graded as low quality evidence by authors.
Gastric	Meta-analysis (updated April 2020)	3 cohort, 1 case-cohort (2343 incident cases) and 3 case-control studies (1517 prevalent cases)	RR = 0.70 (0.61–0.80)	Morze, 2021 [43]	
	Case-control	354 cases, 3040 controls	OR = 0.52 (0.28–0.94) OR = 0.25 (0.12–0.52)	Álvarez-Álvarez, 2021 [46]	5 different indexes were used to assess adherence to MedDiet. The detected risk ranged between the 2 presented OR.
Liver	Meta-analysis (updated April 2020)	3 cohort (1274 incident cases) and 1 case-control (518 prevalent cases)	RR = 0.64 (0.54–0.75)	Morze, 2021 [43]	
	Meta-analysis (updated April 2020)	2 cohort and one case-cohort (1436 incident cases) and 1 case-control (688 prevalent cases)	RR = 0.80 (0.60–1.06)	Morze, 2021 [43]	
Pancreas	Meta-analysis (updated October 2022)	6 cohort (mean 15.6 years follow-up) and 2 case-control studies (688 prevalent cases)	HR = 0.82 (0.76–0.88)	Nucci, 2023 [47]	
	Prospective cohort (Melbourne Collaborative Cohort Study)	33,690 followed for a mean of 23.7 years.	HR = 0.79 (0.49–1.26)	Afshar, 2023 [46]	
	Prospective cohort (Multiethnic Cohort Study)	177,313 subjects, average follow-up 19.3 years	HR = 0.98 (0.83–1.16)	Steel, 2023 [49]	

CI: confidence interval. CRC: colorectal cancer. EPIC: European Prospective Investigation into Cancer and Nutrition. HR: hazard ratio. MedDiet: Mediterranean diet. NIH: National Institute of Health. OR: odds ratio. Ref: reference. RR: relative risk. UGIC: upper gastrointestinal cancer.

Conflicting results were also found in two subsequently published studies. The 23.7 years of follow-up of the 33,690 men and women of the Melbourne Collaborative Cohort Study confirmed an almost significant 21 % risk reduction but only in those with strictest adherence to MedDiet ($p = 0.06$ for the trend) [48]. In contrast, no association was found in the follow-up of 177,313 participants for 19.3 years in the Multiethnic Cohort Study [49].

4.2.2. Other cancers

Table 2 summarizes the main findings regarding non-digestive cancers.

4.2.2.1. Breast cancer. One meta-analysis updated to February 2020 analyzed the relationship of the MedDiet with each histological tumor type separately. The data from the seven studies analyzing the effect on invasive ductal cancer detected protection in the five case-control studies, but not in the two cohort studies. The three studies assessing the link of MedDiet with invasive lobular cancer detected risk reduction [50].

In another meta-analysis updated to April 2020, data from 23 observational studies were analyzed to conclude that adherence to MedDiet was linked to a very small reduction of 6 % [43]. One additional randomized controlled trial (RCT) including 4152 participants followed for 4.8 years found a 59 % risk reduction [43].

Protection was also found in a more recent publication analyzing the pooled data of the EPIC studies [51]. Notably, a certain degree of protection, a 20 % risk reduction, was found for tumors negative for estrogen and progesterone receptors. However, no association was detected in the combined data from five Finnish cohorts numbering 6374 postmenopausal women followed for an average of 10 years [52].

Although not unanimous, the published data appear to favor protection. Of particular interest is the effect in estrogen and progesterone receptor-negative cancers. However, the conflicting data call for more and higher quality studies.

4.2.2.2. Prostate cancer. Evidence from two different meta-analyses concur in the lack of association between the MedDiet and prostate cancer (PrC) after evaluating data from 10 and 16 studies, respectively [43,53]. Data from the subsequently published case-control North Carolina-Louisiana Prostate Cancer Project (PCaP) revealed an inverse relationship between MedDiet and high aggressive PrC overall in 1899 men with PrC [54]. Thus, although meta-analyses do not find an association between the incidence of PrC and MedDiet, it may be, according to this latest study, that the risk of aggressive PrC in men adhering to the MedDiet may be lower.

4.2.2.3. Lung cancer. Evaluation of five studies in the meta-analysis by Morze [43] revealed an overall 16 % risk reduction in individuals with high adherence to the MedDiet. Two subsequent meta-analyses, each including nine observational studies, found a rather similar risk reduction of 16 % [55] and 18 % [56], respectively.

4.2.2.4. Bladder cancer. Pooled analysis of 13 prospective studies included in the Bladder Cancer Epidemiology and Nutritional Determinants including 646,222 participants showed a 15 % reduction in risk related with the MedDiet [57]. A similarly small risk reduction was obtained in two meta-analyses evaluating four [43] and six studies [58], with a risk reduction of 13 % and 8 %, respectively.

4.2.2.5. Other cancer types. A meta-analysis of nine observational studies found a substantial 44 % risk reduction in head and neck cancer [43].

Table 2
Results obtained by meta-analyses and subsequently published clinical studies on Mediterranean diet adherence and risk for non-digestive cancer.

Type of cancer	Design	No. of studies/participants	Risk (95 % CI)	Author, year [ref]	Comments
Breast	Meta-analysis (updated February 2020)	5 case-control and 2 cohort studies analyzing MedDiet & invasive ductal cancer. 2 cohort and 1 case-control study analyzing MedDiet & invasive lobular cancer.	Invasive ductal cancer: RR = 0.47 (0.39–0.55) in case-control. RR = 0.98 (0.92–1.05) in cohort studies. Invasive lobular cancer: RR = 0.76 (0.64–0.87)	Dianatinasab, 2020 [50]	
	Meta-analysis (updated April 2020)	12 cohort (35,373 incident cases), 1 RCT (4152 participants followed for 4.8 years), and 11 case-control studies (10,615 prevalent cases)	RR observational = 0.94 (0.90–0.97) RR RCT = 0.41 (0.19–0.87)	Morze, 2021 [43]	
	Pooled data from 5 cohorts	6374 postmenopausal women followed for an average of 10 years.	HR = 0.88 (0.59–1.30)	Männistö, 2021 [52]	
	Systematic review of pooled data from the EPIC study	41 prospective cohort studies including 335,062 women with 10,225 cases and a mean follow-up of 10.0 years.	Overall HR = 0.94 (0.88–1.00) Postmenopausal women HR = 0.93 (0.87–0.99) ER and PR negative tumors HR = 0.80 (0.65–0.99)	Ubago-Guisado, 2021 [51]	
Prostate	Meta-analysis through February 2019.	10 observational studies, 5 cohort and 5 case-control studies, including a total of 33,451 prostate cancer cases.	RR = 0.95 (0.90–1.01)	Cheng, 2019 [53]	
	Meta-analysis through April 2020.	11 observational studies including 5 cohort and 1 case-cohort (36,006 incident cases), and 5 case-control studies (2466 prevalent cases)	RR = 0.98 (0.93–1.04)	Morze, 2021 [43]	
	Case-only North Carolina Louisiana (PCaP)	Association between MedDiet and cancer aggressiveness studied in 1899 men with prostate cancer.	OR = 0.66 (0.46–0.95)	Schneider, 2019 [54]	
Lung	Meta-analysis through April 2020	4 cohort and one case cohort studies (12,730 incident cases)	RR = 0.84 (0.76–0.94)	Morze, 2021 [43]	
	Meta-analysis through May 2021	8 cohort (991,886 participants and 20,575 cases) and 1 case-control (439 participants and 187 cases)	RR = 0.84 (0.77–0.91)	Bahrami, 2022 [55]	
	Meta-analysis through October 2021	7 cohort studies and 2 case-control studies (936,089 participants)	HR = 0.82 (0.74–0.92)	Du, 2022 [56]	
	Pooled analysis of studies included in BLEND study	13 prospective cohort studies (646,222 participants including 3639 cases)	HR = 0.85 (0.77–0.93)	Witlox, 2020 [57]	
Bladder	Meta-analysis through April 2020	3 cohort (5844 incident cases) and one case-control study (690 prevalent cases)	RR = 0.87 (0.76–0.98)	Morze, 2021 [43]	
	Meta-analysis through February 2021	6 cohort and one case-control study.	RR overall = 0.92 (0.87–0.96) RR cohort = 0.93 (0.88–0.97) RR case-control = 0.73 (0.52–0.94)	Dianatinasab, 2022 [58]	
Head & neck	Meta-analysis through April 2020	1 cohort (1868 incident cases) and 8 case-control studies (4601 prevalent cases)	RR overall = 0.56 (0.44–0.72) OR case-control = 0.54 (0.40–0.72) RR cohort = 0.73 (0.60–0.89)	Morze, 2021 [43]	
Skin	E3N cohort. Ongoing study since 1990	67,332 French women. Cases included 404 melanomas, 1367 BCC, and 232 SCC	HR overall = 0.83 (0.73–0.93) HR melanoma = 0.72 (0.54–0.96) HR BCC = 0.77 (0.66–0.90) HR SCC = 1.08 (0.75–1.55)	Mahamat-Saleh, 2019, [59]	
	SUN study	Nested case-control (101 BCC and 404 controls)	OR = 0.28 (0.10–0.77)	Leone, 2020 [58]	
Lymphoma	EPIC study	Prospective cohort 474,160 participants from 10 European countries (1991–2001) followed for an average of 13.9 years	HR = 0.91 (0.80–1.03)	Solans, 2019 [61]	
Thyroid	EPIC study	450,000 participants (712 cases) from 9 European countries followed up for a mean of 14.1 years	HR = 0.94 (0.70–1.25)	Llaha, 2022 [62]	
Ovary	Prospective cohort (NHS)	82,948 women followed for 24 years with 696 incident cases.	HR = 1.03 (0.80–1.34)	Xie, 2014 [63]	
Endometrium	Meta-analysis through April 2020	1 cohort (1392 incident cases) and 3 case-control studies (2355 prevalent cases)	RR observational = 0.67 (0.41–1.11) RR cohort = 0.98 (0.87–1.17) OR case-control = 0.58 (0.35–0.95)	Morze, 2021 [43]	Contrasting findings from cohort and case-control studies

BCC: basal cell carcinoma. BLEND: Bladder cancer Epidemiology and Nutritional Determinants. CI: confidence intervals. E3N: Etude Epidémiologique auprès de femmes de la Mutuelle Générale de l'Education Nationale. EPIC: European Prospective Investigation into Cancer and Nutrition. ER: estrogen receptors. HR: hazard ratio. MedDiet: Mediteranean diet. NHS: Nurses' Health Study. OR: odds ratio. PcaP: prostate cancer project. PR: progesterone receptors. RCT: randomized controlled trial. Ref: reference. RR: relative risk. SCC: squamous cell carcinoma. SUN Seguimiento Universidad de Navarra.

The risk of skin cancer, including melanoma, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), was reduced, 17 %, in the 67,332 French women participating in the prospective Etude Epidémiologique auprès de femmes de la Mutuelle Générale de l'Education Nationale (E3N cohort) [59] as well as in the case-control Seguimiento Universidad de Navarra (SUN) study, a 72 %, in this case focused only on BCC [60].

In the EPIC study, which included 476,160 participants followed for an average of 13.9 years, a small degree of protection (9 %) was found against lymphoma [61], while no association was found for thyroid cancer [62].

A systematic review evaluated the risk for ovarian and endometrial cancer, with null results in the case of ovary [63] and a small protective effect in the case of endometrium, as concluded from two studies, in which the pooled RR for each one-point increase in the MedDiet score was 13 % [64]. Discrepant results were found between three case-control studies and one cohort study when performing meta-analysis evaluation [43].

5. Mediterranean diet and cancer survivors

Cancer survivors are an especially vulnerable population, who face a risk of recurrence and higher risk for a new cancer, stemming from having previously experienced cancer, or from the oncogenic effects of anti-cancer treatments [65]. Cancer therapy also causes side effects that may occur during treatment or at a later stage, due principally to radiotherapy, chemotherapy or hormonal deficiencies provoked by treatment in endocrine-related cancer [66].

Lifestyle plays a central role in strategies to manage the conditions associated with cancer survivorship. Diet is currently recommended to reduce the metabolic syndrome and bone loss linked with some cancer treatments, as well as to fight the cachectic syndrome accompanying several more aggressive cancers. In addition, the microbiota, which is highly susceptible to diet, can modulate the effect of immunotherapy and chemotherapy, improving therapeutic response and decreasing side effects [67]. The role of the MedDiet in the management of clinical needs associated with cancer treatment and beyond remains an understudied area. Evidence comes mainly from preclinical models, as quality clinical studies remain scarce and small in size.

5.1. The effect of the MedDiet

Evidence has already been published supporting a protective role for the MedDiet against cancer recurrence [43] but a more holistic approach to the potential of this diet in cancer survivor management has materialized only in recent years.

5.1.1. Mortality

Both all-cause and cancer-related mortality have attracted research interest. Table 3 shows the data related to the effect of MedDiet on mortality in cancer survivors.

A meta-analysis reviewing papers published up to April 2020 found a reduction of 25 % in all-cause mortality among cancer survivors on reviewing eight cohort studies, but not in cancer-specific mortality after reviewing 4 cohort studies [43]. A more recent study including 6370 subjects asked about their diet after cancer diagnosis confirmed a reduction of 26 % in all-cause and of 29 % in cancer-specific mortality for MedDiet [68].

Data related to specific cancer types are discrepant. One meta-analysis focusing on CRC found no association between MedDiet adherence and reduction in all-cause or CRC-specific mortality after a review of five cohort studies [42]. Inconclusive results were also found in another cohort of metastatic CRC including 1284 individuals with a median follow up of 73 months [69].

An Italian study of 1453 breast cancer survivors who were followed for 15 years found that adherence to the MedDiet was associated with a reduction of 28 % in all-cause mortality across the whole cohort, and of 35 % in breast cancer mortality only in women 55 years and older [70]. Also in breast cancer, the MedDiet adherence of 3660 women amounting to 40,888 person-years suggested a reduction of 21 % in all-cause mortality, but not in breast cancer-specific mortality [71].

The same Italian researchers found MedDiet adherence to be associated with lower overall mortality, a 26 %, in a cohort of 777 men with PrC followed for 10 years [72].

Table 3
Results from meta-analyses and subsequently published clinical studies on Mediterranean diet adherence and all-cause or cancer- specific mortality in cancer survivors.

Outcome	Design	No. of studies/ participants	Risk (95 % CI)	Author, year [ref]
All cancer types	Meta-analysis (updated April 2020)	8 cohort-studies (4883 cases) 4 cohort studies (1790 cases)	RR = 0.75 (0.66–0.86). All-cause. RR = 0.96 (0.82–1.11. Cancer-specific	Morze, 2021 [43]
CRC survivors	Multiethnic Cohort Study Prospective cohort study in US.	6370 cases, 10 years follow-up	HR = 0.74 (0.66–0.84). All-cause. HR = 0.71(0.59–0.85). Cancer-specific.	Park, 2022 [68]
	Meta-analysis (updated September 2019)	4 prospective studies (all-cause) 1 prospective study (CRC-specific)	HR = 0.66 (0.37–1.17). All-cause HR = 0.84 (0.50–1.42) CRC-specific.	Zhong, 2020 [42]
Metastatic CRC	Cancer and Leukemia Group B (Alliance) and Southwest Oncology Group 80405 trial (Prospective cohort study) in US	1284 cases	HR = 0.83 (0.67–1.04). All cause.	Van Blarigan, 2020 [69]
Breast cancer	Prospective cohort study in Northern Italy	1453 cases, 15 years follow-up	HR = 0.72 (0.57–0.92). All-cause. HR = 0.65 (0.43–0.98). Breast cancer-specific in women ≥55 years.	Di Masso, 2021 [70]
	Pathways study in US	3660 cases, 40,888 person-years of follow-up.	HR = 0.79 (0.61–1.03). All-cause. HR = 0.79 (0.54–1.16). Breast cancer-specific.	Ergas, 2021 [71]
Prostate cancer	Prospective cohort study in Northern Italy	777 cases, 10 years of follow-up.	HR = 0.74 (0.56–0.99) All-cause. HR = 0.58 (0.38–0.90) for MedDiet plus high physical activity	Di Masso, 2021 [72]

CI: confidence intervals. CRC: colorectal cancer. HR: hazard ratio. Ref: reference.

5.1.2. Other actions

There is a dearth of data about other roles of the MedDiet within the wide spectrum of cancer survivorship needs. The risk of recurrence has been shown to remain unchanged in a study mentioned in Section 5.1.1 [71], but prolonged in a small study on 114 women with breast cancer [73]. The Canary Prostate Active Surveillance Study could not detect any effect of the MedDiet on grade re-classification in 564 men after 7.8 years of median follow-up [74].

Quality of life (QoL) was evaluated in a small study including 68 women with non-metastatic breast cancer. No association with the MedDiet was found [75]. A subsequent multi-center study recruited 309 women with early breast cancer, concluding that MedDiet adherence was associated with several dimensions of QoL, including physical functioning, better sleep, and lower pain [76].

The effect of MedDiet has also been studied in the context of cancer therapy-related symptoms, like diarrhea in metastatic CRC [77] or fatigue [78]. Both outcomes were improved, but the effect was minimal and the sample size of the groups meager. A similar pattern was confirmed in another study, a RCT of MedDiet vs. usual care in men under androgen deprivation therapy because of prostate cancer. Fatigue was reduced and quality of life was improved by the MedDiet, but the study only included 23 participants [79].

6. Conclusion

The role of diet in cancer has been widely studied, primarily in terms of cancer risk, but more recently for its role in modulating the many needs of cancer survivors, whose main threats are the possibility of another cancer diagnosis (either recurrence or a new type of tumor) and of higher mortality and morbidity. Modulating the risk of a cancer diagnosis shows more solid evidence for tumors of the digestive system. Data on mortality, either overall or cancer-specific, are less robust and conflicting. Finally, knowledge about the effect of diet on the short and long-term side effects of cancer therapy is still in its infancy. More research is needed at all levels. This does not only mean well-designed studies, i.e., RCTs, but studies with larger numbers of participants or designs appropriate to the question. Despite these limitations, given that diet is a modifiable risk factor for cancer, the MedDiet can and should be recommended on a clinical level, even in the context of evidence that still needs to be improved. This conclusion is based on the arguments of reasonable consistency of the observed benefits, replicated in various populations, and confirmation in meta-analyses, which adds robustness to the findings. Furthermore, the observed benefits are pathophysiologically congruent with findings in experimental models and with supporting research in humans, for example, in intermediate outcomes. Finally, the level of evidence, even if of moderate or low quality, is the best available and, equally interesting, there are no data to support any harm.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.maturitas.2023.107841.

Contributors

Aitana Monllor-Tormos participated in the conception of the manuscript and literature search, and was involved in the analysis of the paper's content.

Alicia García-Vigara participated in the conception of the manuscript and literature search, and was involved in the analysis of the paper's content.

Orly Morgan participated in the conception of the manuscript and literature search, and was involved in the analysis of the paper's content.

Miguel-Ángel García-Pérez participated in the conception of the manuscript and literature search, and was involved in the analysis of the paper's content.

Nicolás Mendoza participated in the conception of the manuscript and literature search, and was involved in the analysis of the paper's content.

Juan J Tarín participated in the conception of the manuscript and literature search, and was involved in the analysis of the paper's content.

Antonio Cano participated in the conception of the manuscript and literature search, was involved in the analysis of the paper's content, and wrote the draft of the manuscript.

All authors approved the final version.

Funding

This research was funded by the EU HORIZON 2020 Research and Innovation Program (European Joint Programming Initiative "A healthy diet for a healthy life" "JPI HDHL" and the ERA-NET co-fund HDHL-INTIMIC), GA no. 727565.

Provenance and peer review

This article was commissioned and was externally peer reviewed.

Declaration of competing interest

The authors acknowledge the support of the funder, the EU HORIZON 2020 Research and Innovation program. The funder had no role in the design of the study; in the collection, analyses, or interpretation of the data; in the writing of the manuscript, or in the decision to publish the results.

References

[1] The World Health Organization. The Global Health Observatory. Global health estimates: Leading causes of death. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death. (Accessed 25 August 2023).
[2] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J. Clin. 71 (2021) 209–249, https://doi.org/10.3322/caac.21660.
[3] WHO, International Agency for Research on Cancer. Latest Global Cancer Data. https://www.iarc.who.int/faq/latest-global-cancer-data-2020-qa/. (Accessed 18 June 2023).
[4] K.D. Miller, L. Nogueira, A.B. Mariotto, J.H. Rowland, K.R. Yabroff, C.M. Alfano, et al., Cancer treatment and survivorship statistics, CA Cancer J Clin 69 (2019) 363–385, https://doi.org/10.3322/caac.21565.
[5] S.M. Bluethmann, A.B. Mariotto, J.H. Rowland, Anticipating the "silver tsunami": prevalence trajectories and comorbidity burden among older cancer survivors in the United States, Cancer Epidemiol. Biomark. Prev. 25 (2016) 1029–1036, https://doi.org/10.1158/1055-9965.EPI-16-0133.
[6] J. Emery, P. Butow, J. Lai-Kwon, L. Nekhlyudov, M. Rynderman, M. Jefford, Management of common clinical problems experienced by survivors of cancer, Lancet 399 (2022) 1537–1550, https://doi.org/10.1016/S0140-6736(22)00242-2.
[7] A.M. Lewandowska, M. Rudzki, S. Rudzki, T. Lewandowski, B. Laskowska, Environmental risk factors for cancer - review paper, Ann. Agric. Environ. Med. 26 (2019) 1–7, https://doi.org/10.26444/aaem/94299.
[8] W.C. Willett, F. Sacks, A. Trichopoulou, G. Drescher, A. Ferro-Luzzi, E. Helsing, D. Trichopoulos, Mediterranean diet pyramid: a cultural model for healthy eating, Am. J. Clin. Nutr. 61 (6 Suppl) (1995) 1402S–1406S, https://doi.org/10.1093/ajcn/61.6.1402S.
[9] C. Davis, J. Bryan, J. Hodgson, K. Murphy, Definition of the Mediterranean diet; a literature review, Nutrients 7 (2015) 9139–9153, https://doi.org/10.3390/nu7115459.
[10] W. Willett, J. Rockström, B. Loken, M. Springmann, T. Lang, S. Vermeulen, et al., Food in the Anthropocene: the EAT-lancet commission on healthy diets from sustainable food systems, Lancet 393 (2019) 447–492, https://doi.org/10.1016/S0140-6736(18)31788-4.
[11] A. Cano, S. Marshall, I. Zolfaroli, J. Bitzer, I. Ceausu, P. Chedraui, et al., The Mediterranean diet and menopausal health: an EMAS position statement, Maturitas 139 (2020) 90–97, https://doi.org/10.1016/j.maturitas.2020.07.001.
[12] M.L. Sánchez-Sánchez, A. García-Vigara, J.J. Hidalgo-Mora, M.A. García-Pérez, J. Tarín, A. Cano, Mediterranean diet and health: a systematic review of epidemiological studies and intervention trials, Maturitas 136 (136) (2020) 25–37, https://doi.org/10.1016/j.maturitas.2020.03.008.
[13] M.S. Farvid, E. Sidahmed, N.D. Spence, K. Mante Angua, B.A. Rosner, J.B. Barnett, Consumption of red meat and processed meat and cancer incidence: a systematic review and meta-analysis of prospective studies, Eur. J. Epidemiol. 36 (2021) 937–951, https://doi.org/10.1007/s10654-021-00741-9.
[14] H.J. Luijendijk, How to create PICO questions about diagnostic tests, BMJ Evid. Based Med. 26 (2021) 155–157, https://doi.org/10.1136/bmjebm-2021-111676.

[15] R. Karki, S.M. Man, T.D. Kanneganti, Inflammasomes and Cancer, Cancer, Immunol. Res. 5 (2017) 94–99, https://doi.org/10.1158/2326-6066.CIR-16-0269.
[16] A. Dandekar, R. Mendez, K. Zhang, Cross talk between ER stress, oxidative stress, and inflammation in health and disease, Methods Mol. Biol. 1292 (2015) 205–214, https://doi.org/10.1007/978-1-4939-2522-3_15.
[17] J.J. Hidalgo-Mora, L. Cortés-Sierra, M.A. García-Pérez, J.J. Tarín, A. Cano, Diet to reduce the metabolic syndrome associated with menopause. The logic for olive oil, Nutrients 12 (2020) 3184, https://doi.org/10.3390/nu12103184.
[18] L. Schwingshackl, J. Morze, G. Hoffmann, Mediterranean diet and health status: active ingredients and pharmacological mechanisms, Br. J. Pharmacol. 177 (2020) 1241–1257, https://doi.org/10.1111/bph.14778.
[19] C.G. Fraga, K.D. Croft, D.O. Kennedy, F.A. Tomás-Barberán, The effects of polyphenols and other bioactives on human health, Food Funct. 10 (2019) 514–528, https://doi.org/10.1039/c8fo01997e.
[20] M. Bonaccio, G. Pounis, C. Cerletti, M.B. Donati, L. Iacoviello, G. de Gaetano, MOLI-SANI Study Investigators, Mediterranean diet, dietary polyphenols and low grade inflammation: results from the MOLI-SANI study, Br. J. Clin. Pharmacol. 83 (2017) 107–113, https://doi.org/10.1111/bcp.12924.
[21] A. Yammine, A. Namsi, D. Vervandier-Fasseur, J.J. Mackrill, G. Lizard, N. Latruffe, Polyphenols of the Mediterranean diet and their metabolites in the prevention of colorectal cancer, Molecules 26 (2021) 3483, https://doi.org/10.3390/molecules26123483.
[22] M. Bucciantini, M. Leri, P. Nardiello, F. Casamenti, M. Stefani, Olive polyphenols: antioxidant and anti-inflammatory properties, Antioxidants (Basel) 10 (2021) 1044, https://doi.org/10.3390/antiox10071044.
[23] R. Moral, E. Escrich, Influence of olive oil and its components on breast cancer: molecular mechanisms, Molecules 27 (2022) 477, https://doi.org/10.3390/molecules27020477.
[24] R.M. de Pablos, A.M. Espinosa-Oliva, R. Hornedo-Ortega, M. Cano, S. Arguelles, Hydroxytyrosol protects from aging process via AMPK and autophagy; a review of its effects on cancer, metabolic syndrome, osteoporosis, immune-mediated and neurodegenerative diseases, Pharmacol. Res. 143 (2019) 58–72, https://doi.org/10.1016/j.phrs.2019.03.005.
[25] A. Beam, E. Clinger, L. Hao, Effect of diet and dietary components on the composition of the gut microbiota, Nutrients 13 (2021) 2795, https://doi.org/10.3390/nu13082795.
[26] E.K. Mitsou, A. Kakali, S. Antonopoulou, K.C. Mountzouris, M. Yannakoulia, D. B. Panagiotakos, et al., Adherence to the Mediterranean diet is associated with the gut microbiota pattern and gastrointestinal characteristics in an adult population, Br. J. Nutr. 117 (2017) 1645–1655, https://doi.org/10.1017/S0007114517001593.
[27] G. Merra, A. Noce, G. Marrone, M. Cintoni, M.G. Tarsitano, A. Capacci, et al., Influence of Mediterranean diet on human gut microbiota, Nutrients 13 (2020) 7, https://doi.org/10.3390/nu13010007.
[28] L. Crudele, E. Piccinin, A. Moschetta, Visceral adiposity and cancer: role in pathogenesis and prognosis, Nutrients 13 (2021) 2101, https://doi.org/10.3390/nu13062101.
[29] W.S. Garrett, Cancer and the microbiota, Science 348 (2015) 80–86, https://doi.org/10.1126/science.aaa4972.
[30] C.A. Brennan, W.S. Garrett, Gut microbiota, inflammation, and colorectal cancer, Annu. Rev. Microbiol. 70 (2016) 395–411, https://doi.org/10.1146/annurev-micro-102215-095513.
[31] T.M. Karpiński, M. Ożarowski, M. Stasiewicz, Carcinogenic microbiota and its role in colorectal cancer development, Semin. Cancer Biol. 86 (Pt 3) (2022) 420–430, https://doi.org/10.1016/j.semcancer.2022.01.004.
[32] T. Irrazábal, A. Belcheva, S.E. Girardin, A. Martin, D.J. Philpott, The multifaceted role of the intestinal microbiota in colon cancer, Mol. Cell 54 (2014) 309–320, https://doi.org/10.1016/j.molcel.2014.03.039.
[33] A. Koh, F. De Vadder, P. Kovatcheva-Datchary, F. Bäckhed, From dietary Fiber to host physiology: short-chain fatty acids as key bacterial metabolites, Cell 165 (2016) 1332–1345, https://doi.org/10.1016/j.cell.2016.05.041.
[34] G. Pagliai, E. Russo, E. Niccolai, M. Dinu, V. Di Pilato, A. Magrini, et al., Influence of a 3-month low-calorie Mediterranean diet compared to the vegetarian diet on human gut microbiota and SCFA: the CARDIVEG study, Eur. J. Nutr. 59 (2020) 2011–2024, https://doi.org/10.1007/s00394-019-02050-0.
[35] T.S. Ghosh, S. Rampelli, I.B. Jeffery, A. Santoro, M. Neto, M. Capri, et al., Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries, Gut 69 (2020) 1218–1228, https://doi.org/10.1136/gutjnl-2019-319654.
[36] O. Illescas, M. Rodríguez-Sosa, M. Gariboldi, Mediterranean diet to prevent the development of colon diseases: a meta-analysis of gut microbiota studies, Nutrients 13 (2021) 2234, https://doi.org/10.3390/nu13072234.
[37] A. Trichopoulou, A. Kouris-Blazos, M.L. Wahlqvist, C. Gnardellis, P. Lagiou, E. Polychronopoulos, et al., Diet and overall survival in elderly people, BMJ 311 (1995) 1457–1460, https://doi.org/10.1136/bmj.311.7018.1457.
[38] M. de Lorgeril, P. Salen, J.L. Martin, I. Monjaud, P. Boucher, N. Mamelle, Mediterranean dietary pattern in a randomized trial: prolonged survival and possible reduced cancer rate, Arch. Intern. Med. 158 (1998) 1181–1187, https://doi.org/10.1001/archinte.158.11.1181.
[39] M. Schulpen, P.A. van den Brandt, Adherence to the Mediterranean diet and overall cancer incidence: the Netherlands Cohort Study, J. Acad. Nutr. Diet. 121 (2021) 242–252, https://doi.org/10.1016/j.jand.2020.07.025.
[40] I. Yiannakou, M.R. Singer, P.F. Jacques, V. Xanthakis, R.C. Ellison, L.L. Moore, Adherence to a Mediterranean-style dietary pattern and cancer risk in a prospective cohort study, Nutrients 13 (2021) 4064, https://doi.org/10.3390/nu13114064.
[41] L. Serra-Majem, B. Román-Viñas, A. Sanchez-Villegas, M. Guasch-Ferré, D. Corella, C. La Vecchia, Benefits of the Mediterranean diet: epidemiological and molecular aspects, Mol. Asp. Med. 67 (2019) 1–55, https://doi.org/10.1016/j.mam.2019.06.001.
[42] Y. Zhong, Y. Zhu, Q. Li, F. Wang, X. Ge, G. Zhou, et al., Association between Mediterranean diet adherence and colorectal cancer: a dose-response meta-analysis, Am. J. Clin. Nutr. 111 (2020) 1214–1225, https://doi.org/10.1093/ajcn/nqaa083.
[43] J. Morze, A. Danielewicz, K. Przybyłowicz, H. Zeng, G. Hoffmann, L. Schwingshackl, An updated systematic review and meta-analysis on adherence to Mediterranean diet and risk of cancer, Eur. J. Nutr. 60 (2021) 1561–1586, https://doi.org/10.1007/s00394-020-02346-6.
[44] A. Castelló, M. Rodríguez-Barranco, N. Fernández de Larrea, P. Jakszyn, A. Dorronsoro, P. Amiano, et al., Adherence to the Western, prudent and Mediterranean dietary patterns and colorectal cancer risk: findings from the Spanish cohort of the European prospective investigation into cancer and nutrition (EPIC-Spain), Nutrients 14 (2022) 3085, https://doi.org/10.3390/nu14153085.
[45] S. Moazzen, K.W.J. van der Sloot, R.J. Vonk, G.H. de Bock, B.Z. Alizadeh, Diet quality and upper gastrointestinal cancers risk: a Meta-analysis and critical assessment of evidence quality, Nutrients 12 (2020) 1863, https://doi.org/10.3390/nu12061863.
[46] L. Álvarez-Álvarez, F. Vitelli-Storelli, M. Rubín-García, N. Aragonés, E. Ardanaz, G. Castaño-Vinyals, et al., Relationship between the risk of gastric cancer and adherence to the mediterranean diet according to different estimators. MCC-Spain Study, Cancers (Basel) 13 (2021) 5281, https://doi.org/10.3390/cancers13215281.
[47] D. Nucci, M. Nardi, A. Cinnirella, E. Campagnoli, M. Maffeo, P.M. Perrone, et al., Adherence to Mediterranean diet and risk of pancreatic cancer: systematic review and meta-analysis, Int. J. Environ. Res. Public Health 29 (2023) 2403, https://doi.org/10.3390/ijerph20032403.
[48] N. Afshar, A.M. Hodge, N. Shivappa, J.R. Hébert, G.G. Giles, D.R. English, et al., Dietary inflammatory index, alternative healthy eating Index-2010, Mediterranean Diet Score and the risk of pancreatic cancer, Cancer Epidemiol. 82 (2023), 102295, https://doi.org/10.1016/j.canep.2022.102295.
[49] H. Steel, S.Y. Park, T. Lim, D.O. Stram, C.I. Boushey, J.R. Hébert, et al., Diet quality and pancreatic cancer incidence in the multiethnic cohort, Cancer Epidemiol. Biomark. Prev. 32 (2023) 123–131, https://doi.org/10.1158/1055-9965.EPI-22-0564.
[50] M. Dianatinasab, M. Rezaian, E. HaghighatNezad, Z. Bagheri-Hosseinabadi, S. Amanat, S. Rezaeian, et al., Dietary patterns and risk of invasive ductal and lobular breast carcinomas: a systematic review and meta-analysis, Clin. Breast Cancer 20 (2020) e516–e528, https://doi.org/10.1016/j.clbc.2020.03.007.
[51] E. Ubago-Guisado, M. Rodríguez-Barranco, A. Ching-López, D. Petrova, E. Molina-Montes, P. Amiano, et al., Evidence update on the relationship between diet and the Most common cancers from the European prospective investigation into cancer and nutrition (EPIC) study: a systematic review, Nutrients 13 (2021) 3582, https://doi.org/10.3390/nu13103582.
[52] S. Männistö, K. Harald, T. Härkänen, M. Maukonen, J.G. Eriksson, S. Heikkinen, et al., Association between overall diet quality and postmenopausal breast cancer risk in five Finnish cohort studies, Sci. Rep. 11 (2021) 16718, https://doi.org/10.1038/s41598-021-95773-2.
[53] S. Cheng, Q. Zheng, G. Ding, G. Li, Mediterranean dietary pattern and the risk of prostate cancer: a meta-analysis, Medicine (Baltimore) 98 (2019), e16341, https://doi.org/10.1097/MD.0000000000016341.
[54] L. Schneider, L.J. Su, L. Arab, J.T. Bensen, L. Farnan, E.T.H. Fontham, et al., Dietary patterns based on the Mediterranean diet and DASH diet are inversely associated with high aggressive prostate cancer in PCaP, Ann. Epidemiol. 29 (2019) 16–22.e1, https://doi.org/10.1016/j.annepidem.2018.08.012.
[55] A. Bahrami, S. Khalesi, E. Makiabadi, S. Alibeyk, M. Hajigholam-Saryazdi, E. Hejazi, Adherence to the Mediterranean diet and the risk of lung cancer: a systematic review and dose-response meta-analysis of observational studies, Nutr. Rev. 80 (2022) 1118–1128, https://doi.org/10.1093/nutrit/nuab117.
[56] H. Du, T. Cao, X. Lu, T. Zhang, B. Luo, Z. Li, Mediterranean diet patterns in relation to lung cancer risk: a meta-analysis, Front. Nutr. 9 (2022), 844382, https://doi.org/10.3389/fnut.2022.844382.
[57] W.J.A. Witlox, F.H.M. van Osch, M. Brinkman, S. Jochems, M.E. Goossens, E. Weiderpass, et al., An inverse association between the Mediterranean diet and bladder cancer risk: a pooled analysis of 13 cohort studies, Eur. J. Nutr. 59 (2020) 287–296, https://doi.org/10.1007/s00394-019-01907-8.
[58] M. Dianatinasab, E. Forozani, A. Akbari, N. Azmi, D. Bastam, M. Fararouei, et al., Dietary patterns and risk of bladder cancer: a systematic review and meta-analysis, BMC Public Health 22 (2022) 73, https://doi.org/10.1186/s12889-022-12516-2.
[59] Y. Mahamat-Saleh, I. Cervenka, M. Al Rahmoun, I. Savoye, F.R. Mancini, A. Trichopoulou, et al., Mediterranean dietary pattern and skin cancer risk: a prospective cohort study in French women, Am. J. Clin. Nutr. 110 (2019) 993–1002, https://doi.org/10.1093/ajcn/nqz173.
[60] A. Leone, M.A. Martínez-González, A. Martin-Gorgojo, R. Sánchez-Bayona, R. De Amicis, S. Bertoli, et al., Mediterranean diet, dietary approaches to stop hypertension, and pro-vegetarian dietary pattern in relation to the risk of basal cell carcinoma: a nested case-control study within the Seguimiento Universidad de Navarra (SUN) cohort, Am. J. Clin. Nutr. 112 (2020) 364–372, https://doi.org/10.1093/ajcn/nqaa127.
[61] M. Solans, Y. Benavente, M. Saez, A. Agudo, S. Naudin, F.S. Hosnijeh, et al., Adherence to the Mediterranean diet and lymphoma risk in the European prospective investigation into cancer and nutrition, Int. J. Cancer 145 (2019) 122–131, https://doi.org/10.1002/ijc.32091.

[62] F. Llaha, V. Cayssials, M. Farràs, A. Agudo, M. Sandström, A.K. Eriksen, et al., Adherence to Mediterranean diet and the risk of differentiated thyroid cancer in a European cohort: the EPIC study, Front. Nutr. 9 (2022), 982369, https://doi.org/10.3389/fnut.2022.982369.
[63] J. Xie, E.M. Poole, K.L. Terry, T.T. Fung, B.A. Rosner, W.C. Willett, et al., A prospective cohort study of dietary indices and incidence of epithelial ovarian cancer, J. Ovarian Res. 7 (2014) 112, https://doi.org/10.1186/s13048-014-0112-4.
[64] Y.H. Zhang, Z. Li, M.Z. Tan, Association between diet quality and risk of ovarian and endometrial cancers: a systematic review of epidemiological studies, Front. Oncol. 11 (2021), 659183, https://doi.org/10.3389/fonc.2021.659183.
[65] C.L. Shapiro, Cancer survivorship, N. Engl. J. Med. 379 (2018) 2438–2450, https://doi.org/10.1056/NEJMra1712502.
[66] M. Jefford, D. Howell, Q. Li, K. Lisy, J. Maher, C.M. Alfano, et al., Improved models of care for cancer survivors, Lancet 399 (2022) 1551–1560, https://doi.org/10.1016/S0140-6736(22)00306-3.
[67] A.J. Kim, D.S. Hong, G.C. George, Dietary influences on symptomatic and non-symptomatic toxicities during cancer treatment: a narrative review, Cancer Treat. Rev. 108 (2022), 102408, https://doi.org/10.1016/j.ctrv.2022.102408.
[68] S.Y. Park, M. Kang, Y.B. Shvetsov, V.W. Setiawan, C.J. Boushey, C.A. Haiman, et al., Diet quality and all-cause and cancer-specific mortality in cancer survivors and non-cancer individuals: the multiethnic cohort study, Eur. J. Nutr. 61 (2022) 925–933, https://doi.org/10.1007/s00394-021-02700-2.
[69] E.L. Van Blarigan, S. Zhang, F.S. Ou, A. Venlo, K. Ng, C. Atreya, et al., Association of diet quality with survival among people with metastatic colorectal cancer in the cancer and leukemia B and southwest oncology group 80405 trial, JAMA Netw. Open 3 (2020), e2023500, https://doi.org/10.1001/jamanetworkopen.2020.23500.
[70] M. Di Maso, L. Dal Maso, L.S.A. Augustin, A. Puppo, F. Falcini, C. Stocco, et al., Adherence to the Mediterranean diet and mortality after breast cancer, Nutrients 12 (2020) 3649, https://doi.org/10.3390/nu12123649.
[71] I.J. Ergas, E.M. Cespedes Feliciano, P.T. Bradshaw, J.M. Roh, M.L. Kwan, J. Cadenhead, et al., Diet quality and breast cancer recurrence and survival: the pathways study, J.N.C.I. Cancer Spectr. 5 (2021), pkab019, https://doi.org/10.1093/jncics/pkab019.
[72] M. Di Maso, L.S.A. Augustin, F. Toffolutti, C. Stocco, L. Dal Maso, D.J.A. Jenkins, et al., Adherence to Mediterranean diet, physical activity and survival after prostate cancer diagnosis, Nutrients 13 (2021) 243, https://doi.org/10.3390/nu13010243.
[73] M. Mantzorou, M. Tolia, A. Poultsidi, G.K. Vasios, D. Papandreou, S. Theocharis, et al., Adherence to Mediterranean diet and nutritional status in women with breast cancer: what is their impact on disease progression and recurrence-free patients' survival? Curr. Oncol. 29 (2022) 7482–7497, https://doi.org/10.3390/curroncol29100589.
[74] J.M. Schenk, M. Liu, M.L. Neuhouser, L.F. Newcomb, Y. Zheng, K. Zhu, et al., Dietary patterns and risk of Gleason grade progression among men on active surveillance for prostate cancer: results from the canary prostate active surveillance study, Nutr. Cancer 75 (2023) 618–626, https://doi.org/10.1080/01635581.2022.2143537.
[75] M. Barchitta, A. Maugeri, R. Magnano San Lio, A. Quattrocchi, F. Degrassi, F. Catalano, et al., The effects of diet and dietary interventions on the quality of life among breast cancer survivors: a cross-sectional analysis and a systematic review of experimental studies, Cancers (Basel) 12 (2020) 322, https://doi.org/10.3390/cancers12020322.
[76] G. Porciello, C. Montagnese, A. Crispo, M. Grimaldi, M. Libra, S. Vitale, et al., Mediterranean diet and quality of life in women treated for breast cancer: a baseline analysis of DEDiCa multicentre trial, PLoS One (2020), e0239803, https://doi.org/10.1371/journal.pone.0239803.
[77] S. Artale, N. Grillo, S. Lepori, C. Butti, A. Bovio, S. Barzaghi, et al., A nutritional approach for the management of chemotherapy-induced diarrhea in patients with colorectal cancer, Nutrients 14 (2022) 1801, https://doi.org/10.3390/nu14091801.
[78] A.S. Kleckner, J.E. Reschke, I.R. Kleckner, A. Magnuson, A.M. Amitrano, E. Culakova, et al., The effects of a Mediterranean diet intervention on cancer-related fatigue for patients undergoing chemotherapy: a pilot randomized controlled trial, Cancers (Basel) 14 (2022) 4202, https://doi.org/10.3390/cancers14174202.
[79] B.J. Baguley, T.L. Skinner, D.G. Jenkins, O.R.L. Wright, Mediterranean-style dietary pattern improves cancer-related fatigue and quality of life in men with prostate cancer treated with androgen deprivation therapy: a pilot randomized control trial, Clin. Nutr. 40 (2021) 245–254, https://doi.org/10.1016/j.clnu.2020.05.016.