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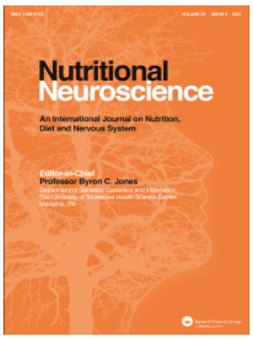

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A comprehensive examination of the evidence for whole of diet patterns in Parkinson's disease: a scoping review

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ABSTRACT

Both motor and non-motor symptoms of Parkinson's disease (PD), a progressive neurological condition, have broad-ranging impacts on nutritional intake and dietary behaviour. Historically studies focused on individual dietary components, but evidence demonstrating ameliorative outcomes with whole-of-diet patterns such as Mediterranean and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) is emerging. These diets provide plenty of antioxidant rich fruits, vegetables, nuts, wholegrains and healthy fats. Paradoxically, the ketogenic diet, high fat and very low carbohydrate, is also proving to be beneficial. Within the PD community, it is well advertised that nutritional intake is associated with disease progression and symptom severity but understandably, the messaging is inconsistent. With projected prevalence estimated to rise to 1.6 million by 2037, more data regarding the impact of whole-of-diet patterns is needed to develop diet-behaviour change programmes and provide clear advice for PD management. Objectives and Methods: Objectives of this scoping review of both peer-reviewed academic and grey literatures are to determine the current evidence-based consensus for best dietary practice in PD and to ascertain whether the grey literature aligns. Results and Discussion: The consensus from the academic literature was that a MeDi/MIND whole of diet pattern (fresh fruit, vegetables, wholegrains, omega-3 fish and olive oil) is the best practice for improving PD outcomes. Support for the KD is emerging, but further research is needed to determine long-term effects. Encouragingly, the grey literature mostly aligned but nutrition advice was rarely forefront. The importance of nutrition needs greater emphasis in the grey literature, with positive messaging on dietary approaches for management of day-to-day symptoms.

KEYWORDS

Parkinson's disease; vegetables; fruits; diet; ketogenic; grey literature; disease progression; symptom severity

1. Introduction

Parkinson's disease (PD) is a progressive neurological condition that is primarily characterised by a triad of motor symptoms, principally resting tremor, bradykinesia, rigidity, with postural instability appearing as the disease progresses [1,2]. These symptoms are caused by loss of dopaminergic neurones from a region of the brain known as the substantia nigra pars compacta, with the pathological signature of intracellular aggregates of protein α-synuclein (Lewy bodies and Lewy neurites) [2]. PD also causes significant non-motor symptoms such as disturbances in autonomic function (e.g. hypotension, gastrointestinal symptoms), sleep disturbances, neuropsychiatric symptoms, and dementia [3]. Symptoms, therefore, can have broad-ranging impacts on health-related quality of life (QoL) [4]. The cause of PD is still unknown, but it is believed that a complex interplay between multiple factors such as environment, genetics, advancing age and chemical exposure increase the risk of developing the condition [5].

In terms of burden, PD is estimated to affect 6 million individuals worldwide and cause 3.2 million disability affected life years (DALYs) each year [6]. Globally, in 2015 it was the fastest growing neurological disorder [7], estimated to have increased by a factor of 2.4 between 1990 and 2016 [6]. In 2017, the total economic burden of PD in the US was estimated at approximately USD $51.9 billion, with direct medical costs of $25.4 billion and indirect and non-medical costs of $26.5 billion [8]. Yang et al. estimate the projected PD prevalence to be greater than 1.6 million and projected total economic burden to surpass $79 billion by 2037 [8]. These

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trends are thought to be driven by increasing life expectancy and therefore, longer disease duration, as well as environmental and population health factors that include diet [6,9].

There also exists a social burden of the disease caused by emotional and communicative changes that disrupt social functioning and can disadvantage daily life [10]. These less recognised social symptoms can lead to isolation and loneliness that may cause severe negative consequences for an individual's well-being [10]. As the disease progresses, increasing severity of both motor and non-motor symptoms can significantly impact dietary choices and nutritional intake. In particular, non-motor symptoms such as hyposmia, constipation, cognitive impairment and depression may have a negative influence [5]. Additionally, the increasing disruption caused by psychosocial and physical symptoms can lead to feelings of stigma and dehumanisation that are experienced equally by both the individual with PD and their caregiver, thereby contributing further to their QoL burden [10–12].

Whilst there remains no cure for PD, current medical management of PD is predominantly targeted at alleviating motor symptoms [13], with levodopa being the mainstay of pharmacotherapy since 1960s [13,14]. Levodopa is the precursor to dopamine and therefore levodopa-based medications are designed to counterbalance depleting dopamine levels in the brain [13]. Issues arise with levodopa therapy however, as the medication causes problematic side effects, which increase as the illness progresses and are a major part of the individual's disease experience [13]. Side-effects include nausea, diarrhoea, constipation, dry mouth, tiredness, indigestion and heartburn as well as vitamin B12 and folate deficiency, all of which have the potential to significantly affect nutritional intake and status [13,14]. Moreover, the efficacy of levodopa decreases as the disease progresses leading to longer 'off' times and worsening symptoms [14]. Bioavailability is greatest if consumed on an empty stomach but this can increase nausea side effects therefore, it is often recommended to be taken with meals. For some individuals the responsiveness to levodopa is blunted, possibly due to 'protein competition', or to non-motor symptoms such as delayed gastric emptying and constipation [15]. The timing of meals with medication and strategies to improve levodopa efficacy continues to be a well-researched topic [13–15].

Despite the already-high economic, physical and social burden of PD and predictions of increasing prevalence, the evidence for interventions to improve disease progression, symptom severity and QoL for individuals living with PD is still inconclusive [16]. Whilst many non-pharmacological intervention studies focus on self-management and target exercise regimes [17], there are fewer that involve a whole of diet approach [16], particularly those that take into consideration symptom-related limitations and QoL [10]. The role of nutrition therapy is gaining momentum but there is still a critical need for research to support nutrition focussed interventions and inform policies on sustainable treatment and self-management options for individuals living with this condition [16,18–20].

1.1. Academic research

To date, much of the research has focussed on the protective effects of specific nutrients against symptom severity and the risk of progression of PD, with examples including (but not limited to) caffeine [21,22]; alcohol [23]; Omega-3 [24]; vitamins E [24], C, [25] and B [26]; anti-oxidants and phytochemicals present in fruit and vegetables [27]; soy [28]; and minerals such as iron, zinc, and copper [29]. Other areas of research include dietary approaches to improve levodopa therapy [14,15,30] and the role of the gut microbiome in PD [31–34]. However, much of the evidence is inconclusive for example, large-scale cohort and cross-sectional studies on dairy foods [22,35] have reported both positive and negative associations with the risk of developing PD. The study of individual components of diet does not adequately capture many of the other influencing factors in PD, in particular those that have an effect on, or are affected by daily living experiences. Again, this suggests that employing a whole of diet approach may not only answer outstanding questions surrounding disease risk, progression, symptom severity, but also be more practical for those living with PD.

Recent research has demonstrated positive health outcomes for an overall high quality diet for reducing the risk of PD [36]. Likewise, diets high in fruits, vegetables, whole grains and healthy fats, such as the Mediterranean diet (MeDi) [37], and the Mediterranean-DASH Intervention for Neurodegenerative Delay diet (MIND) [38] are protective against PD and have been associated with improved motor and nonmotor symptom severity and slowing disease progression [38–43]. Paradoxically, the ketogenic diet (KD) which comprises high fats, moderate proteins and very low carbohydrates (CHO) [44] has also been associated with improved cognition and health outcomes in PD [45,46]. However, the KD is highly restrictive and many find it hard to adhere to outside of a clinical setting [47].

Poor nutritional status and malnutrition are significant feature in PD [48] that have been associated with

reduced QoL and increasing disease severity and progression [49–51]. Both non-motor and motor symptoms can impact normal eating behaviours such as shopping, preparing and cooking meals, leading to reduced intake, often of poorer quality, that therefore cannot be overlooked [3,52,53].

Lifestyle strategies employed by individuals with PD to maintain optimal health have been poorly researched [54]. Health advice providing practical nutrition information on whole of diet patterns would present a more global approach which may be more achievable for the individual [19]. Therefore, clinical findings supporting the impact of whole of diet patterns are necessary to develop diet behaviour change programmes and evidence-based advice for individuals living with PD [19].

1.2. The internet and its emerging role in PD management

Given the increasing prevalence and isolating nature of many neurological conditions, the internet provides a particularly appealing method of sourcing disease-related information and connecting with the community [55]. Patients, their caregivers and family members often turn to the internet, to learn more about their condition, including advice on diet [54]. This reliance on the internet may not necessarily be perceived as a problem as it provides relief for over-stretched healthcare providers; however, despite these advantages, the quality and validity of the information varies [54]. The landscape of health-care delivery, whether being provided by accredited health care professionals or others, is changing due to the emergence of e-health [56]. In an environment where there is a growing trend towards active self-management of one's disease or condition, the internet offers a way to increase efficiency of care delivery whilst reducing economic burden [54,56]. A recent survey of 346 Swedish individuals living with PD found that amongst those under 65 years, the most valued source of disease-specific knowledge was found online, whereas the older age groups more frequently sought information from patient organisations [54]. The potential downfall of the internet is the existence of web based low-quality information, misinformation, or insufficient information in the community, which may be detrimental for health outcomes and QoL among people with PD. False or misleading claims lacking in scientific evidence are also easy to access and could provide questionable health advice, which then represents a key challenge [57].

Nevertheless, the internet provides an increasingly popular avenue for information and advice for people with PD, the validity of which may be variable and possibly misleading. Therefore, the first objective of this scoping review was to appraise the peer-reviewed academic literature and synthesise the research evidence surrounding whole of diet patterns which offer the best outcomes for the management of PD. The underlying aim was to determine the informed consensus on best practice for reducing risk, slowing disease progression and improving management and severity of symptoms. The second objective of this review was to scope the grey literature for dietary advice from professional bodies, governments, not-for-profit agencies and patient communities. The purpose was to determine whether the academic and grey literature align, and to investigate if the content of informal dietary advice is supported by evidence-based recommendations for those living with PD. For clarification, differences between academic and grey literature are described below.

2. Methods

This scoping review was conducted and reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [58].

2.1. Eligibility criteria

To be included in the review, peer-reviewed studies needed to have been published in the last 10 years and to evaluate whole of diet patterns (e.g. overall diet quality, MeDi, KD) and their impact on adults' risk of PD, PD status, PD symptom alleviation or disease progression. Eligible grey literature included any web pages that provided dietary pattern recommendations for individuals to reduce their risk of PD, or alleviate PD symptoms, or slow disease progression. A detailed overview of study eligibility criteria is provided in Table 1.

2.2. Information sources

2.2.1. Academic literature

Academic literature has been described as '*scholarly publications that report original empirical and theoretical work in the natural and social sciences*' [59] and it is generally commercially published. Five academic databases were searched: Medline, Embase, Scopus, CIHNAL, and PsychInfo.

2.2.2. Grey literature

In 2010 Schöpfel defined grey literature as '*manifold document types produced on all levels of government, academics, business and industry in print and electronic formats that are protected by intellectual property rights,*

Table 1. Eligibility criteria.

Criteria	Inclusion: Academic literature	Exclusion: Academic literature	Inclusion: Grey literature	Exclusion: Grey literature
Participants	Adults, 18 years and over, at risk of or having a diagnosis of PD. Includes populations with co-morbidities including PD.	Samples younger than 18 years old, healthy samples with no diagnosis of PD or not identified as at elevated risk of PD. Non-human (i.e. animal) populations. Animal models.	N/A	N/A
Concept	Studies that included assessment of whole of diet patterns and measures of PD risk, PD symptom severity/alleviation and PD progression.	Studies that did not include dietary assessment. Studies investigating the impact of single nutrients on PD (risk, symptom alleviation, disease progression), or interactions with medications. Studies focussing solely on nutritional status (e.g. malnutrition, sarcopenia, dynapenia).	Diet and nutrition (focussing on whole of diet) advice for people with or at risk of PD.	Non-dietary advice. Diet or nutrition recommendations focussed on a single nutrient or ingredient.
Types of peer-reviewed evidence sources	Original and peer-reviewed studies evaluating the impact of a specific dietary pattern on PD risk, symptom severity/ alleviation, or disease progression. Must have a health outcome. Eligible study designs include observational studies (e.g. cross-sectional, qualitative) and experimental designs (e.g. RCT).	Non-original study types, e.g. systematic, narrative, and scoping reviews, commentaries, letters to the editor, corrigendum, study protocol, conference abstracts. Single-person case studies.	Whole of diet or nutrition pattern recommendations found online on relevant websites of government and non-government organisations (e.g. American Parkinson Disease Association, European Parkinson's Disease Association), community blogs, news articles, and social media.	
Geography	Not limited			
Setting	Not limited: Includes community-based, acute care, clinical settings			
Date	Last 10 years			
Language	English			

PD, Parkinson's disease.

of sufficient quality to be collected and preserved by library holdings or institutional repositories, but not controlled by commercial publishers i.e. where publishing is not the primary activity of the producing body' [60]. The grey literature search included only sites that provided diet and nutrition advice and were recently published (i.e. 2012 onward). The search comprised two government websites, seven peak professional bodies, two university or medical websites, seven foundations, seven news/other, seven influential blogs, eight social media/Facebook, seven YouTube videos and seven books (Supplementary Table 1).

2.3. Search strategy

Concepts: (1) PD and (2) Dietary pattern.

A search strategy was developed for Medline and then adapted for the other databases. The search strategy was developed with the assistance of an academic librarian and validated through comparison with previous reviews [19,20,36,58].

TI Parkinson's OR AB Parkinson's		
TI (((diet* OR nutrition) and (behavi* OR quality OR pattern OR factor OR eating OR consumption OR intake OR food* OR change OR ketogenic OR Mediterranean OR DASH OR whole food plant based OR low fat OR McDougall OR MIND OR Western OR Wahls OR Swank OR anti-inflammatory OR 'high animal fat' OR vegetarian OR 'lacto-ovo vegetarian' OR fasting)))	OR	AB (((diet* OR nutrition) and (behavi* OR quality OR pattern OR factor OR eating OR consumption OR intake OR food* OR change OR ketogenic OR Mediterranean OR DASH OR whole food plant based OR low fat OR McDougall OR MIND OR Western OR Wahls OR Swank OR anti-inflammatory OR 'high animal fat' OR vegetarian OR 'lacto-ovo vegetarian' OR fasting)))

TI, terms in the title. AB, terms in the abstract.

2.4. Selection of sources of evidence

Articles were screened using a combination of Endnote (v.20) software [61] and web-based collaboration

software platform, Covidence [62]. Articles were screened independently by two researchers (JR and JR) using an elimination process (based on title, abstract, key terms, full articles in ascending order). The results were compared and consolidated through consensus between the two researchers with any disagreements resolved through discussion.

2.5. Data extraction (charting)

Data were extracted by members of the authorship team. Data extracted were related to publication details, study characteristics (country, aims, design), participant sample (population, health status, sample size, sex, age), methodology (study duration, intervention description, comparator), main findings, and statistical significance of findings.

3. Results

Searches identified 2159 articles from five databases, 732 duplicates were removed leaving 1427 records remaining. In total 1395 articles were removed during screening leaving a total of 32 studies included in the review (Figure 1).

The dietary patterns included in this review are detailed in Table 2.

3.1. Study characteristics

As summarised in Table 3, studies were conducted across the globe with six from USA [39,64,65,68,70,71]; four from Italy [72–75]; three from UK [67,76,77]; two studies each from Greece [78,79] and Iran [80,81]; and one study from Australia [82]; Belgium [83]; Canada [40], China [84]; Germany [85]; Ghana [86]; India [87]; Japan [88]; Mexico [89]; the Netherlands [90]; New Zealand [63]; Poland [91]; Finland [69]; Sweden [92]; and Turkey [66]. Studies were categorised into their study type (Table 3) and included twelve cross-sectional studies [39,40,67,68,70,76,77,79,83,87,89,91]; ten case studies [71–75,82,84–86,88]; six randomised controlled trials [63,64–66,80,81]; and four cohort studies [69,78,90,92].

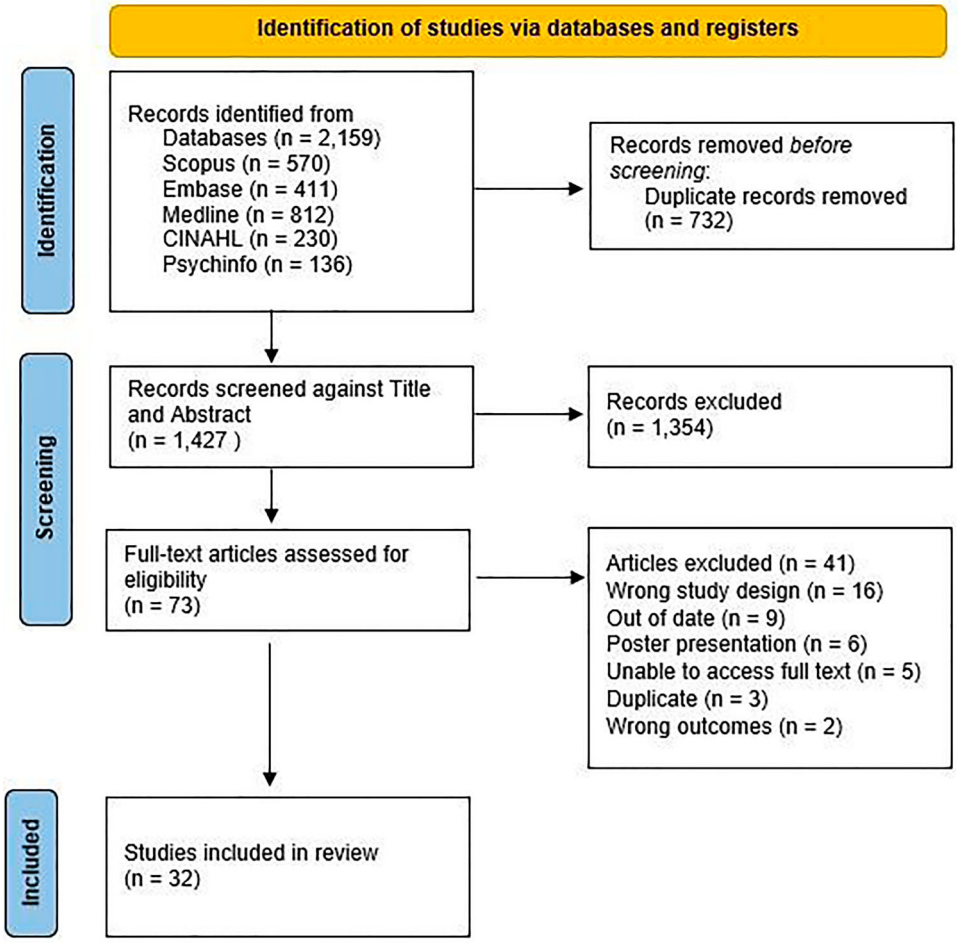

Figure 1. Study flow diagram. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Table 2. Dietary patterns diet quality scoring methods studied.

Dietary patterns

Mediterranean diet (MeDi) diet – characterised by high intake of vegetables, fruits, nuts, legumes and unprocessed cereals; low consumption of meat and meat products: low consumption of dairy (with the exception of the long-preservable cheeses); moderately high consumption of unsaturated fatty acids (mostly in the form of monounsaturated fatty acids from olive oil); moderately high intake of fish (contributing omega-3 fatty acids); and regular but moderate consumption of alcohol, primarily in the form of wine, generally during meals [37]. Versions included the Ordinary Mediterranean Diet (OMeDi), similar to MeDi and the Greek Mediterranean Diet (GMeDi). The latter has similar food groups to MeDi but also promotes potato intake and limits poultry consumption.

Dietary Approaches to Stop Hypertension (DASH) diet – includes foods that are rich in potassium, calcium and magnesium, nutrients that help control blood pressure.

Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet – combines DASH and MeDi to create a diet aimed at reducing the risk of dementia and the decline in brain health experienced with natural aging. Almost identical to MeDi but uniquely promotes leafy green vegetables (daily), berries (2 x week), and poultry and/or fish (1 x week). It also recommends limiting consumption of butter/margarine (≤ 1tbsp/week), cheese, fried/fast food (≤ 5 x week), pastries, sweets and cakes (< 5 x week) [38].

Ketogenic Diet (KD) – a high fat, low carbohydrate (CHO) diet (typically 152 g fat/75 g protein/16 g CHO [63,64]); or **Low carbohydrate (Low CHO), high fat diet** – involves restricted CHO intake (max 20 g/day from vegetables, no fruit, grains or sweets [65]) and up to 90% of daily kJ from fat [66].

Low fat diet/high CHO diet – a low fat, high CHO diet (typically 42 g fat/75 g protein/ 246 g CHO [63])

Diet quality scoring methods

Healthy Diet Index (HDI) – based on the most recent (2018) WHO and global dietary guidelines [67].

Dietary Inflammatory Index (DII) – widely used literature-derived, population-based index designed to compare diverse populations on the inflammatory potential of their diets [67].

Alternative Healthy Eating Index (AHEI) – defined by 11 components: vegetables, fruits, whole grains, sugar-sweetened beverages and fruit juice, nuts and legumes, red and processed meat, trans fat, long-chain (n-3) fats, polyunsaturated fatty acids, sodium, and alcohol [68,69].

3.2. Study population characteristics

Study samples encompassed populations from around the globe and two studies were conducted on the same cohort [80,81]. The balance of male and female participants was fairly equal (mean female participants = 46.8%, SD = 14.7), with one study including only females [92]. The median age was 64.3 (IQR 61–69) and study population sizes varied according to study type with sample numbers ranging between 52 and 18,529 for cross-sectional studies; 67–1200 for case studies; 16–105 for RCT studies; and 4524–47,128 for cohort studies.

3.3. Dietary pattern characteristics

Table 2 provides details of the main whole of diet patterns studied and Table 3 provides details of the diet included in each study. Findings are displayed in Figure 2. Where relevant, various different scoring indexes were used to measure dietary intake and diet quality such as adherence to MeDi, DASH, MIND, AHEI, DII and HDI [39,40,67–69,71,74,79–81,92]. Three studies examined quality or adequacy of diet compared to the country's dietary guidelines [83,89,90]. Six studies compared dietary intakes between PD and healthy controls (HC) [72,74,82,86,89,91]. Eleven studies investigated the effect of dietary intake on the risk of PD; five of these examined overall diet [73,75,78,87,88]; and four adherence to MeDi diet [39,40,90,92]; two reported MIND adherence [39,40]; and one AHEI adherence [69]. Risk of PD was measured by PD incidence, age of onset and adjusted disease duration, details for each study are included in Table 3. There were six studies that examined the effects of a specific dietary intervention on PD outcomes, these included two with a MeDi intervention [80,81] and four with a KD, or low CHO ketogenic style diet intervention [63–66]. Philips et al. [63] compared KD with a low fat dietary intervention and Krikorian et al. [65] compared KD with a high CHO dietary intervention typical of a Western diet. Sauerbier et al. [77] compared dietary intakes of PD patients from three ethnic groups from UK and Okubo et al. [88] categorised and then compared three dietary patterns from Japan. Gupta et al. [87] investigated environmental factors which included vegetarian versus non-vegetarian diets in India; and Hegelmaier et al. [85] explored the effects of a 2-week vegetarian diet on PD symptoms and the gut microbiome in Germans.

3.4. Dietary related PD outcomes

Dietary patterns differed across the studies, mostly due to the variety of ethnic and cultural backgrounds of the study populations. Regardless, the underlying theme reported throughout was that a healthy diet incorporating higher intakes of fruit, vegetables, fish and healthy fats such as MeDi, was associated with lower incidence of PD, milder symptom severity and slower disease progression (Figure 2). Adherence to either MeDi or MIND dietary pattern was found to be protective in seven studies [70,73,80,81,88,90,92] with reasons given that these foods are rich in antioxidants and therefore exert anti-inflammatory properties that are protective against the underlying aetiology of PD [39,40,67,68,71,73,80,81,92]. Additionally, higher dietary fibre intakes were suggested to support the gut microbiome [68,72,79,85] and may also help to improve the PD symptoms of constipation [82,86]. Conversely, in studies where processed meats [75], alcohol, and discretionary foods [75,82] were measured, intakes were reported to be negatively associated with PD outcomes. These foods were considered to exacerbate PD symptoms and disease progression due to their capacity to

Table 3. Study characteristics and outcomes.

Author	Population	PD tool	Study description	Diet tool	Other outcome variables
CROSS SECTIONAL					
Agarwal USA [39]	US adults without PD ($n = 706$, 75% F, mean age 80.3)	26-item modified UPDRS. Incidence = first occurrence over 4.6y follow-up of ≥2 signs of PD. Progression = change in UPDRS score.	Compared MIND, MeDi and DASH scores at baseline with signs of PD incidence and progression.	Modified Harvard FFQ (v), 12mo, 144 items, measured g/d, MIND, MeDi and DASH adherence scores	1 model adjusted for depressive symptoms
Baert Belgium [83]	Belgian A adults with PD, ($n = 52$, 29.7% F, age range 49–84)	Self-administered general questionnaire for PD medication use, knowledge of drug-food interactions	Compared overall dietary intake with Institute of Medicine EAR recommendations	Food diary, 2 non-consecutive 24 h periods, measured macronutrients and micronutrients g/d (included data for % eaten at each eating occasion)	
Coe UK [76]	UK adults with PD, ($n = 90$, 73.1% F, mean age 68 ± 9.6)	Not measured	Investigated feasibility of assessing diet in PD with FFQ. Compared overall diet quality in PD with UK Govt. Science Advisory Committee on Nutrition (SACN) Guidelines.	EPIC-Norfolk FFQ (v), 12mo measured macro and micronutrient intakes g/d	
Gupta India [87]	Indian adults with PD ($n = 97$, 29% F, mean age 56.3 ± 9.6); compared with HC ($n = 97$, 30% F, mean age 53.3 ± 8.3)	PD age of onset	Investigated association between environmental risk factors including dietary habits and PD risk. Vegetarian v non vegetarian included as environmental factors.	How dietary intakes were collected was not reported.	Environmental exposure (chemicals, source of drinking water)
Lawrie UK [67]	UK adults with PD ($n = 162$, 52.5% F, mean age 67 ± 9)	UPDRS (Part I)	Investigated the relationship between PD symptom severity and MIND index; HDI; DII diet scores	EPIC FFQ (v), 12mo, food groups, measured g/d, MIND, HDI and DII scores	Depression (BDI, HADS, ESS, MoCA)
Maraki Greece [79]	HEllenic study Greek older adults without PD ($n = 1731$, 59% F, median age 73 [69,77])	MDS probability score for PD, UPDRS (Part III)	Investigated the probability of PD and signs and symptoms of PD compared with MeDi adherence	Semi-quantitative FFQ (v), 1wk and 1mo, measured g/d, MeDi score adherence	Environmental exposure Depression (GDS, HADS, MOSS, BDS)
Metcalfe-Roach Canada [40]	Canadian adults with PD ($n = 167$, 31.7% F, mean age 64.9); compared with HC ($n = 119$, 60.7% F, mean age 61.8)	PD risk (age of onset, disease duration)	Investigated associations between MIND and MeDi and age of onset of PD	EPIC Norfolk FFQ (v), 12 mo, measured g/d, MIND, OMeDi and GMeDi scores	
Mischley USA [70]	US adults with PD ($n = 1053$, 53% F, mean age 63.1 ± 9.2)	Patient reported outcomes in PD (PRO-PD) PD severity defined by cumulative PRO-PD, PD progression defined by PRO-PD adjusted for disease duration	Investigated association between dietary practices and PD progression	FFQ (nv), 6mo, 40 items, 25 nutritional supplements (serves)	Dietary supplement intake and PD risk
Molsberry USA [68]	Nurses Health study and Health professionals Follow-up study US adults without PD ($n = 18529$, 62% F, age IQR 46.7–48.7)	Prodromal features of PD (constipation, pRBD, hyposmia, excessive daytime sleepiness, impaired colour vision, depressive symptoms, body pain)	Investigated relationship between MeDi and AHEI scores with prodromal features of PD	Semi-quantitative FFQ (v) measured g/d, MeDi adherence score and AHEI score	Sleep, depression
Navarro-Meza Mexico [89]	Mexican adults with neurodegeneration ($n = 20$, 7% F, mean age 66 ± 2); compared with HC ($n = 41$, 57% F, mean age 72 ± 1); 13/20 with PD	UPDRS score used to identify PD	Compared dietary intake between PD and HC. Adequacy of diet compared with Mexican guidelines	24 h dietary recall = 186 foods/15 food groups measured macronutrients and antioxidant vitamins g/d	
Sauerbier Finland/UK [77]	Multi-ethnic UK adults with PD ($n = 139$, 38.8% F, mean age 66.8 ± 11.6)	HY, NMSS	Compared differences in dietary intakes of multiethnic PD patients (Asian, Black African and Caribbean, White) and their relationship with non-motor PD symptom severity	FFQ, 6mo measured diet restrictions (calorie-restricted, paleo, KD, vegetarian, low-sugar), vitamin or supplement use (y/n)	Depression (HADS)

(*Continued*)

Table 3. Continued.

Author	Population	PD tool	Study description	Diet tool	Other outcome variables
Zapała Poland [91]	Polish adults with PD ($n = 59$, 41% F, mean age 69 ± 7); compared with HC ($n = 108$, 58% F, mean age 64 ± 7)	PD status HY, UPDRS (Part III), MMSE, MoCA	Compared diet preferences and oral microbiota profiles between PD and HC	FFQ (nv) 33 foods, food groups. Nutrition behaviour, cooking methods	Oral microbiome
CASE STUDY					
Alcalay USA [71]	US adults with PD ($n = 257$, 44.7% F, mean age 68.2 ± 11); compared with HC ($n = 198$, 48.5% F, mean age 72.4 ± 9.6)	UDPRS (Part III), PD duration, age of onset	Investigated the association between MeDi adherence and PD	Willett semi-quantitative FFQ (v) 12mo, measured g/d, MeDi score adherence	
Barichella Italy/Ghana [86]	Ghanian adults with PD ($n = 55$, 33% F, mean age 65.8 ± 10.5); compared with HC ($n = 60$% F, mean age 61.1 ± 7.8)	UK Brain Bank criteria for PD, PD duration	Described dietary habits and assess nutritional status of Ghanian patients with PD compared with HC. Included data on prevalence of nutrition related PD symptoms	FFQ (nv), 13 item and 2–4 h dietary recall, measured overall diet quality, macro and micronutrients. Fluid intake, number of meals per day.	Dysphagia (Swallowing Disturbance Questionnaire) Constipation (Rome III constipation criteria)
Barichella Italy [72]	Italian adults with PD ($n = 600$, 46.2% F, mean age 68.6 ± 9.4) compared with HC ($n = 600$, 46.2% F, mean age 69.3 ± 8.8)	PD duration, UDPRS (Part I–IV), severity HY, pharmacological therapy	Investigated the relationship between dietary habits and features of PD (body weight, energy balance, constipation and levodopa therapy) and comparisons with HC	Semi-quantitative FFQ (v) 12mo, 66 item, measured g/d, macro and micronutrients, fluid intake	
Belingheri Italy [73]	Italian adults with PD ($n = 347$, 39.5% F, mean age 71.9 ± 9.6); compared with HC ($n = 389$, 40.6% F, mean age 69.5 ± 9.7)	PD defined by presence of 2 of bradykinesia, akinesia, rigidity tremor, postural instability	Investigated the association of nutritional factors and agrochemical exposure with PD risk	FFQ (nv) based on Italian population, measured intakes (serves) categorised into food groups	Environmental exposure
Cassani Italy [74]	Italian adults with PD ($n = 600$, 46.2% F, mean age 68.6 ± 9.4); compared with HC ($n = 600$, % F NR, mean age 68.6 ± 9.4)	UPDRS (Part I–IV), HY	Assessed dietary habits, food preferences and adherence to MeDi in Italian PD patients compared with HC	24 h dietary recall and FFQ (v) 12mo, 66 item measured g/d, MeDi score adherence.	Compared PD with dysphagia and PD without
Fukushima China [84]	Chinese adults with PD + depression ($n = 24$, 54% F, mean age 63.0 ± 9.6); PD no depression ($n = 58$, 37.9% F, mean age 64.3 ± 9.4); compared with HC ($n = 81$, 41.9% F, mean age 63.7 ± 9.4)	UK PD Society's Brain Bank Criteria to identify PD	Investigated the nutritional factors associated with PD and compared PD patients with depression vs PD without depression	Structured closed-ended FFQ (nv) measured intakes (units not reported) prior to PD onset for PD group, and current diet for HC group	Depression (HAMD-17)
Hegelmaier Germany [85]	German adults with PD ($n = 54$, 50% F, mean age 61 ± 9.2); compared with HC ($n = 34$, 58.8% F, mean age 52.8 ± 12.6)	UPDRS (Part I-IV)	Investigated the influence of a 2wk vegetarian diet on clinical course of PD and gut microbiome compared with HC	Balanced vegetarian intervention for 14 days (3 meals/d 45% of dishes contained ghee)	Bristol stool scale. Gut microbiome
Okubo Japan [88]	Japanese adults with PD ($n = 249$, 46.2% F, mean age 68.5 ± 8.6); compared with HC ($n = 368$, 61.7% F, mean age 66.6 ± 8.5)	Not measured	Investigated OR's for PD according to quartile of dietary pattern scores	Current diet history questionnaire (v), 150 food and beverage items, 3 dietary patterns identified (healthy, Western, light)	
Palavra Australia [82]	Australian adults with PD ($n = 103$, 45% F, mean age 67.1 ± 12.2); compared with HC ($n = 81$, 55% F, mean age 62.4 ± 15.6)	UDPRS (Part III), HY, MoCA, NMSS, chronic pain (Visual Analogue Scale)	Investigated the nutritional intake of an Australian PD cohort compared with HC and associations between diet and clinical features of PD symptom severity	Semi-quantitative FFQ (v), 12mo, 145 item, measured g/d macro and micronutrients, included data on added sugars (sucrose, dextrose, fructose, lactose, sugar syrup)	Dyspepsia (Leeds Dyspepsia Questionnaire), constipation (Cleveland Constipation Score) QoL (PDQ-39), Mood (BDI)
Torti Italy [75]	Italian adults with PD ($n = 634$, 42.4% F, age groups classified ≤59 17.7%; 60–64 14.0%; 65–69 19.9%; 70–74 25.4%; ≥ 75 23.0%); compared with HC ($n = 532$, 50.9% F, age groups classified ≤59 26.5%; 60–64 16.5%; 65–69 19.2%; 70–74 19.2%; ≥ 75 18.6%)	UK PD Society's Brain Bank Criteria to identify PD, how PD risk measured not clearly defined	Investigated the role of occupational, environmental and lifestyle factors have on the risk of PD	FFQ (v) assessed dietary habits pre PD, measured food groups	Job categories, family history of PD, smoking

(*Continued*)

Table 3. Continued.

Author	Population	PD tool	Study description	Diet tool	Other outcome variables
RCT					
Koyuncu Turkey [66]	Turkish adults with PD and a speech and voice disorder ($n = 68$, 29.9% F, mean age 66.9 ± 6.9) RegD ($n = 34$, 29.4% F, mean age 69.7 ± 7.3); KD ($n = 34$, 26.5% F, mean age 64.2 ± 6.5)	PD defined with International PD and MDS diagnostic criteria, speech and voice disorders VHI-10	Compared the effect of RegD and KD on voice disorders in PD	Diets not defined, duration of intervention and how intakes were monitored not stated. Intro suggests RegD typically characterised by 30% kJ from fat; KD typically characterised by 90% kJ from fat	
Krikorian USA [65]	US adults with PD ($n = 14$), High CHO ($n = 7$, mean age 64.5 ± 6.5); Low CHO ($n = 7$, mean age 66.0 ± 5.5)	PD identified with UK Brain Bank criteria, MoCA, Controlled Oral Word Association task, California Verbal Learning Test, Verbal Paired Associate Learning Test, UPDRS (Part III), Finger Tapping Task	8w randomised controlled parallel group study investigated effects of Low CHO on cognitive performance	High CHO diet modelled on Western dietary pattern, Low CHO target of 20 g CHO/d from vegetables only, no fruit, grain-based foods or sweets. Diets monitored using 3d food diary in week prior and during each week of intervention	
Paknahad Iran [80]	Iranian adults with PD ($n = 70$), MeDi ($n =$ 35, 38.2% F, mean age 59.3 ± 8.3); control ($n = 35$, 44.4% F, mean age 58.6 ± 9.3)	MoCA	10w single-centre randomised clinical controlled trial to investigate the effect of MeDi on cognitive function in PD	MeDi designed by nutrition expert based on individual's requirements, control group were recommended to eat more fruits and vegetables and less refined grains and red meat. Dietary intakes were monitored using a 24 h recall	
Paknahad Iran [81]	Iranian adults with PD ($n = 70$), MeDi ($n =$ 36, 44.4% F, mean age 59.3 ± 8.3); control ($n = 34$, 38.2% F, mean age 58.6 ± 9.3)	UPDRS (Part I–IV)	10w single-centre, two parallel arm, single blind randomised clinical trial to investigate the effects of MeDi on control of PD symptoms and PD drug side effects compared with traditional Iranian diet	MeDi group consumed greater amounts of foods typical for MeDi dietary pattern (17% protein, 51% CHO, 32% fat), control group followed traditional Iranian diet (12% protein, 58% CHO, 30% fat). Dietary intakes measured using 24hr recall every 2w, phone call and interview 1/m	
Phillips New Zealand [63]	NZ adults with PD ($n = 47$), Low fat ($n = 23$, 39% F, mean age 61.5 ± 7.1); KD ($n = 24$, 29% F, mean age 64.3 ± 6.7)	UDPRS (Part I-IV)	8w single phase parallel group (1:1 randomisation) to examine the plausibility and safety of maintaining an 8w either Low fat or KD on PD outcomes	Both 4w diet plans included weekly shopping lists, daily set menus, simple recipes. Low fat = 42 g of fat (10 g SFA), 75 g of protein, 246 g net CHO; KD = 152 g of fat (67 g SFA), 75 g of protein, 16 g net CHO.	Blood ketone monitoring, metabolic biomarkers
Tidman USA [64]	US adults with PD ($n = 16$, 31.2% F, mean age 64.5 ± 11.9)	UDPRS (Part I-IV), PAS, CESD-R-20, HY	Pre-test/post-test single-group study investigated the effect of LCHO/high fat KD on motor symptoms, anxiety and depression and general health biomarkers in PD	LCHO/high fat KD intervention 12w 1750 kcal/day, 152 g of fat, 67 g SFA (approx. 78%), 75 g protein (approx. 17%), 16 g net CHO (approx. 3–4%), 11 g DF (included in CHO %)	Depression
COHORT					
Kyrozis Greece [78]	EPIC-Greece cohort Greek adults with possible incident PD ($n =$ 25,407), 59.3% F, 66.5% ≤ 60, 33.5% > 60; incident PD ($n = 88$), 58% F, 18.2% ≤ 60, 81.8% > 60	PD identified with UK Brain Bank criteria	Investigated age-adjusted incidence rates of PD and identified dietary and lifestyle factors associated with PD	Semi-quantitative EPIC-Greece FFQ (v) 12mo, 150 items, administered by trained interviewer. measured g/d, food groups, macro and micronutrients	

(*Continued*)

Table 3. Continued.

Author	Population	PD tool	Study description	Diet tool	Other outcome variables
Sääksjärvi Finland [69]	Finnish Mobile Clinic Survey Finnish adults ($n = 4524$), 47.2% F; no PD ($n = 4439$, 47.2% F, mean age 53.3); incident PD ($n = 85$, 47.4% F, mean age 52.2)	PD identified through Drug Imbursement Register and National Institute of Neurological Disorders and Stroke diagnostic criteria	Investigated if food groups or overall diet quality (AHEI) predict PD incidence	Diet history interview using FFQ (v) 12mo, 100 item, measured g/d, food groups macro and micronutrients, AHEI score	
Strikwerda Netherlands [90]	Rotterdam Study Dutch adults ($n = 9414$, 57.8% F, mean age 62.2); incident PD ($n = 129$, 47.3% F, mean age at diagnosis 76.6 ± 7.4)	PD incidence evaluated by a panel of experienced neurologists and confirmed diagnosis	Investigated the association between diet and risk of PD through pre-defined diet scores and data-driven dietary patterns. Additionally investigated specific food groups on risk of PD	FFQ (v) 12mo, 170 item measured g/d, macro and micronutrients, calculated Dutch diet score (based on Dutch Dietary Guidelines), MeDi diet score	
Yin Sweden [92]	Swedish Women's Lifestyle and Health study Swedish adult females ($n = 47{,}128$, 100% F, mean age 62.)	PD incidence ascertained through Swedish National Patient Register and 8th and 10th ICD codes to identify PD	Investigated the association between MeDi adherence at middle age with PD risk in Swedish women	FFQ (v) 6mo, 80 item measured g/d macro and micronutrients, food groups, MeDi adherence score	

PD, Parkinson's disease; F, female; UPDRS, Unified Parkinson's Disease Rating Scale; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MeDi, Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; FFQ, food frequency questionnaire; (v), validated; (nv), not validated: EAR, Estimated Average Requirement; EPIC, European Prospective Investigation into Cancer; HC, healthy control; HDI, Healthy Diet Index; DII, Dietary Inflammatory Index; BDI, Beck Depression Inventory; HADS, Hospital Anxiety and Depression Scale; ESS, Epworth Sleepiness Scale; MoCA, Montreal Cognition Assessment; MDS, Movement Disorder Society; GDS, Geriatric Depression Scale; MOSS, Medical Outcomes Sleep Scale; BDS, Blessed Dementia Scale; OMeDi, original Mediterranean diet; GMeDi, Greek Mediterranean diet; pRBD, Probable REM sleep behaviour disorder; AHEI, Alternative Healthy Eating Index; HY, Hoehn and Yahr Scale; NMSS, Non-Motor Symptom Scale; KD, ketogenic diet; MMSE, Mini Mental State Examination; HAMD-17, Hamilton Depression Rating Scale; QoL, quality of life; PDG-39, Parkinson's Disease Questionnaire; RegD, Regular diet; CHO, carbohydrate; PAS, Parkinson's Anxiety Scale; CESD-R-20, Centre for Epidemiological Studies Depression Scale-revised; LCHO, low carbohydrate; SFA, saturated fat; DF, dietary fibre; AHEI, Alternative Healthy Eating Index.

		MIND	MeDi	DASH	VEG	DII	HDI	AHEI	KD	HIGH CHO	DIET QUALITY
CROSS SECTIONAL	Agarwal (2018)	+	+	no association							
	Baert (2020)										PD inadequate
	Coe (2020)										PD mildly inadequate
	Gupta (2014)				no association						
	Lawrie (2022)	no association				no association	+				
	Maraki (2018)		+								
	Metcalfe-Roach (2021)	+	+								
	Mischley (2017)										+
	Molsberry (2020)		+					+			
	Navarro-Meza (2013)										PD inadequate
	Sauerbier (2013)										no association
	Zapała (2022)										PD poorer quality
Case study	Alcalay (2012)		+								
	Barichella (2013)										PD lower energy
	Barichella (2017)										no difference
	Belingheri (2020)										+
	Cassani (2017)		no association								PD altered preferences
	Fukushima (2012)										PD higher fat intake
	Hegelmaier (2020)				+						
	Okubo (2012)										+
	Palavra (2021)										PD higher sugar intake
	Torti (2020)										+
RCT	Koyuncu (2020)								+		
	Krikorian (2019)									+	
	Paknahad (2020)		+								
	Paknahad (2022)		+								
	Phillips (2018)								+	+	
	Tidman (2021)								+		
Cohort	Kyrozis (2013)										Dairy & PUFA associated with PD risk
	Sääksjärvi (2013)							no association			Dairy mildly associated with PD risk
	Strikwerda (2021)		+								+
	Yin (2020)		+								

Figure 2. Overview of academic literature findings. Green (+) fields indicate an inverse association between dietary pattern and PD risk, onset, or symptom severity. Beige fields indicate no association and purple fields report outcomes. [NR, not reported].

increase oxidative stress [39,80] and be unfavourable for the gut microbiome [68,85]. As has been reported previously, higher intakes of dairy, specifically milk, [69,78,89] were associated with an increased risk of PD [69,78]. Speculated reasons for this were pesticide exposure and altered uric acid metabolism [78].

Another underlying theme was that diet quality appeared to decline with PD onset and progression.

Of the studies that compared PD diets with their national guidelines, all three reported PD diets to be inadequate [76,83,89]. Where PD dietary intakes were compared with HC [72,74,82,86,89,91], all reported either inadequate intakes or poorer diet quality for PD compared to HC. Metcalfe-Roach et al. [40] found higher adherence to MeDi was associated with delayed onset of PD, yet Alcalay et al. [71] found those with PD had poorer adherence to MeDi, which suggests an effect of reverse causality [79]. Indeed, altered food preferences in PD were reported to influence intakes by Cassani et al. [74] and Palavra et al. [82]. Macronutrient differences were varied, again, possibly due to different traditional diets across the study populations. Only Barichella et al. [72] reported a significantly higher energy intake in PD than HC. They, as well as Palavra et al. [82], observed higher CHO intakes. Protein intakes were found to be higher in PD in three studies [72,76,82]. Barichella et al. reported higher protein intake for those not adhering to a protein redistribution diet ($n = 233$) compared to those who were ($n = 277$) [72]. Higher fat intakes (unhealthy fats) were observed in four studies [72,74,84,91], purportedly due to increased discretionary food intakes [74,82,84]. Fruit and vegetable intakes were generally similar across healthy subjects and those with PD, with only Navarro-Meza et al. [89] and Zapala et al. reporting intakes that were significantly lower in PD than HC.

Alterations to food preferences with PD were suggested as reasons for dietary intake differences due to concerns about protein/drug interactions and PD symptoms such as dysphagia, olfactory changes (hyposmia), constipation, and depression [74,82,84]. In addition, Palavra et al. [82] suggested altered dopaminergic signalling and cognition affecting food reward and mood to be the reasons for higher CHO intakes in the form of added sugars. Four studies reported higher intakes of discretionary type foods such as added sugars, animal fats and refined cereals [72,74,82,89]. Inadequate fluid intake was frequently observed in those with PD [72,74,76,83,86] and linked to PD symptoms such as dysphagia and hyposmia [72,74,83,86]. Constipation, another prevalent PD symptom that can be exacerbated by low fluid intake, was observed in two studies [72,83].

Findings from the four KD intervention studies all indicated some positive associations with various PD outcomes after the KD or high fat low CHO intervention [63–66]. Tidman et al. [64] saw improvements in anxiety and metabolic biomarkers; Koyuncu et al. [66] found improved voice quality; and Krikorian et al. [65] reported enhanced cognitive performance in mild PD cognitive impairment after an 8-week period of ketosis. Interestingly, Phillips et al. [63] observed equally positive benefits in motor and non-motor symptoms from both their KD and low fat, high CHO intervention arms [63]. All authors recommend further studies with larger sample sizes and longer duration to elucidate the pathophysiology and central mechanisms of these findings [63–66].

3.5. Content of grey literature

A detailed description of the sources for the grey literature search is provided in Supplementary Table 1 and the findings are summarised in Supplementary Table 2 (Accurate as of 17.01.2023). Thirteen peak nutrition and dietetics bodies such as Dietitians Australia and American Nutrition Association were identified, none had links to information specific to PD. The main government health websites rarely commented on PD but the US National Institutes of Health website [93] and Health Direct Australia website [94] provided brief advice and links to nutrition-related resources. The MIND diet was mentioned with reference to dementia but not PD specifically. The overall theme across peak PD bodies was that, although there is no specific diet for PD, a diet rich in fruit, vegetables and dietary fibre, wholegrains and healthy fats such as the MeDi, was repeatedly recommended, as well as plenty of fluids. Information provided by the majority of the peak bodies focused more specifically on timing of medications and drug efficacy, such as redistribution of protein, to optimise efficacy of levodopa. They also covered symptomatic management for swallowing, constipation and related malnutrition.

Most PD foundations were involved in research and the recruitment of participants for their studies with relevant discussion on their pages thereof. The main topics of information included the importance of healthy nutrition to alleviate PD symptoms such as constipation; how to manage dysphagia and hyposmia; and potential gut microbiome links with PD. Most foundations also had links to at least one blog site, and/or had links to YouTube videos. PD-specific medical news and magazine circulars reported the latest findings from studies and included special features on these. Although there were commonalities and divergences in the advice, most were based on scientific evidence.

As was expected, social media sites were plentiful and appeared to have an even mix of private and public groups, where posts ranged from evidence-based advice to the furthest extreme of fad cures and miraculous recoveries. YouTube videos were mostly produced by peak bodies and/or foundations and covered practical tips for maintaining a healthy diet and overcoming barriers to cooking and eating healthy arising from PD and

PD drug related symptoms. Finally, with the advent of e-books, there appeared to be many available titles that were independently published within the past 2–3 years. This review selected a sample of these including two whose authors were qualified nutritionists and two authors with PD. The selected titles covered healthy plant-based dietary advice, backed up by recipes.

In summary, dietary advice in the grey literature tended towards a common theme that there is not one particular diet for PD. However, whole food plant-based diets that include higher intakes of olive oil, legumes, vegetables and fruit as well as lower intakes of processed foods, meat, and animal fats, were generally recommended. This pattern of eating recapitulates the MIND diet, the DASH diet and the MeDi. Concurrently, there was emerging favourable evidence supporting a KD, but most reported on small trials and suggested further research would be prudent. Other categories that featured were interactions between levodopa and certain nutrients (predominantly protein), dysphagia and poor nutrition or malnutrition. The importance of maintaining good hydration was also emphasised. Overall diet and nutrition generally featured as low priority and, in many cases, had to be specifically searched for, rather than being presented on the main page. This may imply a lack of felt importance and/or a lack scientific consensus, which is reflected in the placing of the information.

4. Discussion

The results from the review of the academic literature were that adherence to a healthy diet with higher intakes of fruits, vegetables, fish and healthy fats such as MeDi or MIND diet patterns are associated with better outcomes for PD. The grey literature, although following the same theme, did not feature diet as a main priority in PD management, more as an additional benefit. Adherence to MeDi or MIND diet patterns were found to lead to improved outcomes in all but two of the studies where they were measured in this review. Both the MeDi and MIND diets include plentiful antioxidant-rich fruits, vegetables and olive oil, all of which are rich sources of dietary fibre and polyphenolic phytochemicals [39,40,68,71,79–81,90,92,95,96]. In addition, the diets provide a good source of fermentable dietary fibre required to maintain a healthy gut microbiome [68,79,80] and the inclusion of plenty of healthy fats for cell repair and brain health [80,81]. Neuroinflammation caused by oxidative stress is known to participate in the pathogenesis of PD [97]. Therefore, these antioxidant-rich diets represent a potential mechanism to alleviate PD pathology [98]. A dietary fibre-deprived gut microbiome has also been associated with higher circulating cytokines and chronic low grade inflammation [99]. Furthermore, gut microbiome profiles have recently been found to differ in individuals with PD compared to the general ageing population [85,100]. Evidence from a 2021 [32] review suggests that gut dysbiosis may precede the onset of motor symptoms of PD, therefore demonstrating how the MeDi and MIND diets offer a preventive effect. These topics were well covered by the grey literature.

A KD broadly describes a diet that restricts CHO intake thereby inducing a state of ketogenesis in the individual [44,45]. The diet has consistently been shown to be effective in the management of epilepsy with some positive findings also reported for Alzheimer's and PD [46], but studies have lacked rigour [45]. Two suggested mechanisms behind the benefits of the KD were covered in both the academic and the grey literature. The first was that ketosis could potentially enhance central and peripheral neurone energy metabolism through increased mitochondrial adenosine triphosphate production [45,63,64]. The second was that a high fat diet stimulates dopaminergic activation in the central nervous system [66]. Krikorian et al. further proposed that metabolic disturbance and insulin resistance exhibited by 80% of PD patients may be a contributing aetiological factor. In this review, the studies investigating KD reported beneficial outcomes for cognitive performance [65], speech and voice disorders [66], both motor and non-motor symptoms [63] and anxiety and body composition [64] in PD. All authors emphasised the need for further research and none explored long term effects on PD outcomes, or long or short-term effects on the gut microbiome. The fact that KD restricts most of the protective foods included in MeDi and MIND (vegetables, grains, legumes and fruit), thereby limiting dietary fibre and phytochemicals, the need for studies into the longer-term safety of KD and the impact on the gut microbiome is warranted [47]. In the grey literature, KD was occasionally featured by PD news websites but generally only recommended by the KD-specific sites.

In this review, the academic literature demonstrated that diet quality in those with PD was frequently suboptimal, with dysphagia, constipation and loss of smell (hyposmia) being the most prevalent PD symptoms leading to detrimental changes in habitual intakes. Additionally, intakes of CHO in PD were often of the more refined variety, being synonymous with a Western dietary pattern [82,91], which was associated with greater symptom severity and poorer PD outcomes [70,88,91,101]. Although the importance of healthy eating by including plenty of fruits, vegetables, wholegrains

and oily fish were well covered in the grey literature, there was little information covering the detrimental consequences of consuming a Western dietary pattern on PD symptom severity. A dietary regimen of fruits, vegetables and soluble dietary fibre, in conjunction with adequate fluids is recommended as a management strategy to improve constipation in PD [101]. When measured, it was found that fluid intakes were frequently below recommendations and/or lower in PD than HC [72,74,76,83,86] which is an often overlooked issue in PD management [102,103]. About half of the sources of nutrition advice in grey literature mentioned the elevated risks associated with dehydration, the need to maintain fluid intake and how to do this with dysphagia.

While not significant, energy intakes in PD were often higher than in the control groups [74,82,84], however, as has been found elsewhere, lower BMI or body weight was also observed amongst PD in this review [72,74,82,86,87,89]. Dietary protein and drug-nutrient interactions with levodopa [13,104] have been extensively researched in the past decades, however in this review only one study included protein redistribution diet and protein intake [72]. Their data suggested that drug-nutrient interactions could be better managed in terms of motor symptom fluctuations, with a protein redistribution diet [72]. Indeed, nutrition interventions that include protein redistribution, dietary fibre, vitamin C and caffeine have been recommended to improve levodopa therapy [30]. In contrast, protein restriction diets have been linked to weight loss and impaired nutritional status [104]. PD associated malnutrition, sarcopenia and dynapenia are key issues that increase with severity of symptoms and are associated with poorer outcomes and QoL [50,51,105,106]. Protein intake and levodopa interactions were well covered in the grey literature, with the general consensus recommending that protein should not be restricted but medications should be consumed 30–60 min prior to a meal.

Both non-motor symptoms and motor symptoms can lead to elevated metabolic demands in PD [105,107] due to degenerative nature of the disease and altered gut motility that may affect absorption of nutrients [105]. In addition to increased energy demands, other PD symptoms such as impaired fine motricity and dysphagia requiring texture modification of foods, as well as depression, cognitive impairment, hyposmia, and constipation all contribute to diminished appetite and poorer nutrition quality [74,82,84,105,106]. Nutrition interventions to reverse malnutrition in PD patients, especially in advanced age, have been found to lead to improvements [49,50,63,108]. In the grey literature, the importance of maintaining body weight and preventing muscle loss was well covered by the peak bodies. YouTube videos were arguably the best resource for providing information on how to manage daily symptoms and facilitate healthy eating. Often these were presented by individuals with PD themselves, however, this information mostly required some prior searching and was not front and foremost.

Interestingly, all of the intervention studies in this review led to improvements in PD symptoms, regardless of the dietary pattern being implemented [63–66,80,81]. This implies that provision of nutritional guidance in the form of a suggested daily/weekly menu plan is of value in the care of those with PD. This was well covered in the grey literature, where many of the peak bodies had links to recipes and menus for healthy eating that were based on MeDi-style ingredients. Other sectors of the grey literature, especially e-books, also provided plenty of guidance and recipes for how to follow particular dietary patterns; however, these were not always based on scientific evidence.

4.1. Strengths and limitations of this study

This study was the first to review both the current peer-reviewed academic literature and the grey literature i.e. public discourse through peak bodies, social media, blogs and other electronic forums worldwide, on the association between whole of diet patterns with PD risk, symptom severity and disease progression. The search strategy included electronic databases with peer-reviewed literature as well as grey literature sources, focussing on the general adult population at risk of or diagnosed with PD. To our knowledge, this is the first time the information provided in open electronic forums, or the grey literature, has been compared with the consensus in the academic literature. Our findings provide valuable insight into the content, integrity and gaps in information that represent a major communication source for those with PD.

Studying the grey literature will always be limited by the fact that social media and e-health platforms are constantly evolving and it is, therefore, impossible to capture everything. The academic literature review spanned the globe and highlighted similarities and differences experienced by those with PD from various cultural and ethnic backgrounds, particularly emphasising the need to consider the typical diet of the study population when providing dietary advice. The grey literature review included mostly US sources (20 from US, 5 from UK, 4 from Australia and 3 from Canada) and was limited to those in English, therefore may not be a true representation of available information. In addition, the grey literature is targeted to those who

already have a diagnosis; therefore, advice on how to reduce the risk of PD is generally not relevant and would fall under the general population nutrition websites.

4.2. Conclusion

The general consensus in the academic literature is that a MeDi/MIND whole of diet pattern with plenty of fresh fruit, vegetables, wholegrains, omega-3 fish and olive oil is best practice for slower progression of disease, improved PD symptoms and decreased PD incidence. Support for the KD is emerging, but long-term studies are needed to further investigate enduring effects on PD, microbiome and sustainability. There was no evidence in either academic or grey literatures to suggest that the diet alone is better than currently available medicine, rather that it should be considered as an adjunct. Encouragingly, the grey literature mostly aligned with the academic literature; however, the topic of nutrition was rarely forefront and, as is often the case with the internet, contained conflicting advice that could be confusing. More emphasis on the importance and significance of good nutrition in the grey literature is needed with positive messaging on dietary approaches to manage day-to-day symptoms. Considering the complex and multifactorial nature of the disease, a personalised approach that considers each patient's unique needs and symptoms would be ideal. Nevertheless, based on the current evidence, some dietary patterns that may be beneficial for Parkinson's disease include the Mediterranean diet, the DASH diet, and the MIND diet.

Data availability statement

Authors agree to make data and materials supporting the results or analyses presented in their paper available upon reasonable request.

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