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REVIEW

Mediterranean diet and cancer risk: Current understanding and epidemiological evidence

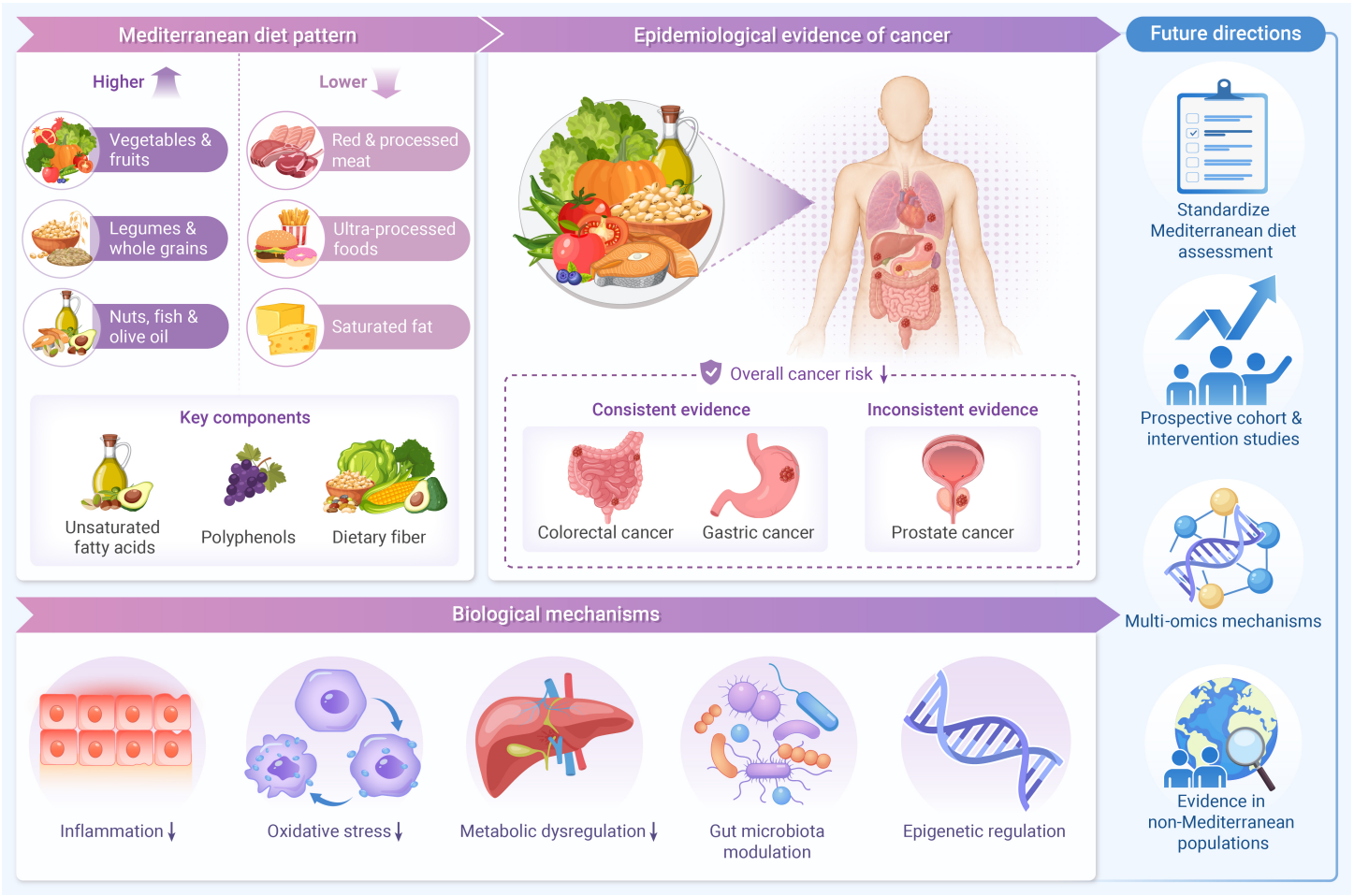
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GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Higher Mediterranean diet adherence is generally associated with a lower overall cancer risk.
- Evidence is more consistent for colorectal and gastric cancers than for other cancer types.
- Potential mechanisms involve inflammation, oxidative stress, metabolism, gut microbiota, and epigenetics.
- More studies in Asian and other non-Mediterranean populations are needed to inform cancer prevention.

REVIEW

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Mediterranean diet and cancer risk: Current understanding and epidemiological evidence

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Cancer is a major public health threat, leading to substantial mortality and disease burden worldwide. Carcinogenesis is modulated by a multitude of genetic, environmental, and lifestyle-related determinants, among which diet constitutes a critical modifiable risk factor. In recent years, Mediterranean diet (MedDiet), characterized by high intake of plant foods and low intake of red meat and processed foods, has garnered widespread attention for its potential health benefits. This narrative review synthesizes recent epidemiological studies, meta-analyses, and mechanistic research on the association between MedDiet and cancer. Current evidence generally suggests an inverse association between MedDiet adherence and overall cancer risk, particularly for colorectal and gastric cancers, whereas findings regarding other cancers remain controversial. Potential underlying mechanisms of MedDiet include the modulation of chronic inflammation, oxidative stress, metabolic dysregulation, gut microbiota, and epigenetics. In addition, key dietary components such as unsaturated fatty acids, polyphenols, and dietary fiber may play important roles in cancer prevention. However, variable exposure definitions, dietary measurement bias, between-site cancer heterogeneity, and regional disparities in dietary profiles limit the interpretation and generalizability of existing findings. Particularly, most available evidence has been derived from European and American populations, and its applicability to Asian and other non-Mediterranean populations requires further validation. Moreover, the predominance of observational studies limits causal inference. In the future, research should prioritize high-quality prospective and interventional studies, alongside multi-omics studies on mechanisms, to clarify the real effects and key biological mechanisms of MedDiet, thereby providing a more reliable scientific basis for cancer prevention and dietary guidance.

INTRODUCTION

Cancer is a major public health issue that poses serious threats to human health and socioeconomic development worldwide. According to GLOBOCAN 2024 released by the International Agency for Research on Cancer (IARC), there were approximately 20.6 million new cancer cases and 9.8 million cancer-related deaths globally in 2024, with lung cancer, breast cancer, colorectal cancer, prostate cancer, and gastric cancer being the most common types.[1] Cancer is the result of the long-term combined effects of genetic susceptibility, environmental exposures, and lifestyle factors. Existing research indicates that approximately 38% of new cancer cases worldwide in 2022 were attributable to modifiable risk factors, including smoking, alcohol consumption, and unhealthy breastfeeding practices, among others.[2] This suggests that cancer prevention should not only rely on early screening, diagnosis, and treatment, but should also emphasize lifestyle interventions such as diet.

In recent years, a large body of research has shown that dietary patterns play an important role in the onset, progression, and prognosis of cancer.[3] The cancer prevention recommendations jointly issued by the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) also emphasize the importance of following appropriate dietary patterns and viewing diet and lifestyle as an integrated whole.[4] Unlike traditional studies that focus on a single nutrient or food component, dietary pattern analysis captures overall dietary structure and the synergistic effects among foods, and has therefore become an important approach in nutritional epidemiology. Among different dietary patterns, the Mediterranean diet (MedDiet) has attracted widespread attention due to its potential protective role against cardiovascular, metabolic, and neurodegenerative diseases.[5-7] Its potential value in cancer prevention has also been gradually recognized.[8]

As a dietary pattern derived from the traditional dietary structure of Mediterranean coastal countries, MedDiet is rich in dietary fiber, polyphenolic compounds, polyunsaturated fatty acids, and other antioxidant compounds, which are believed to be a key basis for its health benefits.[8] Previous studies have suggested that MedDiet may influence carcinogenesis through multiple mechanisms, including chronic inflammation, oxidative stress, metabolic changes, gut microbiota alterations, and influencing epigenetics.[8-10]

This narrative review aims to provide a structured synthesis of epidemiological evidence regarding the association between MedDiet and the risk of overall cancer and various cancer types, and to analyze the potential biological mechanisms involved. We also identify the limitations in current research regarding study design, exposure assessment, and causal inference, as well as outline future research directions, with the aim of providing guidance for the development of primary cancer prevention and nutritional intervention strategies.

As a narrative review, this article was developed through a structured literature search and critical synthesis. We searched PubMed, Embase, and Web of Science for articles published up to August 2026. The search strategy combined terms related to the MedDiet, dietary assessment tools, cancer outcomes, site-specific cancers, and potential biological mechanisms. Representative search terms included "Mediterranean diet", "Mediterranean diet score", combined with "cancer", "neoplasm", as well as mechanism-related terms such as "inflammation", "oxidative stress", "gut microbiota", "metabolomics", or "epigenetics". We also manually screened the reference lists of included articles and relevant reviews to identify additional eligible studies. Only studies published in English were considered. We prioritized systematic reviews and meta-analyses, large prospective cohort studies, randomized intervention studies, representative case-control studies, and mechanistic studies related to MedDiet and cancer-related biological pathways. Studies were excluded if they were not clearly related to MedDiet, focused only on isolated nutrients without reflecting the overall dietary pattern, or were weakly relevant to cancer outcomes or cancer-related mechanisms.

DEFINITION AND ASSESSMENT OF MEDDIET

Origins and development of MedDiet

MedDiet is a traditional dietary pattern derived from a specific historical, geographical, and cultural context. The concept of MedDiet can be traced back to Ancel Keys and his Seven Countries Study, which originally referred to a dietary pattern followed by residents of Mediterranean olive planting areas in the 1960s, such as Greece and southern Italy, and characterized by low intake of saturated fat and high intake of vegetable oils, particularly olive oil.[11-12] In the Seven Countries Study, Keys found that this dietary pattern was associated with a lower risk of coronary heart disease, thereby promoting subsequent scientific interest in MedDiet.[11]

With socioeconomic development and changes in dietary patterns driven by globalization, the specific composition of MedDiet is evolving. Estruch and Salas-Salvadó point out that while the traditional MedDiet provides a solid foundation for health, it can be further optimized in the modern context based on new evidence of chronic diseases. Rather than simply replicating the traditional diet of the 1960s, the modern MedDiet has been updated by emphasizing extra-virgin olive oil, nuts, fatty fish, whole grains, and lower sodium intake while preserving its core dietary structure.[13]

In recent years, with advances in nutritional science and public health, the concept of MedDiet has gradually expanded from a traditional dietary pattern to a comprehensive lifestyle model that integrates nutritional health, cultural heritage, and environmental sustainability. The MedDiet was first inscribed on the Representative List of the Intangible Cultural Heritage of Humanity by United Nations Educational, Scientific and Cultural Organization (UNESCO) in 2010, and was then expanded in 2013 to become a transnational cultural heritage project involving multiple countries.[14-15] The definition given by UNESCO is not limited to food types or nutritional composition; rather, it regards MedDiet as a set of skills, knowledge, rituals, symbols and traditions concerning crops, harvesting, fishing, animal husbandry, conservation, processing, cooking, and particularly the sharing and consumption of food.[15] This broader interpretation is also reflected in the updated MedDiet pyramid proposed by Bach-Faig et al., which incorporates moderation, socialization, culinary activities, physical activity, adequate rest, seasonality and traditional, local, eco-friendly and biodiverse products.[16] The new model proposed by the Italian Society of Human Nutrition also reflects this change, emphasizing the principles of sustainability, including local, seasonal, and minimally processed foods while discouraging food waste. However, though the concept of the MedDiet has now become quite broad, it is worth noting that the current research on the role of MedDiet in cancer risk is generally limited to the traditional definition of diet pattern.

MedDiet-related assessment scores

Since MedDiet is a holistic dietary pattern rather than a single food component or nutrient, adherence is usually assessed using dietary scores. In epidemiological and nutritional intervention studies, MedDiet is typically assessed using an *a priori* dietary index, in which predefined food groups and scoring method are used to quantify adherence, rather than *a posteriori* dietary index extracting dietary patterns from the data using statistical methods such as factor analysis and principal component analysis.[17] The most widely used tools include the Mediterranean Diet Score (MDS), the Alternate Mediterranean Diet Score (aMED), and the Mediterranean Diet Adherence Screener (MEDAS).[18-20] These tools differ in food group classification, cutoff selection, and alcohol scoring, which may influence exposure classification, effect estimates, and the comparability of findings across cancer studies.

The MDS proposed by Trichopoulou et al. is believed the earliest index used to assess adherence to MedDiet in the general population.[17] This original index was based on eight characteristics of the traditional MedDiet (vegetables, legumes, fruits and nuts, grains, meat and meat products, ethanol, dairy products, and the ratio of monounsaturated fats to saturated fats) among older adults in rural Greece.[18] In the later 9-point version, fish intake was additionally incorporated.[21]

The core of MDS is the dichotomization of each food group based on the population's median intake. For components considered beneficial, an intake above the median is assigned 1 point; for components considered detrimental, an intake below the median is assigned 1 point. Ethanol intake within moderate limits is assigned 1 point. Ultimately, a higher total score indicates better adherence to the MedDiet.[18,21] The advantage of this score is its simple structure, ease of use in large cohorts, and the ability to incorporate overall dietary patterns as a single exposure variable into the model. However, its major limitation is the use of median within study population as the cut-off point, which highly relies on the distribution of the sample. The same score may represent substantially different absolute intake in different countries and dietary contexts. This undermines the comparability between different studies and may also make "high adherence" not truly representative of traditional MedDiet.

In order to adapt to the dietary structure of populations outside the Mediterranean region, Fung et al. further proposed the aMED based on MDS. While retaining the core principles of the traditional MedDiet, aMED makes adjustments to certain food categories. For example, it excludes potato products from the vegetable group, separates fruit and nuts into two groups, eliminates the dairy group, includes whole-grain products only, and includes only red and processed meats for the meat group.[19] The modified aMED has been widely used in epidemiological studies in the United States and other non-Mediterranean countries. However, as a score using the median value within the study population as a cutoff point, it still has limitations similar to those of the MDS.

Different from the median-based MDS and aMED, MEDAS used in the Prevención con Dieta Mediterránea (PREDIMED) study is a 14-item rapid screening tool based on preset intake targets. MEDAS consists of twelve questions on food consumption frequency and two questions on food intake habits considered characteristic of the Spanish MedDiet. Each question was scored 0 or 1. Questions on food intake habits include whether using olive oil as the principal source of fat for cooking and preferring white meat over red meat. Twelve foods of concern include olive oil, vegetables, fruit, red meat or sausages, animal fat, sugar-sweetened beverages, red wine, pulses, fish, commercial pastries, nuts and sofrito (a traditional sauce of tomatoes, garlic, onion, or leeks) respectively.[20]

The advantage of MEDAS lies in its use of predefined, absolute intake thresholds, which facilitates intervention monitoring, rapid screening, and comparisons across studies. As an index originally designed for the Spanish region, its shortcomings lie in the fact that there are too many items reflecting the background of Spanish cuisine, such as sofrito being a specialty sauce in Spain, while the intake thresholds for red wine and olive oil may require cultural adaptation in non-Mediterranean countries. Validation studies in Turkish and German populations suggest that MEDAS has potential for cross-cultural application, but item-level agreement varies across dietary contexts, supporting the need for local validation before direct application.[22-23]

In addition to the three commonly used MedDiet-related indexes mentioned above, there are also some less frequently used scores, such as the relative Mediterranean Diet score (rMED), the modified Mediterranean Diet score (mMED), and the Mediterranean Style Dietary Pattern Score (MSDPS). While these indexes differ in terms of food group selection and score calculation, they are generally based on the three indexes mentioned above.

When it comes to MedDiet-related cancer risk, there are still some specific issues related to the assessment of MedDiet that need to be considered. Firstly, the practice of assigning points for moderate alcohol consumption in above three traditional indexes is controversial in the context of cancer prevention. Though moderate red wine consumption with meals is part of the traditional MedDiet, alcohol itself is a well-established risk factor for various cancers. Therefore, in the study of breast cancer, head and neck cancer, liver cancer, colorectal cancer and other cancers, the inclusion of alcohol may weaken, mask, or even reverse the true association between the MedDiet and cancer risk. Some cancer-related studies have therefore used alcohol-excluded MedDiet scores, ultimately obtaining a significant inverse association between MedDiet and cancer risk. Secondly, traditional MDS and aMED rely on sample-specific medians, which are suitable for relative ranking of populations within a single cohort, but are not conducive to cross-regional comparisons, for high adherence may correspond to different absolute intakes in different regions. Besides, the current diverse MedDiet scoring system also creates additional barriers to such cross-study comparisons, as studies using different indexes are typically not directly comparable. Finally, the application of MedDiet in non-Mediterranean regions requires following core principles rather than mechanically replicating. Martínez-González et al. emphasize that, while it is possible to adapt MedDiet to non-Mediterranean countries, cultural adaptation is needed by preserving core characteristics such as olive oil, plant-based foods, low red meat, and low processed foods.[24] Therefore, the choice of a MedDiet score should not be viewed merely as a technical and operational detail, but as an important methodological source of heterogeneity that may lead to inconsistent findings in MedDiet-related cancer research. Future studies on the association between MedDiet and cancer risk should clearly report the composition of the index, and conduct sensitivity analyses using alcohol-excluded scores when appropriate. At the same time, efforts should be made to develop a new MedDiet assessment index that is more suitable for cancer prevention and cross-cultural comparisons.

MEDDIET AND CANCER RISK: EPIDEMIOLOGICAL EVIDENCE

Epidemiological studies have examined the association between MedDiet adherence and the risk of overall cancer incidence, cancer mortality, and several site-specific cancers, suggesting a potential protective role of MedDiet (Table 1). To facilitate interpretation across cancer types, we applied a descriptive grading framework rather than a formal GRADE assessment.

Table 1. Representative epidemiological studies and meta-analyses on Mediterranean diet adherence and cancer risk.

Section	Cancer site	Representative study	Study design	Effect estimates	Evidence level and pattern
Overall cancer risk	/	Trichopoulou et al.[21]	Cohort study	All-cause mortality: HR=0.75, 95% CI: 0.64-0.87; Cancer mortality: HR=0.76, 95% CI: 0.59-0.98	Moderate; Relatively consistent inverse association
		Schwingshackl et al.[25]	Meta-analysis	Incidence/mortality: RR=0.90, 95% CI: 0.86–0.95	
		Morze et al.[26]	Meta-analysis	Mortality: RR=0.87, 95% CI: 0.82-0.92; All-cause mortality among cancer survivors: RR=0.75, 95% CI: 0.66-0.86	
Digestive system cancers	Colorectal cancer	Zhong et al.[27]	Meta-analysis	Incidence: RR=0.90, 95% CI: 0.84-0.96; Per 2-point increment, RR=0.96, 95% CI: 0.94-0.99; Rectal cancer, RR=0.82, 95% CI: 0.71-0.95	Moderate; Relatively consistent inverse association
		Ungvari et al.[28]	Meta-analysis	Incidence: HR=0.84, 95% CI: 0.78-0.91	
		Moazzen et al.[29]	Meta-analysis	Incidence: OR=0.84, 95% CI: 0.78-0.90	
		Jafari Nasab et al.[30]	Meta-analysis	Colorectal adenomas incidence: OR=0.79, 95% CI: 0.73-0.85	
	Gastric cancer	Bai et al.[31]	Meta-analysis	Incidence: OR=0.43, 95% CI: 0.29–0.63 (case-control studies); OR=0.84, 95% CI: 0.77–0.92 (cohort studies)	Moderate; Relatively consistent inverse association
		Zhu et al.[32]	Meta-analysis	Incidence: RR=0.71, 95% CI: 0.59-0.84; per 1-point increment, RR=0.95, 95% CI: 0.94-0.96	
		Schulpen et al.[33]	Cohort study	Male incidence: gastric cardia adenocarcinoma, HR=0.48, 95% CI: 0.26-0.89; gastric non-cardia adenocarcinoma, HR=0.65, 95% CI: 0.45-0.94	
	Pancreatic cancer	Nucci et al.[34]	Meta-analysis	Incidence: HR=0.82, 95% CI: 0.76-0.88	Low; Suggestive inverse association
		Julián-Serrano S et al.[35]	Cohort study	Incidence: HR=0.82, 95% CI: 0.73-0.93	
Hormone-dependent cancers	Breast cancer	van den Brandt et al.[36]	Cohort study	ER- incidence: HR=0.60, 95% CI: 0.39-0.93; overall risk excluded alcohol: HR=0.92, 95% CI: 0.87-0.98	Low; Subtype-specific inverse association
		Buckland et al.[37]	Cohort study	Overall risk excluded alcohol: HR=0.94, 95% CI: 0.88-1.00; postmenopausal: HR=0.93, 95% CI: 0.87-0.99; ER-/PR- incidence: HR=0.80, 95% CI: 0.65-0.99	
		Dianatinasab et al.[38]	Meta-analysis	invasive ductal carcinoma: RR=0.77, 95% CI: 0.72-0.82; invasive lobular carcinoma: RR=0.76, 95% CI: 0.64-0.87	
	Prostate cancer	Schwingshackl et al.[25]	Meta-analysis	Incidence: RR=0.96, 95% CI: 0.92-0.99	Low; Inconclusive
		Morze et al.[26]	Meta-analysis	Incidence: RR=0.98, 95% CI: 0.93-1.04	
		Cheng et al.[39]	Meta-analysis	Incidence: RR=0.95, 95% CI: 0.90-1.01	
Head and neck cancers and respiratory system cancers	Head and neck cancer	Zalaquett et al.[40]	Meta-analysis	Incidence: OR=0.56, 95% CI: 0.37-0.86	Low; Suggestive inverse association
		Shrivastava et al.[41]	Meta-analysis	Oral and oropharyngeal cancer: per 1-point increment, OR=0.71, 95% CI: 0.63-0.79	
	Lung cancer	Bahrami et al.[42]	Meta-analysis	Incidence: RR=0.84, 95% CI: 0.77-0.91; per 2-point increment, RR=0.94, 95% CI: 0.91-0.96; former smoker, RR=0.81, 95% CI: 0.74-0.89	Low; Suggestive inverse association
		Anic et al.[43]	Cohort study	Incidence: HR=0.85, 95% CI: 0.79-0.91; former smoker, HR=0.81, 95% CI: 0.74-0.89	
Other types of cancer	Bladder cancer	Dianatinasab et al.[44]	Meta-analysis	Incidence: OR=0.73, 95% CI: 0.52-0.94 (case-control studies); RR=0.93, 95% CI: 0.88-0.97 (cohort studies)	Very low; Limited or emerging evidence
	Skin cancer	Leone et al.[45]	Nested case-control study	Basal cell carcinoma incidence: OR=0.28, 95% CI: 0.10-0.77	Very low; Limited or emerging evidence
	Liver cancer	Morze et al.[26]	Meta-analysis	Incidence: RR=0.64, 95% CI: 0.54-0.75	Very low; Limited or emerging evidence

Note: Evidence level and patterns are descriptive summaries and are not intended to represent formal GRADE ratings. They were assigned according to the type and amount of available evidence, study design, endpoint relevance, consistency of findings, and major methodological limitations. Cancer incidence and mortality were considered more direct endpoints than intermediate biomarkers or precancerous outcomes. Some meta-analyses are updated versions of earlier work and may include overlapping primary studies; therefore, they should not be interpreted as fully independent evidence sources. Abbreviations: HR, hazard ratio; CI, confidence interval; RR, relative risk; OR, odds ratio; ER-, ER negative

Evidence was considered to have high certainty when supported by multiple large prospective cohort studies or randomized intervention studies with direct cancer incidence or mortality endpoints. Evidence was considered to have moderate certainty when supported by several prospective studies or meta-analyses with direct cancer endpoints and broadly consistent findings, but with limitations such as observational design, residual confounding, heterogeneity, or overlap among primary studies. Evidence was considered to have low certainty when findings were based on fewer studies, case-control designs, subgroup-specific results, inconsistent estimates, or substantial concerns about confounding and heterogeneity. Evidence was considered to have very low certainty when cancer-specific evidence was sparse, indirect, based on small studies, or insufficient to support a stable conclusion. Using this framework, no cancer type was classified as having high certainty, largely because most available evidence is observational.

Overall cancer risk

Numerous epidemiological studies have examined the relationship between MedDiet and the risk of overall cancer incidence and mortality. Overall, higher adherence to MedDiet has been consistently associated with a reduced risk of overall cancer incidence and cancer-related mortality, and the level of evidence was graded as moderate.

In a prospective study involving 22,043 Greek adults, each 2-point increase in MedDiet adherence was associated with a 25% lower risk of all-cause mortality and a 24% lower risk of cancer mortality.[21] Evidence from successive meta-analyses further supports this inverse association. One meta-analysis with more than 1.4 million participants reported that individuals with the highest adherence had an approximately 10% lower risk of overall cancer incidence or mortality than those with the lowest adherence.[25] The study was updated three times later, each time incorporating newly published research, and reached similar conclusions.[26,46-47] In the most comprehensive update, which included 117 studies and more than 3.2 million participants, high adherence to MedDiet was associated with a significant reduction in the risk of cancer mortality, as well as a reduction in all-cause mortality among cancer survivors.[26]

Digestive system cancer

Colorectal cancer is one of the most extensively studied cancer types in MedDiet research, with evidence level classified as moderate and generally supporting an inverse association. A meta-analysis of prospective cohort studies showed that compared with the group with the lowest MedDiet adherence, the group with the highest adherence had a 10% lower risk of colorectal cancer incidence. A dose-response analysis further showed that for every 2-point increase in MedDiet adherence, the risk of colorectal cancer decreased by 4%. In subgroup analyses by anatomical site, adherence to the MedDiet was associated with a reduced risk of rectal cancer, but was not statistically significant for proximal or distal colon cancer.[27] Another meta-analysis involving more than 2.21 million participants reported similar findings, showing that individuals with higher adherence to MedDiet had a 16% lower risk of colorectal cancer, and this association was consistent across both sexes.[28] Meta-analysis by Moazzen et al. also reported similar results.[29]

Beyond its association with colorectal cancer risk, MedDiet may also be associated with the development of precancerous colorectal lesions. A meta-analysis incorporating six observational studies found that higher adherence to MedDiet was associated with a 21% lower risk of colorectal adenomas, suggesting that MedDiet may exert its potential effects at various stages of carcinogenesis.[30]

A substantial body of evidence has also been accumulated regarding gastric cancer, and the evidence level was graded as moderate. A meta-analysis incorporating 11 studies showed that adherence to MedDiet was inversely associated with the risk of gastric cancer, and this trend was consistent across both gastric cardia adenocarcinoma and gastric non-cardia adenocarcinoma.[31] Another dose-response meta-analysis involving more than 1.3 million participants reached similar conclusions. Compared with the lowest adherence group, the highest adherence group had a 29% lower risk of gastric cancer; and each 1-point increase in the adherence was associated with a 5% lower risk.[32] In addition, this analysis found that this inverse association was more pronounced in non-Western countries, suggesting that genetic background, basic dietary structure, and environmental exposures may influence the association between MedDiet and gastric cancer.

Particularly, the strength of potential protective role against gastric cancer may differ by sex. A Dutch cohort study containing 120,000 participants showed that the alternate Mediterranean diet score without alcohol (aMEDr) was inversely associated with the risk of gastric cardia adenocarcinoma and gastric non-cardia adenocarcinoma in both genders, but statistical significance was observed only among men.[33] Subgroup analyses in the aforementioned meta-analysis also suggested similar gender differences.[31] This may be related to differences between male and female in dietary structure, alcohol consumption, hormone levels, *Helicobacter pylori* infection, and other lifestyle factors. However, further validation through additional prospective studies is still needed.

With regard to pancreatic cancer, the available evidence is relatively limited compared to that for colorectal and gastric cancers; therefore, the level of evidence was graded as low, though current findings suggest an inverse association. A meta-analysis with more than 1.3 million participants reported that higher adherence to MedDiet was associated with a lower risk of pancreatic cancer.[34] Similarly, an analysis of the prospective National Institutes of Health-American Association of Retired Persons (NIH-AARP) Diet and Health Study, which included 535,824 participants, found that compared with those in the lowest aMED quintile, those in the highest had an 18% lower risk of pancreatic cancer.[35] Besides, it is worth noting that statistical significance was only observed among females in the gender-specific subgroup analysis by Nucci et al., suggesting that the secretion of sex hormones, metabolic status, or other gender-related factors may influence the association between MedDiet and pancreatic cancer.[34]

Hormone-dependent cancer

Breast cancer is one of the most widely studied hormone-dependent cancers; however, the overall evidence was considered to have low certainty because the association appears subtype-specific and is influenced by menopausal status and alcohol scoring. Research suggests that there is a weak or inconsistent association between MedDiet and overall breast cancer risk, but it may be more pronounced in specific molecular and histological subtypes. Furthermore, menopausal status may also influence the effects of MedDiet. In a Netherlands cohort study with 62,573 postmenopausal women, adherence to MedDiet was significantly associated with a reduced risk of ER negative (ER-) breast cancer, whereas the associations with overall breast cancer and ER positive (ER+) breast cancer were weak and not statistically significant. Meta-analytic evidence from the same study also suggested that the inverse association was more apparent for ER- group.[36]

The treatment of alcohol within MedDiet scoring is particularly crucial in breast cancer research. When alcohol was excluded from the MedDiet score in Netherlands study, the score became significantly inversely associated with overall breast cancer risk, suggesting that as an independent risk factor for various cancers, alcohol may attenuate, obscure or even reverse the potential protective role of MedDiet against breast cancer. Evidence from a large European cohort using an alcohol-excluded adapted relative Mediterranean diet (arMED) score yielded similar results, with inverse associations observed for overall breast cancer, postmenopausal breast cancer, and ER-/PR- molecular subtype.[37] These results illustrate that the choice of MedDiet scoring method, especially alcohol treatment, can materially influence the estimated association between MedDiet adherence and cancer risk.

Besides, menopausal status can also influence the potential protective role of MedDiet. Two studies have indicated that no association was found between MedDiet-related scores and breast cancer in premenopausal women.[37,48] As for histopathologic subtypes, a meta-analysis showed that high adherence to MedDiet was associated with a reduced risk of invasive ductal carcinoma and invasive lobular carcinoma.[38]

In contrast, evidence level regarding MedDiet and prostate cancer risk was graded as low, with current findings remaining inconclusive. Though an earlier meta-analysis suggested a slight inverse association between MedDiet adherence and prostate cancer risk,[25] this association did not reach statistical significance in a later updated meta-analysis involving more published research.[26] In addition, subgroup analyses by another meta-analy-

sis for advanced prostate cancer, localized prostate cancer, and fatal prostate cancer also failed to reveal any statistically significant associations.[39]

Head and neck cancers and respiratory system cancers

Head and neck cancers have been a rapidly growing area of research in recent years, with the level of available evidence graded as low because much of it comes from case-control studies. A meta-analysis of case-control studies reported that high adherence to MedDiet was associated with an approximately 44% lower risk of head and neck cancer. Further component analysis revealed that higher intake of fruits and vegetables was associated with a reduced risk, suggesting that a high dietary fiber intake may be an important component in reducing cancer risk.[40] As for oral and oropharyngeal cancers, a category of head and neck cancers, the meta-analysis also suggested that each one-unit increase in MDS was associated with a 29% reduction in cancer risk.[41]

With regard to lung cancer, the level of evidence was graded as low because residual confounding by smoking remains a major concern, though meta-analyses and cohort studies suggest an inverse association. A meta-analysis found that adherence to MedDiet was associated with a reduced risk of lung cancer. Dose-response analysis further showed that for every 2-point increase in MedDiet adherence, the risk of lung cancer decreased by approximately 6%.[42] Another analysis based on the NIH-AARP Diet and Health Study reached similar conclusions. Compared with the lowest quintile adherence group, the highest quintile was associated with a 15% reduction in lung cancer risk.[43]

Particularly, both studies found that the inverse association was more pronounced among former smokers compared to non-smokers and current smokers.[42-43] Bahrami et al. suggested that this might be related to the lifestyle changes of former smokers after quitting. They tend to adopt a healthier lifestyle such as increasing physical activity, and these behaviors may have a synergistic effect with MedDiet.[42]

Other types of cancer

Apart from the types of cancer mentioned above, evidence for other cancer types remains limited, with the overall evidence level considered very low due to sparse cancer-specific evidence. A meta-analysis of bladder cancer found that, whether in case-control studies or cohort studies, high MedDiet adherence was always associated with a reduced risk of bladder cancer.[44] In terms of skin cancer, a nested case-control study found that the risk of basal cell carcinoma was significantly lower in the highest quintile compared with the lowest quintile of MedDiet adherence.[45] As for liver cancer, the current evidence primarily comes from a single, continuously updated comprehensive meta-analysis rather than cancer-specific prospective studies,[26,46-47] and existing evidence is still limited.

POTENTIAL BIOLOGICAL MECHANISMS

The MedDiet is thought to exert its effects through synergistic interactions of multiple dietary components, potentially involving biological pathways related to inflammation, oxidative stress, metabolic regulation, gut microbiota, and epigenetics (Table 2).[8]

Anti-inflammatory effects

Chronic inflammation is a well-recognized contributor to carcinogenesis and tumor progression, and it serves as a key link between dietary factors and cancer development. A chronic inflammatory state can promote DNA damage, abnormal cell proliferation, angiogenesis, and cell invasion, thereby contributing to multiple stages of cancer development.[49] Elevated levels of inflammation-related cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), have been widely recognized as being associated with an increased risk of various types of cancer.[50]

Several studies have shown that MedDiet has anti-inflammatory effects and can significantly reduce levels of inflammatory markers. In a randomized, single-blind trial, MedDiet intervention reduced the levels of high-sensitivity C-reactive protein (CRP), IL-6, IL-7, and IL-18 compared to the control group which followed a prudent diet, while endothelial function was also improved.[51] Other studies have also supported similar findings. A meta-analysis by Koelman et al., which included 22 RCTs, showed that among various dietary patterns, MedDiet was most effective in reducing levels of inflammatory markers, with a mean difference of -1.07 pg/mL for IL-6, -0.46 pg/mL for IL-1β, and -1.00 mg/L for CRP.[52] Another meta-analysis including 17 intervention trials further reported reductions in high-sensitivity CRP, IL-6 and intracellular adhesion molecule-1, as well as improvement in endothelial function.[53]

This anti-inflammatory effect may stem primarily from components in the MedDiet such as polyphenolic compounds, unsaturated fatty acids, and dietary fiber. Hydroxytyrosol, tyrosol, and β-sitosterol in olive oil, as well as n-3 polyunsaturated fatty acids in fish, are believed to have anti-inflammatory effects.[54] In addition, the high dietary fiber content in whole grains, vegetables, fruits, and legumes may further reduce inflammation levels in the human body.[55]

Anti-oxidative stress

Oxidative stress is a key mechanism in carcinogenesis. Excessive accumulation of reactive oxygen species (ROS) can lead to DNA damage, genomic instability, and cell proliferation, thereby promoting genetic mutations and malignant transformation.[56] Previous studies have shown that chronic oxidative stress is closely associated with the development of various cancers, including breast cancer, prostate cancer, colorectal cancer, and ovarian cancer.[57]

MedDiet is rich in natural antioxidants and is therefore considered to have strong antioxidant potential. In an observational study of breast cancer survivors, Negrati et al. found that MDS was significantly positively correlated with the antioxidants β-carotene and lycopene, as well as antioxidant capacity.[58] A RCT conducted by Skouroliakou et al. showed that, compared with the control group, breast cancer survivors who followed a MedDiet had significantly higher levels of vitamin C, an antioxidant biomarker, in their blood.[59]

This antioxidant effect may come from the olive oil polyphenols found in MedDiet, including hydroxytyrosol, oleuropein, and tyrosol. These compounds can scavenge free radicals, reduce lipid peroxidation levels, and enhance the activity of antioxidant enzyme systems.[60] An observational sub-study conducted by Sureda et al. based on the PREDIMED study found that MedDiet supplemented with extra-virgin olive oil or MedDiet supplemented with nuts can increase the activity of superoxide dismutase and catalase, while reducing the activity of xanthine oxidase.[61] In addition, resveratrol, a polyphenol found in red wine, is also believed to have antioxidant and anticancer properties.[62] However, there is still controversy regarding the potential benefits of red wine consumption, as alcohol itself is also a known carcinogen. Therefore, most current studies emphasize the effects of polyphenols themselves rather than encouraging alcohol consumption.

Metabolic regulation

Metabolic dysregulation is considered an important indirect mechanism linking modern lifestyles and cancer risk. The IARC Working Group noted that excess body fat is associated with an increased risk of various cancers; the mechanisms involved include sex hormone metabolism, insulin and insulin-like growth factor (IGF) signaling, and adipokines or inflammatory pathways.[63] Insulin and IGF can promote tumor cell growth through signaling pathways such as Akt and MAP,[64] and dysfunction of adipose tissue can also influence obesity-related cancers through mechanisms such as insulin resistance, chronic inflammation, and adipokines.[65]

Substantial evidence suggests that MedDiet adherence is associated with improvements in metabolic risk factors. Numerous studies have shown that MedDiet can improve insulin sensitivity and reduce the risk of developing type 2 diabetes and metabolic syndrome. A RCT conducted by Esposito et al. in patients with metabolic syndrome found that the MedDiet significantly reduced the insulin resistance index and alleviated the symptoms of metabolic syndrome.[51] Another RCT yielded similar results.[66] In addition, a meta-analysis involving 57 controlled trials and 36,983 participants showed that the MedDiet can significantly improve weight, body mass index (BMI), blood glucose, insulin, the homeostatic model assessment of insulin resistance (HOMA-IR) index, and blood lipid.[67]

Gut microbiota

In recent years, gut microbiota has been recognized as one of the key

Table 2. Putative biological pathways linking Mediterranean diet adherence to cancer-related processes.

Biological pathway	MedDiet-related dietary features	Putative mediating links	Cancer-related implications
Anti-inflammatory effects	Polyphenols, unsaturated fatty acids, and dietary fiber	Reduced systemic inflammation; lower inflammatory cytokines and adhesion molecules, including CRP, IL-6, IL-1β, TNF-α	May reduce inflammation-related DNA damage, abnormal cell proliferation, angiogenesis, and invasion
Anti-oxidative stress	Natural antioxidants and polyphenols	Enhanced antioxidant capacity; reduced reactive oxygen species and lipid peroxidation; improved antioxidant enzyme activity	May reduce oxidative DNA damage, genomic instability, and mutation accumulation
Metabolic regulation	High plant-food intake and healthy fats	Improved body weight control, insulin sensitivity, glucose metabolism, lipid profiles, and obesity-related metabolic dysfunction	May influence cancer risk through insulin/IGF signaling, adipokines, sex hormone metabolism, and chronic low-grade inflammation
Gut microbiota modulation	Dietary fiber and polyphenols	Increased short-chain fatty acid production, especially butyrate; enrichment of fiber-degrading and SCFA-producing bacteria; modulation of bile acid metabolism	May affect cancer through anti-inflammatory effects, epithelial energy metabolism, histone deacetylase inhibition, apoptosis regulation, and reduced unfavorable bile acid profiles
Epigenetic regulation	Polyphenols and folate	Modulation of DNA methylation, miRNA expression, histone-related pathways, and telomere maintenance	May regulate tumor suppressor pathways, inflammatory signaling, cell cycle regulation, genomic stability, and cellular aging

Note: These pathways represent biologically plausible and putative mediating links rather than fully established causal mechanisms. Most mechanistic evidence is derived from biomarker studies, animal experiments, small human interventions, or studies using intermediate molecular outcomes instead of cancer incidence or mortality. Abbreviations: CRP, C-reactive protein; IL, interleukin; TNF-α, tumor necrosis factor-α; IGF, insulin-like growth factor; SCFAs, short-chain fatty acids.

mechanisms underlying the potential protective role of MedDiet. Gut microbiota not only participate in nutrient metabolism, but also profoundly influence the host immune responses, inflammation, and metabolic homeostasis, thereby affecting the onset and progression of cancer.[68]

MedDiet is rich in dietary fiber, which can be fermented by gut microbiota to produce short-chain fatty acids (SCFAs), particularly butyrate. In addition to serving as an important energy source for colonic epithelial cells, butyrate may exert anti-inflammatory and antitumor effects. It can influence the expression of genes related to cell proliferation and apoptosis by inhibiting histone deacetylases.[69-70] A study based on mouse model demonstrated that the potent tumor suppressive effect of fibers can only be exerted through the microbiota and butyrate.[70] Population-based studies further showed that high adherence to the MedDiet is associated with higher levels of SCFAs, *Prevotella*, and *Firmicutes* (two types of bacteria that break down plant polysaccharides and produce SCFAs), while those with low adherence have higher levels of trimethylamine oxide, a cancer risk factor, in their urine.[71] Another RCT yielded similar results: during the MedDiet intervention, levels of *Faecalibacterium prausnitzii* (a gut bacterium responsible for fiber degradation) and genes associated with butyrate metabolism both increased in the participants' intestines.[72]

In addition to SCFAs, bile acid metabolism has also been an important area in recent years. A high-fat diet can promote the abnormal accumulation of secondary bile acids, which are believed to have potential carcinogenic effects.[73] In contrast, the MedDiet may reduce the production of secondary bile acids by modulating the composition of the gut microbiota and bile acid metabolic pathways. A RCT showed that participants in MedDiet intervention group had lower concentrations of both primary and secondary bile acids in their stool compared with baseline levels.[72]

Epigenetics

In addition to the mechanisms mentioned above, MedDiet may also play a protective role through epigenetic mechanisms. Epigenetic alterations include DNA methylation, non-coding RNA regulation, and changes in telomere length. These processes can regulate gene expression without altering the DNA sequence, and abnormal epigenetic reprogramming has been considered an important molecular basis for cancer development.[74-76]

Dietary polyphenols abundant in MedDiet can influence DNA methyltransferases and miRNA networks, thereby influencing aberrant gene silencing and restoring tumor-suppressing pathways.[77] Besides, folate in plants, legumes and grains can also exert its effects by influencing DNA methylation.[78]

In an RCT based PREDIMED-Navarra study, MedDiet combined with extra virgin olive oil or nuts induced methylation at multiple CpG sites in peripheral blood leukocytes compared with a low-fat diet.[79] In patients with familial adenomatous polyposis (FAP), Illescas et al. found that a low-inflammatory MedDiet intervention could modulate fecal miRNA expression, involving pro-inflammatory ERK1/2, cell cycle regulation, and nutritional response pathways.[80] With regard to telomeres, a meta-analysis incorporating 8 cross-sectional studies and 13,733 participants showed that higher adherence to the MedDiet was associated with longer telomere length (standardized mean difference [SMD]=0.130), suggesting MedDiet may contribute to cancer prevention by maintaining genomic stability and delaying cellular aging.[81]

LIMITATIONS AND PROSPECTS

In general, existing research has provided substantial epidemiological evidence for the association between MedDiet and reduced risk of cancer. However, establishing whether these associations are causal remains a major research priority. Multiple systematic reviews and meta-analyses have shown that higher adherence to MedDiet is associated with a reduced risk of overall cancer, as well as colorectal, gastric, pancreatic, head and neck, lung, and certain subtypes of breast cancer; however, the strength of the evidence varies across different cancer types. Besides, inconsistencies in the definition of MedDiet across different studies, variations in adjustment factors, and differences in study design may all contribute to high heterogeneity.[47] In addition, the quality of the studies varies. A meta-analysis with 117 studies and more than 3.2 million participants found that except for a few outcomes such as overall cancer mortality and colorectal cancer that met moderate levels of evidence, most cancer types remained at a low or very low level.[26] Therefore, the current evidence may be better understood as indicating that MedDiet may have a general protective trend, with relatively consistent evidence for certain types of cancer, rather than simply concluding that it provides a definitive protective effect against all cancers.

Inconsistencies in exposure assessment are the primary issue limiting the quality of evidence in this field. As a complex dietary pattern, MedDiet often needs to be transformed into scoring tools such as MDS, aMED, rMED, mMED, and MEDAS in epidemiological studies. Though these various scores all aim to measure adherence to MedDiet, there are significant differences in terms of food group selection, score calculation, cutoff point selection, as well as the treatment of alcohol consumption. Furthermore, the scores used in previous studies did not fully align with the traditional MedDiet, especially in terms of distinguishing between whole grains and refined grains, olive oil and monounsaturated fatty acids, as well as red wine and total alcohol consumption,[17] which will make great differences in cancer-related studies. Previous

studies have suggested that refined grains, red meat and processed meat, and alcohol are closely associated with an increased risk of cancer; therefore, greater caution is warranted when conducting research on MedDiet in the context of cancer prevention. For future research, it is necessary to develop a MedDiet-related index that is more suitable for cancer prevention, with a particular focus on clarifying whether alcohol should be included, how it should be scored, and how to distinguish between whole grains and refined grains, extra virgin olive oil and other fat sources.

In addition, measurement error in dietary assessment is a well-recognized limitation. Most prospective cohort studies only assess dietary exposure once at baseline, whereas cancer development typically goes through a long latency period; changes in dietary habits during follow-up may lead to misclassification of exposure, thereby affecting the accuracy of risk estimates.[26,47] In addition, most dietary exposure assessments are currently conducted using questionnaires, but since they rely heavily on participants' recall, results are susceptible to recall bias and social desirability bias.[82] Previous studies have identified discrepancies between self-reported dietary intake and objective nutritional biomarkers,[83] which may bias effect estimates and contribute to inconsistencies across studies. These suggest that future studies should employ repeated dietary assessments, dynamic dietary trajectory analysis, and objective nutritional biomarkers to minimize the impact of misclassification on effect estimates. In recent years, the emergence and application of metabolomics and digital dietary recording tools have opened up new avenues for objective assessment, and such strategies could be further applied to cancer-related cohort studies in future to improve the accuracy and reproducibility of dietary pattern assessments.

In terms of study design, the current evidence regarding the MedDiet and cancer risk remains primarily based on observational studies, with limited ability to draw causal inferences. Due to poor adherence to long-term dietary interventions, high implementation costs, and ethical constraints, the number of RCTs that use cancer-related outcomes as their primary endpoints remains relatively limited in this field. Though prospective cohort studies and meta-analyses are superior to cross-sectional studies and case-control studies in terms of temporal sequence and strength of evidence, they are still short of fully supporting causal inferences. Reverse causation is another challenge that needs to be addressed. Some individuals may proactively change their dietary structures due to obesity, diabetes, metabolic disorders, or other health issues, thereby exhibiting a high level of adherence to MedDiet. In such cases, dietary changes may be the result of an increased risk of disease rather than the cause of a reduced risk. Though many studies have tried to mitigate this bias by excluding cancer cases diagnosed early in the follow-up period or by conducting sensitivity analyses, reverse causality is difficult to completely avoid due to the long incubation period of cancer. Finally, residual confounding remains a significant limitation in nutritional studies. As part of a multidimensional lifestyle complex, individuals with high adherence to MedDiet tend to adopt other healthy lifestyles, such as less smoking, higher levels of physical activity and lower BMI.[47] Therefore, in the future, more high-quality and large-scale RCTs should be designed to not only fully control confounding factors, but also conduct stratified analysis of smoking, drinking, obesity, infection, and genetic susceptibility during the design phase to identify populations for which MedDiet may offer the greatest preventive benefits.

The heterogeneity of cancer itself also determines that research on MedDiet cannot be limited just to overall cancer risk. Different types of cancer have distinct etiological profiles and precancerous progression pathways; even within the same cancer type, different anatomical sites, histological types, and molecular subtypes may exhibit varying sensitivities to dietary exposures. Existing studies have already suggested certain subtype differences in colorectal and breast cancers, but evidence regarding subtypes in other cancers remains insufficient. For cancer types where existing epidemiological evidence is unclear, subgroup analyses may yield new findings. Therefore, future research should make greater use of cancer registry data, pathological information, and molecular subtyping, and try to avoid using overall cancer incidence or a single cancer type as the sole endpoint.

There are also limitations in terms of geographic and population representativeness. The concept of MedDiet is rooted in the traditional lifestyle of the Mediterranean region, and PREDIMED study and several cohorts from Mediterranean countries have provided substantial evidence. However, research in non-Mediterranean regions, such as Asia and Africa, has been relatively limited. As noted by Morze in their meta-analysis, most included studies were conducted in Europe and United States, while there were fewer studies from Asian countries. This geographical imbalance may lead to heterogeneity, as there are differences in cancer spectrum, genetic backgrounds, environmental exposures, and dietary structures across different regions.[26] Recent studies in cardiometabolic and liver-related conditions have provided references for how MedDiet principles can be culturally adapted to Asian populations. In the TANGO randomized controlled trial, Chooi et al. evaluated a Mediterranean-like, culturally contextualized Asian diet in Singapore Chinese women with nonalcoholic fatty liver disease. Rather than directly replicating a MedDiet food list, the intervention preserved core MedDiet features, including high fiber and high-polyphenol extra-virgin olive oil, while preparing meals in line with Asian cuisine and incorporating locally acceptable foods such as soy milk, soy-based protein, oat bran, and millet.[84] A subsequent secondary analysis in women with metabolic dysfunction-associated steatotic liver disease also used this Asian-adapted MedDiet framework.[85] These studies suggest that MedDiet can be translated into an Asian dietary context by preserving its core nutritional principles while adapting food choices, meal formats, and alcohol treatment to local culture. However, such Asian-adapted MedDiet approaches have not yet been sufficiently applied or validated in cancer prevention research. Future studies should develop culturally adapted MedDiet or MedDiet-like scores for Asian populations and evaluate them in prospective cancer cohorts and intervention studies.

Apart from geographic and population applicability, future research on MedDiet should also move toward precision nutrition. Traditional dietary guidelines are typically based on average effects observed in populations. However, there may be significant differences in the biological responses of individuals to the same dietary pattern, which can be influenced by multiple factors including genetic background, age, sex, metabolic state, gut microbiota and lifestyle. As for MedDiet, its potential protective role may not manifest equally across all populations. For example, studies on lung cancer suggest that effects might be influenced by smoking status; similarly, the association observed in breast cancer studies may vary depending on hormone receptor status. These findings suggest that MedDiet should not only serve as a unified universal dietary recommendation; rather, further identification of which populations are likely to benefit most is needed. With the development of genetic susceptibility, metabolomics and gut microbiota, future research can establish individualized response prediction models, thereby advancing MedDiet-related research from the assessment of average effects to precision prevention.

In terms of biological mechanisms, though existing studies provide a plausible explanation for the potential protective role of MedDiet, the evidence currently remains indirect. Rather than directly demonstrating MedDiet's impact on cancer, current studies have focused more on intermediate cancer-related pathways such as inflammation, oxidative stress, gut microbiota, metabolic status, epigenetics. For example, a meta-analysis incorporating RCTs showed that MedDiet can reduce levels of inflammatory markers such as IL-6, IL-1β, and CRP; however, the study consisted primarily of individuals with chronic diseases, and the outcomes were inflammatory markers rather than precancerous lesions or cancer incidence.[52] Illescas et al. found that a low-inflammation MedDiet intervention in patients with FAP could modulate fecal miRNA and intestinal tissue gene expression, involving pathways related to inflammation, the cell cycle, and nutritional responses. This represents one of the most compelling pieces of human evidence to date supporting the chain of evidence linking precancerous state to dietary intervention, and then to molecular changes. However, this study remains a small-sample, single-arm, short-term intervention, and has not demonstrated that these molecular changes in precancerous lesions can translate into a reduced risk of cancer.[80] Therefore, the key limitation in current research on biological mechanisms lies not in a lack of potential pathways, but in the absence of a direct chain of evidence linking these pathways to long-term cancer outcomes.

In future, mechanism research should move from the analysis of single biomarkers to the integration of multi-omics and the validation of causal chains. By synchronously collecting dietary information, blood and fecal

samples, metabolomics, microbiota, inflammatory factors, epigenetics, and outcomes of precancerous lesions or cancer in long-term cohort or intervention studies, we can evaluate whether the improvement of MedDiet adherence precedes molecular changes, and whether these changes further mediate the reduction of precancerous lesions or cancer risk. Analytical approaches such as mediation analysis, Mendelian randomization, and other causal inference methods may further help distinguish true mechanistic mediators from correlated biomarkers.

CONCLUSION

In summary, current research on MedDiet and cancer risk has outlined an overall evidence framework, in which epidemiological studies suggest that it is associated with a reduced risk of various cancers, while mechanism studies indicate that it may exert its effects through pathways such as inflammation, oxidative stress, gut microbiota, metabolism, and epigenetics. However, it still faces challenges such as inconsistent definitions of exposure, errors in dietary measurement, limited ability to draw causal inferences, imbalance across cancer types and subtypes, limited evidence from non-Mediterranean regions, as well as an incomplete chain of mechanisms. In future, research should be built upon a unified and optimized assessment score of MedDiet adherence. By incorporating repeated dietary measurements, nutritional biomarkers, multi-omics data, large-scale prospective cohorts, and rigorous causal inference methods, studies should progressively advance from the general association between MedDiet and cancer risk toward addressing precision nutritional epidemiological questions: which type of MedDiet, in which population, through what mechanisms, confers protection against which specific cancers. This will help further transform the MedDiet from an empirical recommendation as a healthy dietary pattern into an evidence-based strategy that can be applied to primary cancer prevention and nutritional interventions for high-risk populations.

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AUTHOR CONTRIBUTIONS

Dr. WQ Li conceived the study, designed the overall framework and contributed to the manuscript revision; JE Zhao contributed to the literature collection and initial drafting.

DECLARATION OF INTERESTS

The authors declare no competing interests.

DATA AND CODE AVAILABILITY

No new data or code were generated in this study.