

Mediterranean Diet and Oral Health: Is There an Association? A Scoping Review

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Abstract

Mediterranean diet (MDi) has demonstrated a powerful preventing effect on various medical conditions, therefore, a positive effect on oral health may also be speculated. Also, tooth loss, pain or tooth mobility may discourage the consumption of specific food types, with affectance to MDi adherence. The aim of this study was to investigate the association between adherence to MDi and oral health in adult populations. The study protocol was registered in Open Science Framework, <https://osf.io/vxbnh/>, and adhered to PRISMA-ScR guidelines. Principal research questions were: 1) Does better oral health enable adults to better adhere to MDi? and 2) Does better adherence to MDi enable adult individuals to have better oral health? The content of three databases, Clarivate Analytics' Web of Science, Scopus, and PubMed was searched without language, date, or any other restrictions. The search results were imported into the Rayyan environment and from the initial 1127 studies identified only 20 remained after exclusion process. Three articles comprised the first group, revealing significant associations between various oral health parameters and adherence to MDi, with large variations in methodology and no safe conclusions. The studies investigating the effect of the level of adherence to MDi on various oral parameters were more numerous and revealed negative associations with the prevalence of periodontal disease and upper aero-digestive tract cancer. Further studies to explore the existence and direction of the association between oral health and MDi are needed, with public health interventions encouraging MDi to reduce the burden of oral conditions and other non-communicable diseases.

Key words: mediterranean diet; oral health; periodontal disease; oral and neck cancers; masticatory performance; antioxidants

Introduction

Since the first results of the landmark Seven Countries study, it became obvious that the Mediterranean diet (MDi) has a powerful preventing effect on cardiovascular disease^(1, 2). In the following decades, several cross-sectional, longitudinal, interventional, case-control studies, as well as systematic reviews have demonstrated the positive effect of MDi on the prevention of various diseases⁽³⁾. The most prominent benefits were reduction in mortality (4, 5), prevention of cardiovascular disease^(6, 7), metabolic syndrome^(7, 8), obesity^(9, 10, 11, 12) type 2 diabetes^(7, 13, 14), breast and upper aero-digestive tract (UADT) cancer^(15, 16, 17, 18). Also, a positive association was found between better adherence to MDi and lower incidence of cognitive problems^(19, 20, 21, 22), sleep apnea⁽²³⁾, renal diseases⁽²⁴⁾, and selected hormone-related cancers such as endometrial cancer⁽²⁵⁾.

Although MDi is not the only “healthy diet”, other dietary patterns failed to demonstrate such a strong beneficial association with disease prevention. An umbrella review comprising of 80 different meta-analyses examined a wide range of popular diets such as low-carbohydrate, high protein, palaeolithic, low glycaemic index, intermittent energy restriction, Nordic, vegetarian and Dietary Approaches to Stop Hypertension (DASH) and concluded that MDi has shown the most consistent association with cardiometabolic risk factors, without evidence of adverse health effects⁽²⁶⁾. Also, MDi has been recognised as a healthy dietary pattern in the Dietary Guidelines for Americans 2015–2020 from the United States Department of Agriculture⁽²⁷⁾. Due to all aforementioned positive effects on general health, key organisations recognised MDi as a prominent value for human health and supported its international promotion. In 2013, UNESCO proclaimed the MDi as an Intangible Cultural Heritage of Humanity⁽²⁸⁾.

The role of MDi in the prevention of non-communicable diseases (NCD) and cognitive impairment gains more significance considering the growing population of older adults worldwide and the relevant increased morbidity^(29, 31, 31). Although there are established genetic and environmental contributors to NCD risk, modifiable lifestyle-related factors, such as nutrition and physical activity, play an immense role in individual NCD development and prevention^(32, 33).

Since its introduction into the scientific world, MDi has changed in some of its characteristics, prevalence, economic, and ecological importance. The base of the MDi still consists of olive oil, and plants (vegetables, fruits, cereals, nuts) that provide key nutrients

and fibers^(4, 34, 35, 36) and should be consumed in high frequencies. Foods eaten in moderate amounts are dairy products, eggs, legumes, white meat, and fish (seafood) that are a good source of proteins. Consumption of red meat and processed meats should be in small quantities and limited frequency. Olive oil as monounsaturated fat is the principal source of dietary lipids because of its high nutritional quality. A moderate consumption of wine is recommended during meals. Sugar, candies, pastries, and sweetened soft drinks, are avoided and consumed only on special occasions⁽³⁷⁾. Modifications that are introduced in the MDi when applied in non-Mediterranean countries are mainly related to the source of fat, and the varieties of local fruit and vegetables⁽³⁸⁾. Seed oil (sunflower, canola, soya, or other seeds), as polyunsaturated fat, is mostly used in many non-Mediterranean countries. However, these oils don't present the antioxidant capacity of olive oil even though they are better than lard or butter⁽³⁸⁾.

In accordance with the strong positive correlation between MDi and general health, it is expected that a positive impact on oral health also exists. On the other hand, the status of oral tissues and functions may also affect adherence to MDi. A cross sectional study in older Greeks has shown that increased masticatory performance was independently associated with better adherence to the MDi⁽³⁹⁾. The stomatognathic system is the initial part of the digestive tract preparing the bolus for swallowing and its health status may affect food choices^(40, 41,42) including the components of MDi. Functional limitations like tooth loss, pain due to untreated caries, or tooth mobility due to severe periodontal disease may affect masticatory performance^(43, 44) and discourage the consumption of specific food types like fruits, seeds, and raw vegetables^(45, 44, 46,) that are important components of the MDi. Bearing in mind the data scarcity on the association between adherence to MDi and oral health, and especially the lack of any relevant systematic reviews, it was necessary to summarise the existing knowledge in this field and, based on the results, direct further research.

Therefore, the aim of this study was to investigate the association between adherence to MDi and oral health in adult populations.

Methods

Protocol and registration

The present scoping review adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines⁽⁴⁷⁾. The search process is also reported following the PRISMA-ScR guidelines of 2018. The study protocol is registered in Open Science Framework, <https://osf.io/vxbnh/>.

Research question and eligibility criteria

The PEO (Population, Exposure, Outcomes) strategy was used to formulate principal research questions: 1) Does better oral health (E) enable adult individuals (P) to better adhere to MDi (O)? and 2) Does better adherence to MDi (E) enable adult individuals (P) to have better oral health (O)?

In the scoping review, specific eligibility criteria were employed to ensure the relevance and consistency of included studies. Specifically, only research focusing on adult individuals was considered eligible, with studies involving children being excluded. Furthermore, only research exploring the MDi as a whole dietary pattern was included, while studies examining variations, such as "MDi style" diets, "alternative MDi", "healthy diet with Mediterranean components", etc. were excluded. Additionally, studies investigating oral/dental health in relation to the MDi were included. Notably, review papers and meeting abstracts were excluded from consideration to maintain the focus on primary research studies.

Information sources and search strategy

The content of three databases, Clarivate Analytics' Web of Science (including Web of Science Core Collection - WoS, Korean Journal Database - KCI, SciELO Citation Index - SCIELO, Preprint Citation Index, Grants Index, ProQuest™ Dissertations & Theses Citation Index), Scopus, and PubMed (including MEDLINE), was searched until January 6th, 2024, without language, date, or any other restrictions. The complete search strategy, including controlled vocabulary (Medical Subject Headings - MeSH, <https://www.ncbi.nlm.nih.gov/mesh>), free keywords, search operators (AND, OR, NEAR, W), and truncation (*, \$) used according to the searched database, is detailed in Supplementary Table 1. In the pursuit of relevant unpublished manuscripts, conference

papers, doctoral dissertations, and other grey literature, additional searches were conducted in resources like OpenGrey (<http://www.opengrey.eu>) and Google Scholar™ (first 100 returns), as well as other available digital repositories such as the Networked Digital Library of Theses and Dissertations (<http://www.ndltd.org>), Open Access Theses and Dissertations (<https://oatd.org>), DART-Europe E-theses Portal – DEEP (<https://www.dart-europe.org/basic-search.php>), and Opening access to UK theses – EThOS (<https://ethos.bl.uk>). Furthermore, snowballing and screening the reference lists of included studies and relevant previously published reviews were performed using citation indexes (Web of Science and Scopus). During the drafting phase of the paper in March 2024, a complete search of the primary databases was repeated, which led to the identification of three new relevant trials that have been included in this systematic review. The search results were imported into the Rayyan environment⁽⁴⁸⁾ for duplicate removal, initially performed using Rayyan's duplicate identification strategy, and then manually.

Study selection

The screening and study selection process comprised two phases, and two independent reviewers (AP and JJ) assessed the titles and abstracts of the retrieved records. Articles not meeting the inclusion criteria were excluded, and the full texts of the initially selected papers were accessed to determine their eligibility for inclusion. During the second stage of study selection, two independent reviewers (AP and AML) critically evaluated full texts of studies considered possibly relevant during the initial screening stage. Lists of relevant studies were compared, and any disagreements regarding the eligibility of specific studies were resolved through discussion with a third reviewer (AK).

Data extraction and analysis

The two reviewers (AP and EP) independently performed data extraction using a pre-established form (Microsoft Excel™, Microsoft Corporation, USA). Information from each study included in the final review was collected, encompassing the first author's name, journal, year of publication, study design type, setting, study population characteristics, implemented MDi questionnaire, oral health factor investigated, and key results. In case of any disagreements or uncertainties, a third reviewer (AK) was consulted to resolve them through discussion.

To comprehensively assess all aspects and identify variations in study characteristics and outcomes, the collected data were consolidated into evidence tables. These tables served as a descriptive summary, enabling the revelation of similarities and differences between studies, as well as determining their suitability for further synthesis or comparison methods. The adopted approach for data synthesis was the narrative synthesis method. The data were descriptively synthesised based on whether they exhibited significant, positive, negative, or null effects, as reported by the authors of included studies.

Results

Study selection

The sequence and details of the literature search are depicted in Figure 1, the PRISMA flowchart. Initially, 1127 studies were identified through the primary search, and 409 were excluded due to duplicates. Following the screening titles and abstracts, according to exclusion criteria, an additional 695 studies were excluded. In addition, by reviewing the references of relevant papers, one more study was found. Ultimately, 24 studies remained and were subjected to full-text evaluation. After carefully reviewing the full texts, 20 studies were included in the current scoping review. The list of excluded studies, along with the reasons or their exclusion, is provided in Supplementary Table 2. Thereafter, the studies were divided into two groups depending on the direction of causality between the MDi and oral health as indicated by the aims and content. The first group consisted of studies that examined the impact of oral health on adherence to the MDi (**Table 1**) and the second group consisted of studies that aimed to show how MDi adherence affects oral health (**Table 2**).

Does better oral health enable individuals to better adhere to Me Di?

The first group of studies consisted of only three research papers that primarily investigated oral health factors affecting adherence to MDi (Table 1). These studies varied in design, participants' characteristics and methodology. One was carried out in a Mediterranean country (Greece) ⁽³⁹⁾ and the other two ^(49, 50) in non-Mediterranean ones (Northern Ireland and the United States of America). The MDi scales varied among studies. Bousiou et al used the Mediterranean diet Index (MDI_BNC4H), Lohse et al. ⁽⁵⁰⁾ the 14-item Mediterranean Diet Questionnaire, and Logan et al. ⁽⁴⁹⁾ the Mediterranean Diet Score (MDS). Two investigations included older participants ^(39, 49) and one wider age groups ⁽⁵⁰⁾. Two studies

were cross sectional ^(39, 50), and one prospective ⁽⁴⁹⁾. Two studies included both interviews and oral examination ^(39, 49) and one ⁽⁵⁰⁾ only an online interview.

All studies revealed significant associations between various oral health parameters and adherence to MDi with large variation in the investigated factors and the outcomes. The number of teeth that was investigated in all studies revealed inconclusive findings. Logan et al. ⁽⁴⁹⁾ showed that having more than 21 teeth resulted in overall better future adherence to MDi and higher intake of fruit, vegetables, and nuts compared to other dental status categories (with fewer teeth and with dentures). However, Bousiou et al. ⁽³⁹⁾ and Lohse et al. ⁽⁵⁰⁾ didn't find any statistically significant associations between number of teeth and adherence to MDi scales. Bousiou et al. ⁽³⁹⁾ in the multivariate statistical analysis found that objectively recorded masticatory performance was the most important oral factor that was marginally significantly associated with adherence to MDi. Also, Bousiou et al. ⁽³⁹⁾ didn't find any significant association between adherence to MDI_BNC4H and rehabilitation with removable dentures. Logan et al. ⁽⁴⁹⁾ found that those with 21-28 teeth but without dentures had significantly higher MSD scores compared to all other dental status groups with fewer than 20 teeth even when removable dentures were present. Some indicators of periodontal disease (PD) that were examined did not reveal any significant association with better adherence to MDi. Tooth mobility objectively recorded ⁽³⁹⁾, and loose teeth and bleeding gums subjectively reported ⁽⁵⁰⁾ did not reveal any significant associations with the related MDi scales' scores.

Regarding oral hygiene behaviour and dental check ups regularity, the data were also inconclusive. Lohse et al. ⁽⁵⁰⁾ found that participants who followed MDi were more likely to have visited a dentist in the past year than those who did not. However, Bousiou et al. ⁽³⁹⁾ did not find any significant associations between adherence to MDi and dental visitation habits or frequency of oral hygiene.

Does better adherence to MDi enable individuals to have better oral health?

Seventeen studies were identified with the primary aim to investigate the effect of the level of adherence to MDi on various oral parameters (Table 2). Eight studies ⁽⁵¹⁻⁵⁸⁾ investigated the association of adherence to MDi with various PD indicators, three ^(59, 60, 61) with saliva indicators, one with Sjogren syndrome ⁽⁶²⁾ and five ⁽⁶³⁻⁶⁷⁾ with UADT cancers. Of those studies, nine ^(60, 59, 56, 54, 51, 63, 64, 65, 67) were conducted in Mediterranean countries. The MDi

scales applied were variant and included the Mediterranean Diet Adherence Screener (MEDAS) ^(53, 54, 56, 57, 60, 61), the Italian Mediterranean index score (ItMedIndex) ⁽⁵⁷⁾, the Mediterranean Diet Score (MDS) ^(56, 62, 63, 64, 65, 66, 67), the aMed ⁽⁵²⁾, the Mediterranean Diet Index ⁽⁵⁸⁾, the Mediterranean Diet Serving Score (MDSS)⁽⁵⁰⁾, the Mediterranean Dietary Pattern Adherence Index (MDP) ⁽⁶³⁾, and the Mediterranean Adequacy Index (MAI) ⁽⁶³⁾. The study participants were adults of various age groups.

The oral factor most frequently investigated was PD using various indicators such as bleeding on probing (BOP), probing pocket depth (PPD), gingival recession (GR), clinical attachment level (CAL), periodontal inflamed surface area (PISA), self-reported gingival health status, etc. All studies reported a beneficial effect of better adherence to MDi on periodontal health.

Five cross-sectional studies concluded that better adherence to MDi is associated with less frequent PD occurrence ^(51, 52, 54, 58, 53). Altun et al.⁽⁵²⁾ revealed a significant association between higher adherence to the MDi and lower odds of PD, specifically plaque index and bleeding on probing. Moreover, the odds of stage III/IV periodontitis were found to be 6 times higher in subjects with low MDi adherence compared to those with high adherence ⁽⁵⁴⁾. For each point of increase at the Mediterranean Diet Index scale, there were 18% greater odds of self-reporting very good or good gingival health among Chilean adults ⁽⁵⁸⁾. Radic et al. ⁽⁵¹⁾ showed that better adherence to MDi was associated with better periodontal status in kidney transplant recipients. Similarly, Wu et al. ⁽⁵³⁾ found that better MDi adherence was negatively associated with important PD parameters such as pocket depth and clinical attachment loss ⁽⁵³⁾.

In an interventional study, gingival inflammatory parameters (bleeding on probing, gingival index and periodontal inflamed surface area) were significantly reduced by adherence to a 6-week MDi dietary programme even when the plaque index remained constant ⁽⁵⁵⁾. The mechanism of this association was further explained by the effect of MDi on reducing serum omega-6 levels, through a mechanism affecting gingival inflammatory parameters ⁽⁵⁸⁾. Possible mechanisms of the positive effect of the MDi on PD lie in the possibility of changing the composition of saliva and the bacterial biofilm, hence contributing to the host defense immunomodulation ⁽⁵⁹⁾. Laiola et al. ⁽⁵⁹⁾ investigated the changes in the salivary microbial composition in overweight and obese subjects after following individually tailored MDi intervention for 8 weeks and didn't find any changes in the overall microbiota

composition but a significant decrease in the red bacterial complex that may be implicated in PD. Increased MDi adherence was found to lead to a significant decrease in the salivary concentration of periodontopathogenic microorganisms such as *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Treponema denticola* ⁽⁵⁹⁾ together with the increase of *Streptococcus cristatus* levels which has ability to act antagonistically to *P. gingivalis*. Moreover, *P. Intermedia* and *T. Denticola* are members of the “red bacterial complex”, which appear later in biofilm development and represent progressive PD ⁽⁵⁹⁾.

Shaalan et al. ⁽⁶⁰⁾ in their study in patients with diabetes type II and obesity, and controls found that saliva microbiota was associated with the level of adherence to MDi but not to a significant level. However, they showed specific changes in patients associated with the frequency of consumption of individual MDi items (sugar snacks, fish/shellfish and nuts). Iwasaki et al. ⁽⁵⁶⁾ reported a negative but not statistically significant association between better adherence to MDi and periodontitis among University students in Morocco, but his sample was very young (mean age 20.2 years) and only 6.6% had periodontitis. Nonetheless, olive oil consumption, which can be considered as the fundamental component of the MDi, showed a significant inverse association with periodontitis ⁽⁵⁶⁾.

Four case-control ^(63, 64, 65, 67) and one cross sectional ⁽⁶⁶⁾ studies investigated the association of adherence to MDi with UADT cancer and all agreed on a strong protective effect of MDi. The decrease in UADT cancer risk was 30% for a two-unit increase and 41% for a three-unit increase in MDS ⁽⁶⁵⁾. Besides the cancer incidence, better adherence to MDi prior to cancer diagnosis affected 5-year mortality ⁽⁶⁶⁾.

One study ⁽⁶²⁾ investigated the association of MDi with Sjogren syndrome and found that higher adherence to a MDi was associated with a lower likelihood of developing primary Sjogren syndrome.

DISCUSSION

This scoping review revealed 20 studies investigating the association between adherence to MDi and various oral health indicators that were divided into two groups based on the primary direction of this association. The inclusion criteria included only publications that

investigated the effect of full MDi scales' scores and not their individual components because the findings are more reliable, particularly when sample sizes are small ⁽⁶⁵⁾. Only three studies investigated the effect of oral factors on adherence to MDi and safe conclusions cannot be drawn. On the other hand, seventeen studies explored the effect of the level of adherence to MDi on oral health indicators, mainly PD and UADT cancer, showing a systematic negative association between better adherence to MDi and prevalence of disease. It should be noticed that the reviewed papers revealed increased inconsistencies in the methodology applied regarding both oral and MDi indicators posing difficulties in comparisons. Various indexes and scores for quantifying MDi adherence were implemented, using either cut off values classifying participants as high, moderate or low adherers to MDi or various scoring systems to credit or penalise individuals according to their level of adherence to each MDi component.

The effect of oral factors on food choices and nutrient intake are ambiguous, analogue as found in the present study regarding the effect of oral indicators on adherence to MDi. Some studies, conducted in non-Mediterranean countries, have shown that older adults with very few teeth (0-10) were less likely to choose dark green, orange vegetables, and whole grains, and were more likely to consume more calories from solid fat, alcohol and added sugar compared to those with 11 and more teeth ^(46, 68). Furthermore, deficiency of posterior functional units (opposing pair of natural or fixed prosthetic teeth) has been related to avoidance of vegetables and fibers and higher consumption of sugar-rich food ^(69, 70). Removable denture wearers showed less dietary variety and were often discouraged from eating hard food, mostly fruit and vegetables, compared to dentate older adults ^(71, 72, 73). Several studies did not find any significant improvement in food intake after removable dentures provision to edentulous people, ⁽⁷⁴⁾ while others have shown that those satisfied with their removable dentures received significantly higher amounts of vegetables in contrast to those unsatisfied ^(74, 75). A systematic review of the association of mastication with food and nutrient intake in older people found that studies reporting no associations were performed in developed countries where food is often processed to become softer and manageable by individuals with poor dental status ⁽⁷⁴⁾.

The effect of local culture on food choice can be revealed from studies performed in Greece, a Mediterranean country, in comparison to other European countries. Greek studies have shown that tooth loss and dentures' use did not have a significant impact on different food

types consumption^(78, 77). Older Greeks, with dental or chewing deficiencies, still consumed basic elements of MDi, such as cereals, fruits and vegetables, either by selecting those with softer texture or by preparing them to be easier to chew. For example, they ate oranges, grapes, tangerines, and melons, cut harder fruits like apples into small pieces, softened bread crust and rusks in water or milk or minced the meat. Regarding vegetables, “Ladera” (stewed vegetables in olive oil easy to chew) is the common way for their consumption together with boiling them and eating as a salad with the addition of raw olive oil. On the other hand, English complete denture wearers were more likely to avoid vegetables, grains, and other healthy but harder foods and settled for softer, sugary foods⁽⁸⁰⁾. These studies revealed an increased cultural effect on food preparation patterns enabling or impeding older people with poor dental status and/or chewing difficulties eating basic elements of MDi, like cereals, raw vegetables and fruits. Bousiou et al.⁽³⁹⁾ in an older community dwelling sample living in Athens, Greece concluded that the most important oral predictor for better adherence to MDi was good masticatory performance⁽³⁹⁾. The number and location of teeth is not the only predictor of good masticatory performance, that is a complex function affected by several factors such as tooth mobility, neuromuscular coordination, intraoral sensitivity, jaw-closing muscle force, tongue function, saliva quality and quantity, general medical condition, or ageing^(39, 43).

Moreover, apart from chewing process, hyposalivation, swallowing problems or oral neuromuscular dysfunction may affect food choices⁽⁴⁴⁾. Regarding PD, the reviewed studies^(39, 50) did not reveal any statistically significant association with adherence to MDi, but PD was not comprehensively measured using current validated clinical methodology and further investigation is needed. The above findings reveal the complex nature of food selection patterns, associated with various medical, oral, psychological, religious, socioeconomic and cultural factors^(39, 44) and the need to further investigate effective strategies to promote healthy dietary patterns like MDi.

The findings of the opposite direction of the association between adherence to MDi and oral health were clearer and revealed a general tendency for a protective dietary effect. The moderate to strong association between better MDi adherence and lower PD prevalence and severity is not surprising considering current evidence of the effect of certain “healthy foods”, integral to MDi, on the etiopathogenesis of PD. PD is a biofilm-mediated inflammation located in the periodontal tissue in response to the increased presence of bacteria in dental plaque. When an imbalance is created between periodontopathogenic

bacteria and the host's defense mechanisms, inflammation is triggered progressively. This imbalance is subject to the influence of several external factors, including nutrition^(80, 81). It has been shown that the consumption of at least 5 portions a day of vegetables (especially dark green and yellow ones) such as spinach, broccoli, yellow peppers, cabbage, onions, fruits rich in vitamin C such as black currants, grapefruit, oranges, and fruits rich in dietary fibers such as bananas, apples and plums can prevent developing aggressive form of PD and thus tooth loss⁽⁸²⁾. Intake of larger quantities of salad, fruit/vegetables, poultry, seafood, water, whole grains and lower intake of red/processed meat, showed a positive association with lower clinical attachment loss and, consequently, less chances of a more severe form of PD^(83, 84, 85). Particularly, wholegrain cereals are considered to have a prominent effect in the prevention of PD, mostly in lower interdental clinical attachment loss⁽⁵⁴⁾. Wholegrain consumption showed an association with lower systemic inflammatory markers, such as C-reactive protein, and decreased insulin resistance⁽⁸⁶⁾. Consequently, when insulin sensitivity is preserved, the production of glycation end products, oxidative stress and, accordingly, the release of cytokines is reduced, which has a positive effect on the periodontal tissue⁽⁸⁷⁾. Catechins and ellagic acids found in fruits, vegetables and nuts can inhibit the growth of *Prevotella intermedia* which has a significant role in the pathogenesis of PD⁽⁸⁸⁾. Additionally, it is considered that phytochemicals, including vitamin C (ascorbic acid), vitamin E (alpha-tocopherol), vitamin A, beta-carotene, and coenzyme Q-10 and minerals provided by fruits, vegetables, nuts, and whole grains in the MDi are effective for maintaining periodontal homeostasis⁽⁸⁹⁾. Olive oil is a key protective factor for PD, and in some studies, it was shown to be the only effective ingredient^(56, 90). An olive oil-enriched diet was found to protect mononuclear phagocyte system function⁽⁹¹⁾, and phagocyte abnormalities are among the key mechanisms in the pathogenesis of PD⁽⁸⁰⁾.

A significant protective effect of MDi diet was also recorded for UADT cancers^(62, 63, 64, 66, 67). The positive influence of MDi on infectious, inflammation and cancerogenic processes is based on its potential in modifying oxidative stress⁽⁹²⁾. The bioactive components from MDi that mainly act as antioxidants are polyphenols, vitamin C, vitamin E, and β -carotene^(89, 90, 91). Dietary polyphenols play an important role in preventing the disequilibrium between oxidative stress and antioxidant activities in the oral cavity, thereby preventing periodontal tissue destruction. Polyphenol intake was positively associated with S-type cystatins levels in saliva in a study by Louro et al.⁽⁶¹⁾ who investigated the association of MDi with saliva composition. Besides antioxidant capacities, polyphenols also carry anti-inflammatory

properties by interfering with a number of proinflammatory pathways and inhibits them, which results in reduction of synthesis and releasing of proinflammatory cytokines such as interleukin (IL)-1 β , IL-6, IL-8, and tumor necrosis factor (TNF- α)^(95, 96, 97). These positive effects of polyphenols have been demonstrated in other low grade inflammatory diseases such as cardiovascular and endocrine diseases, metabolic and immune disorders^(93, 98). In addition to anticancerogenic effect, phytochemicals that are involved in cellular differentiation and proliferation are also included in the synthesis and repair of DNA and in inhibition of the formation of carcinogenic chemicals in inflammatory response^(93, 99, 100, 101). High adherence to MDi has been associated with a lower risk of pancreatic, colorectum, breast, aerodigestive tract, prostate and liver cancer^(102, 103). Besides polyphenols, omega-3 fatty acids, from fish and nuts can affect cancer cell proliferation, angiogenesis and metastasis, slowing down cancer development⁽¹⁰⁴⁾. Also, animal studies have shown that extra virgin olive oil may induce cancer cell apoptosis and minimise DNA damage⁽¹⁰⁵⁾.

Machowicz et al.⁽⁶²⁾ concluded that adherence to the MDi was associated with a lower likelihood of having primary Sjogren Syndrome (pSS). Increasing MDi score for just one unit, was associated with a 19% decrease in the odds of having pSS. This positive effect was explained in terms of the fish intake since the MDS fish domain was inversely associated with pSS in both univariate and multivariate analysis. Fish intake has also been previously reported to reduce the risk of other autoimmune disorders such as rheumatoid arthritis^(106, 107).

Clarification of the association between oral health and adherence to MDi may lead to large public health benefits. The WHO has raised awareness of importance of good oral health in essential functions such as eating, breathing and speaking, and its contribution to overall health and quality of life, and developed the Global Strategy and Action Plan on Oral Health (2023-2030) stressing the need for a life-long, multi-sectoral approach (WHO 2024)⁽¹⁰⁸⁾. The high rates of oral disease worldwide, particularly among the most vulnerable members of society, pose major challenges to health and social care systems⁽¹⁰⁹⁾. PD, a major cause of tooth loss in middle and older age groups, peaks around 55 years of age and remains highly prevalent among older dentate people, while higher prevalence is expected in the near future due to larger numbers of older individuals and longer lives⁽¹⁰⁹⁾. Oral cancer is closely associated with tobacco use, and still has high mortality and high prevalence with large variation in relation to region, countries, sex and age⁽¹⁰⁹⁾.

It should be noticed that most oral diseases are largely preventable, if early diagnosed, with unhealthy diet, rich in free sugars and poor in fruits and vegetables, being a significant risk factor. Oral health shares common risk factors with other non-communicable diseases (NCDs) and may benefit from common preventive strategies in research agendas and policy development. Based on WHO recommendations, enabling actions on the prevention and control of NCDs, including oral health, include development and implementation of national nutrient-and food-based dietary guidelines, and nutrient profile models for different applications ⁽¹¹⁰⁾. A healthy lifestyle requires to reduce the intake of free sugars and increase the consumption of legumes, fruits and vegetables that are basic components of MDi ⁽¹¹⁰⁾. It is a significant opportunity that MDi has progressively become globally well-known even in non-Mediterranean countries, because of wider availability of olive oil, fresh fruits and vegetables, whole grains, legumes, seeds, and nuts in many world regions ^(3,6). On the other hand, a decrease in MDi adherence has been recently observed in Mediterranean countries, due to modern stressful lifestyles, prompting people to consume fast and sugary foods ⁽³¹⁾.

Therefore, effective strategies need to be developed and implemented at national levels to promote diet literacy and encourage adoption of MDi diet. Food education campaigns may play an important role in the nutritional behaviour change, and MDi adherence should be encouraged worldwide, aiming to promote Healthy Ageing. Mass media and targeted client communication messaging services with mobile phones like the BeHe@lthy BeMobile WHO applications, may promote healthy behaviors through propagating balanced information. Exposure to information delivered by mass media was associated with a greater adherence to both Mediterranean diet and Mediterranean diet-like eating pattern in a representative large sample of a general adult Italian population ⁽¹¹¹⁾.

Nutrition education for all healthcare providers, including dental professionals, and multidisciplinary collaboration may improve both oral and general health as studies have shown improvement in nutritional status of dental patients when accompanying dental rehabilitation with nutritional advice ⁽¹¹²⁾.

Study limitations

The present review had some limitations. Although non-English language publications were not excluded, many of them may be missing from the databases that were searched. Most articles analysed had a cross-sectional design and clear causative effects between adherence

to MDi and oral health indicators cannot be concluded. Moreover, there was large variability in study design, population recorded, and MDi scales applied precluding direct comparison between findings. Finally, this study included only articles where the total MDi scale scores were considered and the specific effect of different MDi elements could not be identified.

Implications for future research

The high prevalence of oral diseases and their negative impact on general health and quality of life necessitate enhancement of knowledge about the benefits of MDi to population oral health. More interventional studies are necessary to clarify the protective effect of MDi on oral health and the related mechanisms. The individual components of MDi should also be investigated to identify their specific protective role on oral diseases' prevention and control. Regarding PD, further studies should contribute to the elucidation of the mechanism of action on cytokines, phagocytes system and the overall inflammatory process. Apart from PD and UADT cancer, other components of oral health and function should be investigated in relation to adherence to MDi such as dental decay, masticatory performance, oral dryness, bite force etc.

Since evidence on the impact of oral health on MDi adherence is not clear, further studies should be conducted taking into consideration the complexity of sociomedical and oral factors involved in food selection. Interventional studies should investigate the effect of different types of prosthodontic rehabilitation on food selection and the best strategies to improve nutritional habits of fully and partially edentulous individuals. The role of a multidisciplinary care team in improving adherence to MDi could also be further studied.

Multi-center studies in different Mediterranean and non-Mediterranean countries would be particularly useful to elucidate the combination of environmental and oral health factors on the MDi adherence.

Finally, further studies should be conducted on effective interventions to educate the public and the healthcare providers on the benefits of MDi on oral health and NCDs prevention and control and drive changes in food selection behaviour. As required by WHO, research findings should be translated into practice aiming at country, location and population group specific evidence based clinical practice guidelines⁽¹¹⁰⁾.

Conclusions

The findings in this scoping review revealed systematic negative associations between better adherence to MDi and prevalence of PD and UADT cancer. As a Healthy Diet, MDi is a significant tool for prevention and control of NCDs and its specific effect and mechanisms in prevention and control of oral diseases require further investigation.

On the other hand, few studies investigated the effect of oral factors on adherence to MDi with inconclusive findings. It would be important to further elucidate the effect of various oral health indicators, such as number of teeth, prosthodontic rehabilitation, masticatory performance, severe periodontal disease, biting force, tongue force, oral dryness etc on adhering to MDi and inform dental professionals and other members of the multidisciplinary healthcare team on more effective oral rehabilitation and nutritional improvement strategies.

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Conflict of interest

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Table 1. Studies retrieved on the primary effect of oral health indicators on the level of adherence to MDi.

Author	Aim of study	Study population, country, setting, research type	Questionnaire related to MDi implemented	Oral health factors investigated in relation to MDi	Key results related to oral factor and adherence to MDi
Bousiou et al., <i>Aging Clinical and Experimental Research</i> , 2021 https://doi.org/10.1007/s40520-021-01861-8	To investigate the effect of oral factors on adherence to MDi in an older population	Cross-sectional study; 130 community-dwelling older adults, 33 men and 91 women over 60 years, with mean age 74 ± 8.4 years (range: 60–93 years), were interviewed and clinically examined in open care community centers for older people in Athens, Greece.	Mediterranean diet Index (MDI_BNC4H)	Oral interview including subjective assessment of oral health, oral pain and chewing ability; oral hygiene habits; xerostomia using the Xerostomia Index; denture related complaints; dental visitation habits. Oral examination: number of natural teeth, degree of tooth mobility, number of occluding tooth-pairs, prevalence and quality of removable dentures (Modified Kapur Index), masticatory performance using a mixing ability test with a two-color chewing gum.	Multivariate analyses revealed that higher masticatory performance was statistically significantly associated with better adherence to MDi. Number of teeth and chewing contacts were not significantly associated with the MDI_BNC4H score.
Lohse and Masters, <i>The Journal of Dental Hygiene</i> , 2019	To determine the association of oral health factors with adherence to MDi and eating competence, and examine their impact on food insecurity and oral health.	Cross-sectional study; online survey among 93 adults, 63 women and 30 men, with mean age 41.2 ± 12.3 years, range 18-71 years, who attended free clinics or a community clinic in Pennsylvania, USA	14-item Mediterranean Diet Questionnaire	Self-perceived and reported oral health and behaviors. These included: recent oral health problems such as toothaches, sensitive teeth, bleeding gums, missing teeth, loose teeth, and fillings, impact of oral health issues on daily life, toothbrushing and flossing habits, having a family dentist, last dentist visit, reasons for visiting a dentist, and reasons for not visiting a dentist.	Participants who followed Me Di were more likely to have visited the dentist in the past year than those who didn't (82% vs. 46%, $p=.026$). No other differences related to oral factors were found.

Logan et al., Journal of Dentistry, 2020	To investigate whether oral health status was associated with dietary intake and diet quality in older men after an average time period of 13 years.	Prospective study; 1096 older community dwelling men in Belfast Northern Ireland participating in “The Prospective Epidemiological Study of Myocardial Infarction (PRIME)” study;. Oral health was assessed between 2001 and 2004 (baseline) when they were 63.5 ±2.9 years, and dietary intake in 2015.	Mediterranean Diet Score (MDS)	Number of natural teeth and presence of dentures, categorised into 5 groups: 21–28 teeth with dentures. 21–28 teeth without dentures, 1–20 teeth with dentures and 1–20 teeth without dentures.	Having 21 or more natural teeth was positively significantly associated with higher future MDS scores and intake of fruits, vegetables and nuts, after an average period of 13 years compared to those with 1-20 teeth or being edentate. Dentures improved future adherence to MDS and intake of fruits, vegetables and nuts in those with more than 21 teeth.
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Table 2. Studies retrieved on the primary effect of adherence to Me Di on oral health indicators.

Research/ Author	Aim of study	Study population, country, setting, research type	Questionnaire related to MDi implemented	Oral health factors investigated in relation to MDi	Key results related to oral factor and adherence to MDi
Shaalán et al., <i>Frontiers in Nutrition</i> 2022; doi: 10.3389/fnut.2022.914715	To compare the composition of the salivary microbiome in older patients with type 2 diabetes mellitus (T2DM) and high body mass index (BMI) and controls and determine whether BMI status or MDi adherence influenced salivary microbiome composition.	Nested case-control cohort study in 121 individuals (67–84 years) recruited from the Seniors-ENRICA-2 cohort in Madrid, Spain. Cases (n = 61): individuals affected by T2DM Controls (n = 60): were diabetes free seniors	Mediterranean Diet Adherence Screener (MEDAS)	Salivary composition	Saliva microbiome was associated with MeDAS score but not to a significant level. The microbial community structure of saliva is changed in patients with diabetes II and obesity. Changes are associated with altered consumption of particular MDi food items.
Laiola et al., <i>Appl Environ Microbiol</i> 2020 DOI: 10.1128/AEM.00777-20	To investigate the changes in the salivary microbial communities in overweight and obese subjects after an 8-week individually tailored MD- based nutritional intervention.	Randomised interventional nutritional study in 49 healthy overweight/obese individuals aged 20 - 60 years, 29 in the MDi group and 20 in the control group, at the University of Naples Federico, Italy	Italian Mediterranean index score (ItMedIndex)	Salivary composition	No changes in the overall salivary microbiota composition, but a significant decrease in the relative abundances of species-level operational taxonomic units annotated as <i>Porphyromonas gingivalis</i> , <i>Prevotella intermedia</i> , and <i>Treponema denticola</i> and increased levels of <i>Streptococcus cristatus</i> in the M Di group after 8 weeks of intervention. The MDi modulates the salivary levels of the red bacterial complex, and may be implicated in reducing periodontal bacteria

Louro et al., <i>Nutrients</i> 2021; doi.org/10.3390/nu13041246	to assess the differences in salivary protein profile among groups with different adherence levels to Me Di; and (2) to investigate if salivary protein profiles relate with the levels of total polyphenols and flavanols in diet	Cross-sectional study; 122 adults, 61 men and 61 women, 18 to 65 years old, in Portugal	Mediterranean Diet Adherence Score (MEDAS) score	Salivary composition	Saliva composition was associated with adherence to MDi but this was dependent on the BMI. It can be hypothesized that salivary proteome can have a role in the acceptance of polyphenol-rich foods.
Machowicz et al., <i>Clinical and Experimental Rheumatology</i> 2020;	To examine the association of Mediterranean diet with Sjogren syndrome (SS)	81 participants with primary SS and 51 with non-SS sicca (signs and/or symptoms of dryness) treated at the multidisciplinary Sjögren's clinic at Queen Elizabeth Hospital Birmingham, UK. Age: over 18; mean age for SS (56±14), sicca (57.4±11).	Mediterranean Diet Score (MDS)	Sjogren syndrome	Higher adherence to a MDi was associated with a lower likelihood of developing primary Sjogren syndrome.
Altun et al., <i>Nutrients</i> 2021 https://doi.org/10.3390/nu13114167	To investigate the relationship between DASH diet and MDi and the prevalence of periodontal disease.	Cross sectional, population-based cohort study from the Hamburg City Health Study (HCHS) in Germany with 6209 participants over 45 years; 1453 participants with none/mild periodontal disease (PD) and 1176 participants with severe PD.	Mediterranean Diet Adherence Screener (MEDAS)	Periodontal disease (probing depth, gingival recession, bleeding on probing - 6 sites per tooth, determination of the plaque index - 4 sites per tooth, DMFT (decayed, missing, filled teeth) and clinical attachment loss)	Significant association between higher adherence to the MDi and lower odds to be affected by periodontal diseases. Fish intake was the main item contributing to this effect.
Iwasaki et al., <i>J Period Research</i> 2021; https://doi.org/10.1111/jre.12833	To investigate the potential association between adherence to the MedDiet and PD	Cross-sectional cohort study; 1075 university students in Rabat, Morocco with mean age 20.2 years	The Mediterranean Diet score (MDS)	Periodontal Disease (probing pocket depth and gingival recession at six sites on every tooth, clinical attachment loss) number of teeth, brushing frequency, dental visits frequency	There was no statistically significant association between total MDS and periodontitis but only a negative tendency. Olive oil consumption presented a significant inverse association with periodontitis

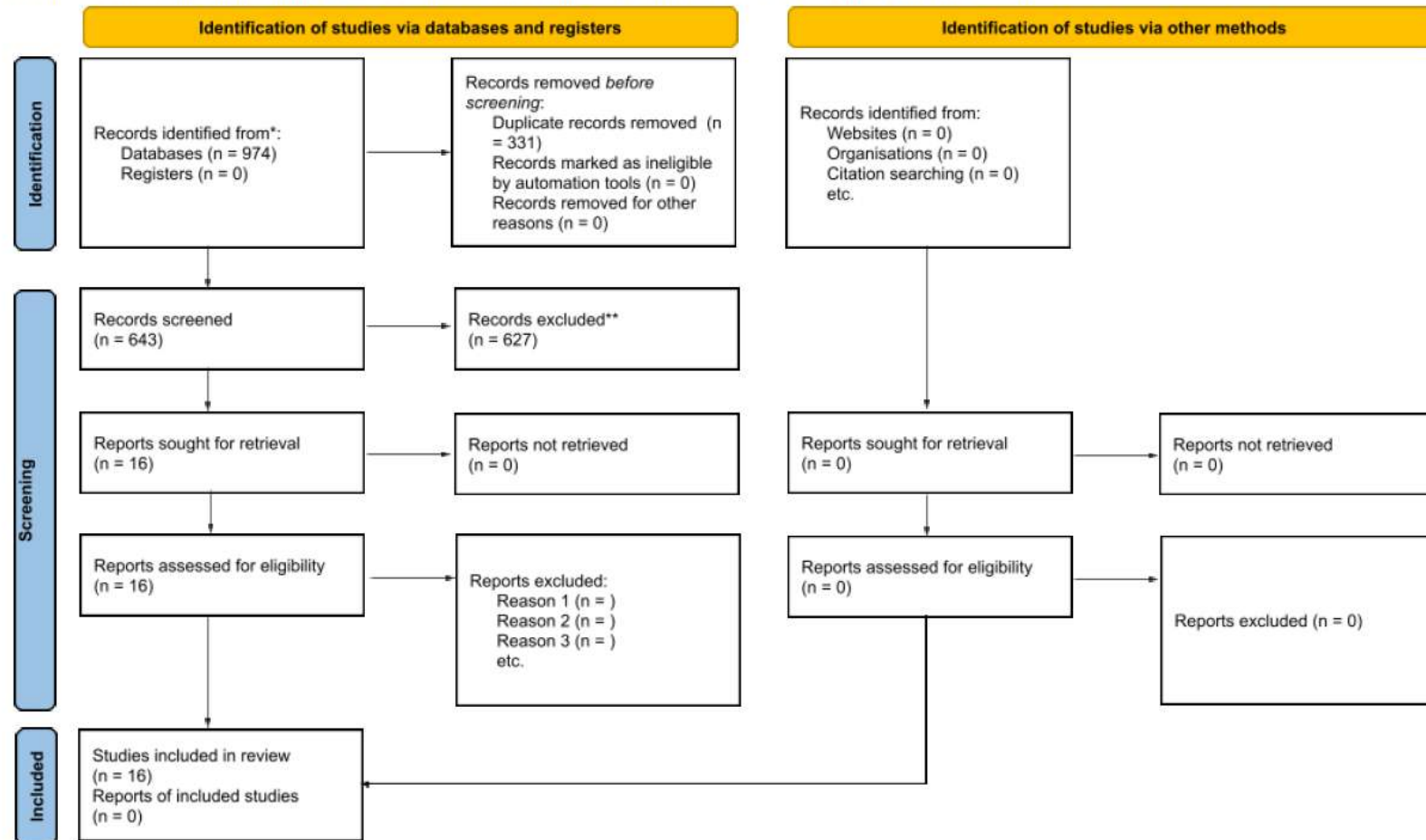
Bartha, V, Exner, L, Schweikert D, Woelber JP, Vach K, Meyer A.-L, Basrai M, Bischoff SC, Meller C, Wolff D. 2022 J CI Period DOI: 10.1111/jcpe.13576	To investigate the effects of a 6-week Me Di intervention on gingival inflammatory and anthropometric parameters of patients with gingivitis.	Single-blind randomised controlled trial; 37 participants, 17 males and 20 females, aged 18-49 years with generalised gingivitis, at the University Hospital Tübingen, Germany	Mediterranean Diet Adherence Screener (MEDAS)	Gingivitis (dental status, periodontal status - probing pocket depths at six sites per tooth, bleeding on probing, the gingival index and the plaque index, periodontal inflamed surface area (PISA))	Gingival inflammatory parameters (BOP, GI, and PISA) were significantly reduced in the Me Di group, but not the plaque index.
Bartha V, Exner L, Basrai M, Bischoff CM, Schweikert D, Adolph M, Bruckner T, Grueninger D, Klein D, Meller C, Woelber JP, Wolff D. J Periodont Res. 2022 DOI: 10.1111/jre.13056	To analyze any changes in serum PUFA levels after a six-week randomized controlled trial in individuals following the Me Di and to determine possible correlations of diet with oral inflammatory parameters.	Randomised clinical trial, 37 participants aged 18-49 years; 18 in the MedD group and 19 in the western diet group at the University Hospital Tübingen, Germany,	Mediterranean Diet Adherence Screener (MEDAS)	Periodontal disease (percentage of site with bleeding on probing (BOP), the Gingival Index, and the Plaque Index)	Adherence to a Me Di was associated with a decrease in serum omega-6 levels, which positively affected the omega-6/omega-3 ratio. This may be a mechanism with positive effects on gingival inflammatory parameters
Marrungati et al. J Periodontol 2022; DOI: 10.1002/JPER.21-0643	To evaluate the association between adherence to MDi and physical activity (PA) level with the periodontal status.	Cross-sectional study at the Unit of Periodontology at the University of Siena in Italy; 235 participants aged 18-70 years with mean age 53.9 years	aMed drawn from the QueMD questionnaire	Periodontal disease. (Clinical attachment level (CAL), periodontal probing depth (PPD), gingival recession (REC), plaque and Bleeding on Probing (BoP) in six sites per tooth, third molars excluded, presence of furcation, tooth mobility)	High adherence to MD was significantly associated to a lower prevalence of Stage III/IV periodontitis (29.66%) compared to those with low adherence (70.34%) Individuals with low adherence to MDi are more than 9 times more likely to have severe manifestations of periodontitis, irrespective of physical activity level

Saenz-Ravello G et al J Appl Oral Sci. 2/13 2023;31:e20230100	To determine the association between adherence to a Mediterranean diet and self-reported gingival health status in an adult population living in Chile	Cross-sectional, analytical, observational study; 351 people, aged 30 (IQR 21), range 218-60, 72.9% women, filled in an online questionnaire, in Chile	Mediterranean Diet Index	Periodontal disease (self-reported gingival health status (SGH)), oral hygiene and oral care habits, dental attendance	Adherence to the MDi was associated with better self-reported gingival health status. Specifically for each point where the MDi increased, there were 18% greater odds of self reporting very good/good gingival health, 12% greater odds of self-reporting the absence of bleeding on toothbrushing, and 24% greater odds of self-reporting the absence of clinical gingival inflammatory signs.
Wu Y, He B, Chen Q, et al. J Periodont Res. 2024;59:32-41. doi:10.1111/jre.13195	To assess the relationship between MDi adherence and PD in the US adult population and to explore the mediating role of obesity indicators in this relationship.	Cross-sectional; 8290 participants aged 30–80 (4159 participants with periodontitis and 4131 without periodontitis) Data used from the National Health and Nutrition Examination Survey (NHANES) Dietary data are collected through two 24-h diary recalls.	Me Di adherence score (MEDAS)	Gingival recession, periodontal pocket depth (PPD), clinical attachment loss (CAL)	MedDiet adherence score was negatively associated periodontitis. Participants with PD had a lower MDi adherence score than those without PD. Me Di adherence score was negatively associated with mean PPD and mean CAL. Obesity indicators may partially mediate this association (nearly 10% of the total effect)

Radić et al., Scientific Reports, 2022 doi.org/10.1038/s41598-022-15589-6	To determine the associations between MDi, nutritional status parameters, muscle strength and periodontal status in kidney transplant recipients.	Cross-sectional study; 89 kidney transplant recipients (40 women and 49 men) with a median age of 61 years in Dalmatia, Croatia.	Mediterranean Diet Serving Score (MDSS)	Periodontal disease (full mouth plaque score (FMPS), bleeding on probing (BOP), probing pocket depth (PPD), gingival recession (GR) and clinical attachment level (CAL)), number of teeth. Interview investigating reasons for tooth loss, frequency of dental visits and dental plaque removal, daily oral hygiene methods and frequency, presence of bad breath, bleeding while brushing and loose teeth, Recording of the Croatian version of the OHIP-14 questionnaire.	There were several significant associations between periodontal and nutritional parameters showing that better adherence to MDi and its components were associated with better periodontal status. Higher MDSS score was associated with a higher number of teeth and more frequent dental plaque removal
Giraldi et al. Eur J of Cancer Prev 2017	To evaluate the association between adherence to MDi and head and neck cancer (HNC) overall and by cancer subsite, as well as the effect of the individual food components on the risk of HNC	Case-control study, 500 cases of head and neck cancer (HNC) and 433 controls at the Gemelli Hospital of Rome Italy;	Mediterranean diet score (MDS)	Oral cavity, pharyngeal and larynx cancer	High adherence to MD protects against the development of HNC, particularly among smokers. . A high consumption of fruit, vegetables, and legumes was significantly associated with a lower risk of larynx, oral cavity and pharynx cancers
Samoli et al. British Journal of Nutrition; 2010 doi:10.1017/S0007114510002205	To investigate whether the traditional Greek MDi may protect against upper aerodigestive tract (UADT) cancers	Case – control study based on data from the Alcohol-Related Cancers and Genetic Susceptibility in Europe (ARCAGE) study collected in four major hospitals in Athens Greece; 239 cases, 192 males and 47 females (109 with cancer of the oral cavity or pharynx, 108 with cancer of the larynx and 22 with cancer of the oesophagus) with mean age 61.3 years, and 194 controls, 143 males and 51 females, with mean age 60.6 years.	Mediterranean Diet Score (MDS)	Upper aerodigestive tract (UADT) cancers	Better adherence to the traditional Me Di was associated with reduced risk of cancers of the UADT. The decrease in UADT cancer risk was 30% for a two-unit increase and 41% for a three-unit increase in MDS. This association was stronger than the associations of the individual diet components with UADT cancer risk.

Filomeno et al. British Journal of Cancer 2014; doi: 10.1038/bjc.2014.329	To investigate the association between the MDi and the oral cavity and pharyngeal cancer risk	Case-control study 768 cases, 593 men and 175 women, with median age 58 years and range: 22–79 years; - histologically confirmed oral cavity and pharyngeal cancer cases and 2078 controls, 1368 men and 710 women, median age 59 years, range: 19–79 years in Milan, Italy and Vaud, Switzerland;	Mediterranean Diet Score (MDS) Mediterranean Dietary Pattern Adherence Index (MDP) Mediterranean Adequacy Index (MAI)	Oral cavity and pharyngeal cancer	Strong inverse association between oral cavity and pharyngeal cancer risk and adherence to the MDi, as measured by the 3 indexes. The associations were stronger in subjects below age 60, in those with a higher level of education, and ex-smokers
Saka-Herrán, C.; Pereira-Riveros, T.; Jané-Salas, E.; López-López, J. Nutrients 2023, 15, 2846. https://doi.org/10.3390/nu15132846	To assess the association between Me Di adherence, type of diet, and vitamin C intake and the risk of head and neck cancer.	Case-control study; 101 patients with head and neck cancers (cases) and 101 controls (total 202), in Barcelona, Spain. Age \geq 18 years, mean age 65.8 \pm 9.9 years, and 68.3% were males.	The Mediterranean Diet score (MDS);	Head and neck cancers (HNC) (Oral cavity, Oro/Hypopharynx, Nasopharynx and Larynx)	Me Di adherence was found to be significantly associated with a lower risk of HNC. Specifically, 1-unit increase in the diet score, was associated with a 12% reduction in the risk of HNC (OR = 0.88, 95% CI: 0.79–0.98).
Saraiya V, Bradshaw PT, Meyer K, Lund J, Slade GD, Olshan AF. Cancer Causes Control. 2024 Jan;35(1):77-92. https://doi.org/10.1007/s10552-023-01761-4	To determine association between pre-diagnosis adherence to MDi and mortality among individuals diagnosed with head and neck cancer.	Cross-sectional; 1184 individuals diagnosed with head and neck cancer (HNC); 20 - 80 years old, in central and eastern North Carolina, USA. Part of the Carolina Head and Neck Cancer Epidemiology (CHANCE) study, 2002 - 2006.	The Mediterranean Diet score (MDS); MDS was calculated from data extracted from the National Cancer Institute's Diet History Questionnaire (DHQ), designed to assess past-year consumption.	Head and neck cancers (HNC) (Oral cavity, pharynx, larynx)	MDi adherence was inversely associated with both 5-year all-cause and 5-year HNC-specific mortality.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



*The total number of records identified from each database or register searched is given in Supplementary Table 1.

**Exclusion of records was performed by a human.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>

Figure 1. Prisma 2020 flow diagram.