Migraine and Diet

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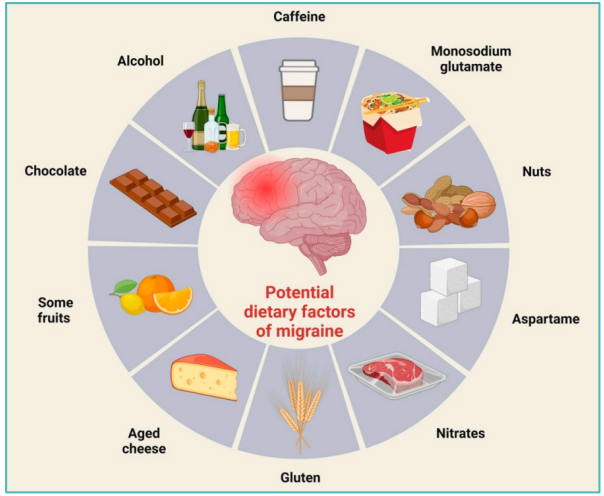
The 5th Nordic Migraine Symposium:
Pearls and Pitfalls in Migraine Management
Nov 10-11 2023 - Copenhagen, Denmark

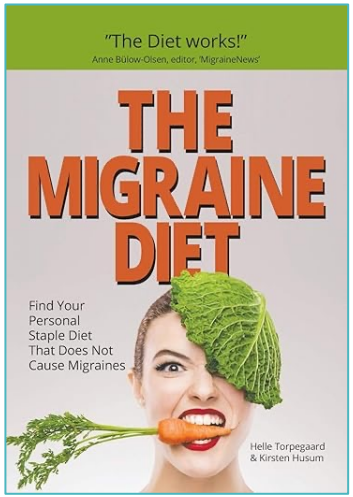
Disclosure

- This is an invited lecture sponsored by Teva Pharmaceuticals.
- The presenter has no relevant point to disclose about the content of this lecture.

Agenda

- Diet: Why diet? Do we have a healthy diet?
- Migraine and Diet: What is proven?
- Future perspectives: Where to focus?





Neurol. Int. 2023, 15, 1174–1190
THE MIGRAINE DIET by Helle Torpegaard and Kirsten Husum, 2018

Diet: Why diet?

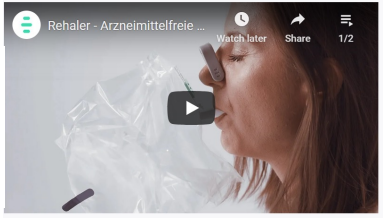
Lifestyle modifications, behavioral therapy

Education, support, managing expectations, and close follow-up

Pharmacologic therapy

Chronic migraine management

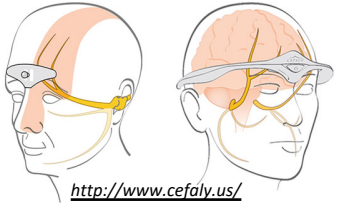
https://theranica.com/nerivio/



https://www.rehaler.io/rehaler-device

Neurostimulation in the treatment of primary headaches

Sarah Miller,[1] Alex J Sinclair,[2] Brendan Davies,[3] Manjit Matharu[1]



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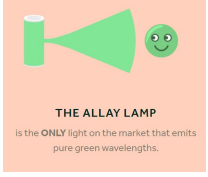

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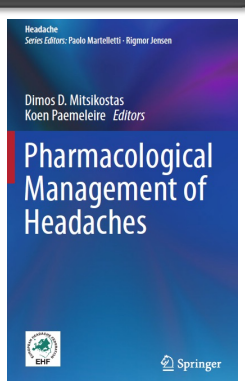
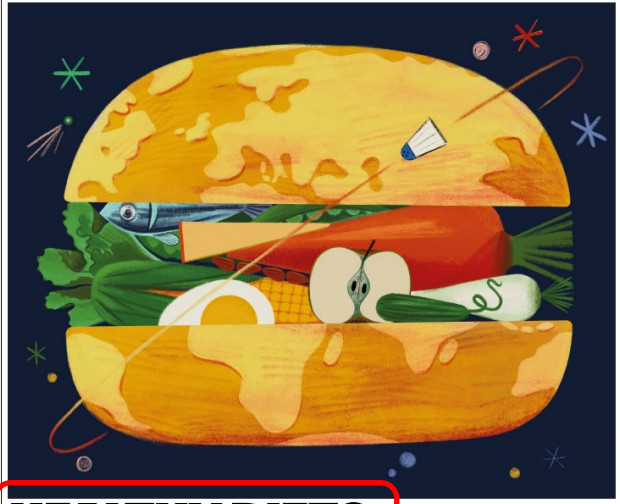


Feature

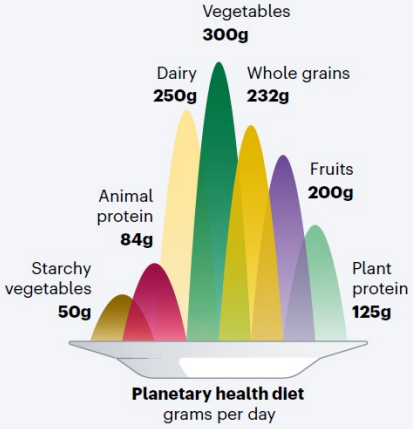


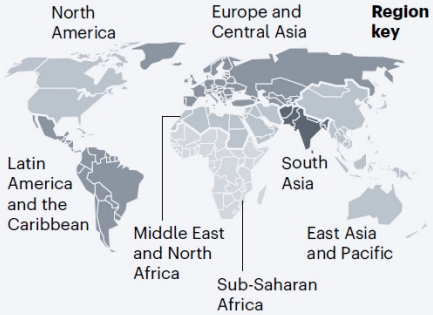
HEALTHY DIETS FOR PEOPLE AND THE PLANET ?

HEALTHY EATING

A commission of food researchers devised a 'planetary health' diet — meant to be nutritious and sustainable — and compared its composition with the average diets in different regions. Further studies showed that, in many regions, following the proposed diet would be prohibitively expensive.

By Kerri Smith
Design by Jasiek Krzysztofiak



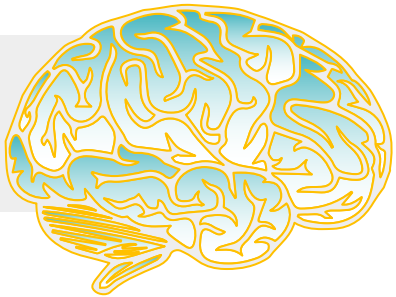


Diets that are lower in fat, meat, and sugar reduce the relative risk of several health conditions

Nature | Vol 600 | 2 December 2021

Migraine and Diet: What is proven?

Migraine - Diet



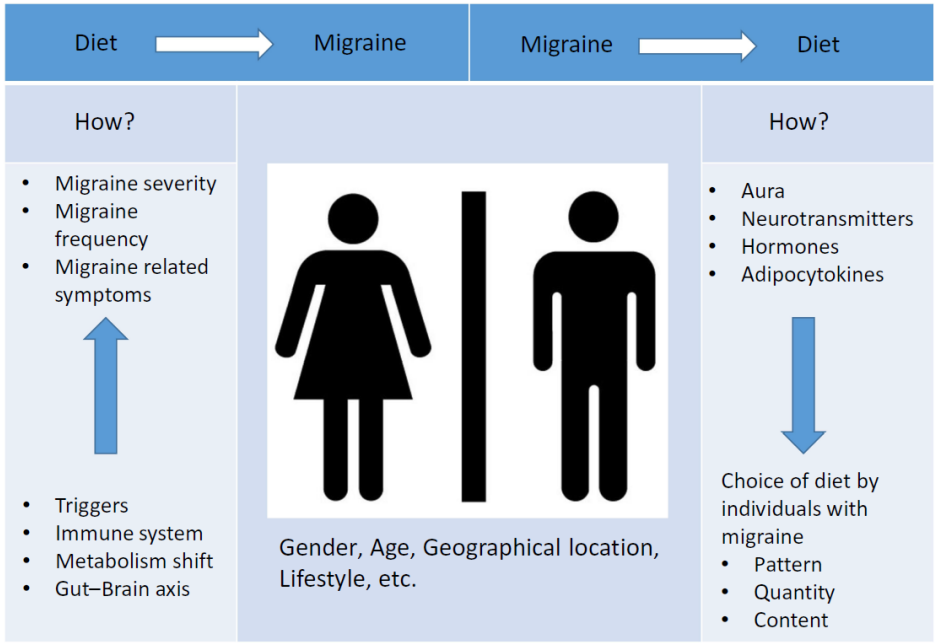


Figure 1 A potential bidirectional relationship between migraine and diet.

The diet-migraine interaction is a dynamic bidirectional phenomenon that requires careful monitoring, review, and justification of dietary choices to yield the optimal outcome while minimizing potential risks.

- How Does Diet Affect Migraine?
- Does Migraine Affect Diet, and How?

EBC
European Brain Council

The cause of migraine attacks is not yet known. It is suspected that they result from abnormal activity in the brain. This can affect the way nerves and brain cells communicate as well as the chemicals and blood vessels in the brain. Genetics may make someone more sensitive to the triggers that can cause migraine attacks. However, the following triggers are likely to set off migraine attacks:

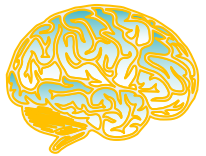
Hormonal changes: Women may experience migraine symptoms during menstruation or during the month, due to changing hormone levels.

Emotional triggers: Stress, anxiety, excitement, and shock can trigger a migraine.

Physical causes: Tiredness and insufficient sleep, shoulder or neck tension, poor posture, and physical overexertion have all been linked to migraine attacks. Low blood sugar, trips in airplaines and jet lag can also act as triggers.

Diet

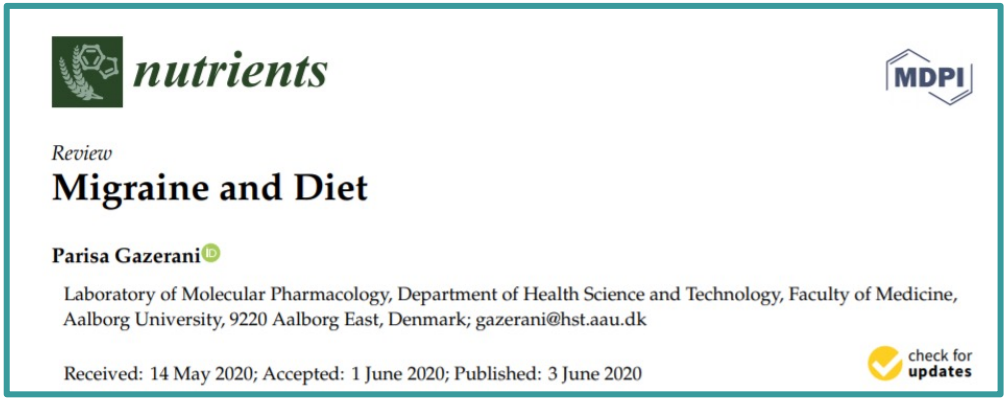
Triggers in the diet: Alcohol can contribute to triggering migraine attacks as well as some normal and usual foods for so many affected people. Additives such as tyramine or histamine can worsen the situation. Migraine triggers are as personal as the fingerprint and each person can be sensitive to different ones. Irregular mealtimes and dehydration have also been named as potential triggers.



Medications: Some sleeping pills, hormone replacement therapy (HRT) medications, antibiotics, the combined contraceptive pill and some others have all been named as possible triggers.

Triggers in the environment: Flickering screens, strong smells, second-hand smoke, and loud noises can set off a migraine. Stuffy rooms, temperature changes, and bright lights are also possible triggers.[8]

https://www.braincouncil.eu/disease-fact-sheets/



nutrients

MDPI

Review

Migraine and Diet

Parisa Gazerani

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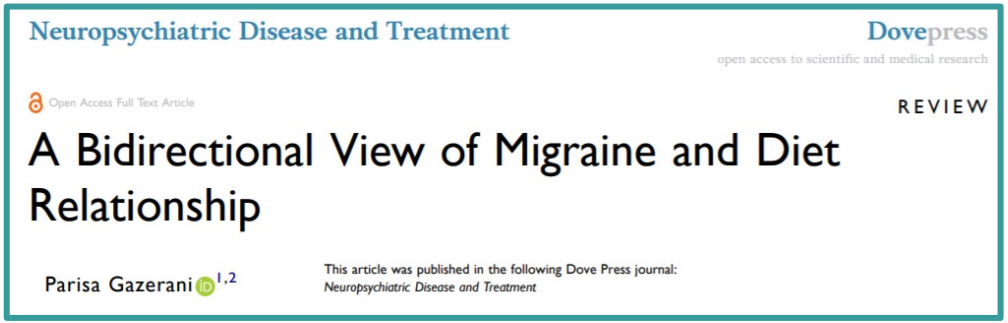
Received: 14 May 2020; Accepted: 1 June 2020; Published: 3 June 2020

check for updates

Altmetric has tracked 24,657,405 research outputs across all sources so far. Compared to these this one has done particularly well and is in the 99th percentile: it's in the top 5% of all research outputs ever tracked by Altmetric.



Neuropsychiatric Disease and Treatment

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REVIEW

A Bidirectional View of Migraine and Diet Relationship

Parisa Gazerani [1,2]

This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment

Altmetric has tracked 23,577,654 research outputs across all sources so far. Compared to these this one has done particularly well and is in the 94th percentile: it's in the top 10% of all research outputs ever tracked by Altmetric.

CURRENT OPINION

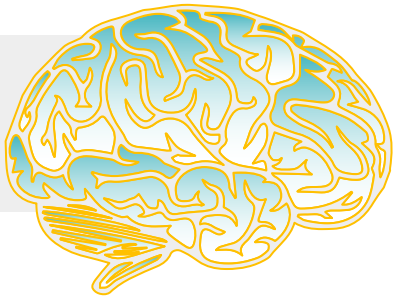
Diet and migraine: what is proven?

Parisa Gazerani [a,b,c]

Curr Opin Neurol. 2023 Sep 20

Altmetric has tracked 24,694,993 research outputs across all sources so far. This one is in the 39th percentile – i.e., 39% of other outputs scored the same or lower than it.

Diet Affects Migraine



Diet Affects Migraine

Element	Modification	Level of Evidence	Reference(s)	Future Considerations
Dietary Triggers Systematic review • Major triggers: Caffeine alcohol • Effect: Migraine frequency	**Dietary Modifications** Promising outcome: (yet, insufficient) • Elimination diets • Low-fat diet • Ketogenic diet	Low	[22]	• Age, sex, puberty, hormonal levels • Other lifestyle factors (eg, sleep, exercise) • Migraine characteristics (with aura, without aura, comorbid conditions, episodic, chronic) • Larger population, longer duration, proper control group
Element	**Modification**	**Level of Evidence**	**Reference(s)**	**Future Considerations**
Obesity and Migraine Systematic reviews and meta-analyses • Effect of weight control: Headache severity, frequency, duration, and associated disabilities	**Weight Control** Promising outcome: (yet, insufficient) • Obesity and being underweight are at higher risk of migraine • Diet quality and maintaining a healthy weight can be the key • Amount of weight loss is not critical • Strategy of weight loss (eg, behavioral weight loss, educational instructions) is not critical	Low	[71–73,77,81]	• Diverse population instead of only at higher obesity risk (ie, middle-aged women) • Age, sex, genetic predisposition, and environmental factors • Neurometabolic features • Nutritional intervention to improve nutrient metabolism, neuroinflammation, oxidative stress • Role of hypothalamus • Comorbidities, eg, irritable bowel syndrome (IBS)
Element	**Modification**	**Level of Evidence**	**Reference(s)**	**Future Considerations**
Gut–Brain Axis, Microbiome Systematic review Probiotic supplementation • Effect: Frequency, severity, number of migraine days, consumed drugs (abortive), quality of life	**Microbiome Modification** • To maintain healthy composition of the gut microbiota • Proper probiotics • Adding mineral and vitamins	Low	[102–,105–,107–,108]	• Microbiome analysis, pre- and post-intervention • Proper inclusion and exclusion for the enrolment • Age, sex, genetic predisposition, and environmental factors • Proper control groups, proper study design and length

- Dietary triggers exist for migraines, for example, coffee and alcohol, according to a new systematic review.
- Elimination diets must be personalized to delineate a balanced diet with acceptable quality and pattern.

Neuropsychiatric Disease and Treatment 2021:17 435–451

MIGRAINE WELLNESS PROGRAM

ASSOCIATION OF MIGRAINE DISORDERS

Diet and Migraine

Preventive - Diet

How and why people react to different foods is not yet well understood. However, it is worth trying to identify if you have a food trigger and then avoid it.

In general, food triggers fall into three main categories:

- Byproducts of food aging and fermentation: red wine, aged cheeses, yeast and yogurt
- Foods with ingredients that affect our nervous system: coffee, chocolate, MSG, aspartame, citrus fruits and the nitrates used as preservatives in many prepackaged foods, particularly cured meats
- Foods you have mild or silent allergies or sensitivities to: such as milk, corn, soy and wheat (gluten). Gluten sensitivity is particularly a common issue for those with migraine.

Blood tests for food allergies may or may not identify a food trigger. The use of an **elimination diet** - a careful removal of specific foods over a specific time period, followed by a reintroduction of the food - is the most reliable method to identify dietary migraine triggers.

Simple rules: Buy fresh foods only - No deli or cheese

MIGRAINE WELLNESS PROGRAM

ASSOCIATION OF MIGRAINE DISORDERS

Common Food & Beverage Triggers

Common Food & Beverage Triggers

Food Additives

- monosodium glutamate (MSG), often in Asian foods and meat tenderizers
- artificial sweeteners, especially aspartame
- nitrates, often found in bacon, ham, and hot dogs
- yellow dye #6, found in some processed foods
- tyramine
- Brewer's yeast

Caffeine
including coffee, many teas, colas, and chocolate

Ripened Cheeses
such as cheddar, brie, and camembert

Alcohol
red wine and beer are the most common culprits

Nuts and Seeds

Aged, Fermented, and Pickled Foods
such as sauerkraut, pickles, olives, soy sauce, miso, and salami

Cultured Dairy Products
including yogurt, buttermilk, and sour cream

Very Cold Foods
cold foods and beverages, such as ice cream or frozen beverages

Migraine-Friendly Foods?

How Triggers Work

There are a number of theories about why some foods trigger migraine including:

- Antibodies that cause allergic reactions may responsible.
- Some foods cause blood vessels in the brain to constrict, which causes an attack.
- migraine may be the result of your body defending itself against unstable molecules called free radicals that can damage healthy cells.

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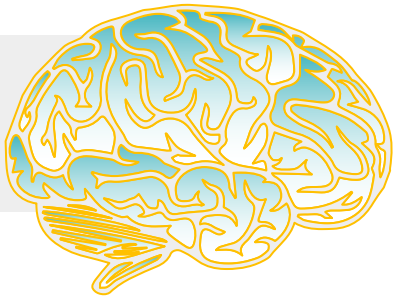
Migraine Diets?



- The literature is rich in studies examining ketogenic and low-calorie diets, modified Atkins diets, low-glycemic diets, Mediterranean diets, healthy diets, prudent diets, Western diets, weight loss diets, and diets with low omega-6 and high omega-3 fatty acid intake.
- A piece of average-quality evidence shows that the ketogenic diet (KD) and the Dietary Approaches to Stop Hypertension (DASH) are effective in reducing the frequency, duration, and severity of migraine headaches in adult patients.
- Mechanisms underlying the effects of these diets against migraine are proposed to be diverse and multidimensional, including neuroprotection, mitochondrial function, and energy metabolism compensating serotoninergic dysfunction, decreasing calcitonin gene-related peptide (CGRP) level, suppressing neuro-inflammation and cortical spreading depression (CSD), and affecting platelet function and regulation of vascular tone, which are proposed to play a role in migraine pathophysiology

DASH diet emphasizes plant-based foods high in potassium, calcium, and magnesium and minimizes foods high in saturated fat, cholesterol, sodium, and sugar.

KD is a regimen that mimics fasting and induces ketone body production. This is obtained through carbohydrate restriction, with the aim of decreasing insulin secretion and increasing glucagon secretion along with the mobilization of fatty acids and production of ketone bodies.

Neuropsychiatric Disease and Treatment 2021:17 435–451

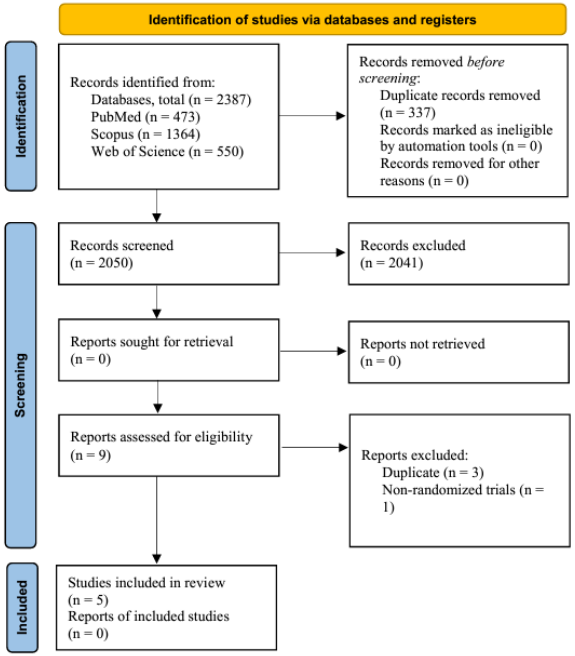


Fig. 1 Literature search and study selection process

SN Comprehensive Clinical Medicine (2022) 4:185
https://doi.org/10.1007/s42399-022-01270-6

REVIEW

Effect of Major Dietary Interventions on Migraine: a Systematic Review of Randomized Control Trials

SN Comprehensive Clinical Medicine
A SPRINGER NATURE journal

Table 2 General characteristics of primary studies included the systematic review

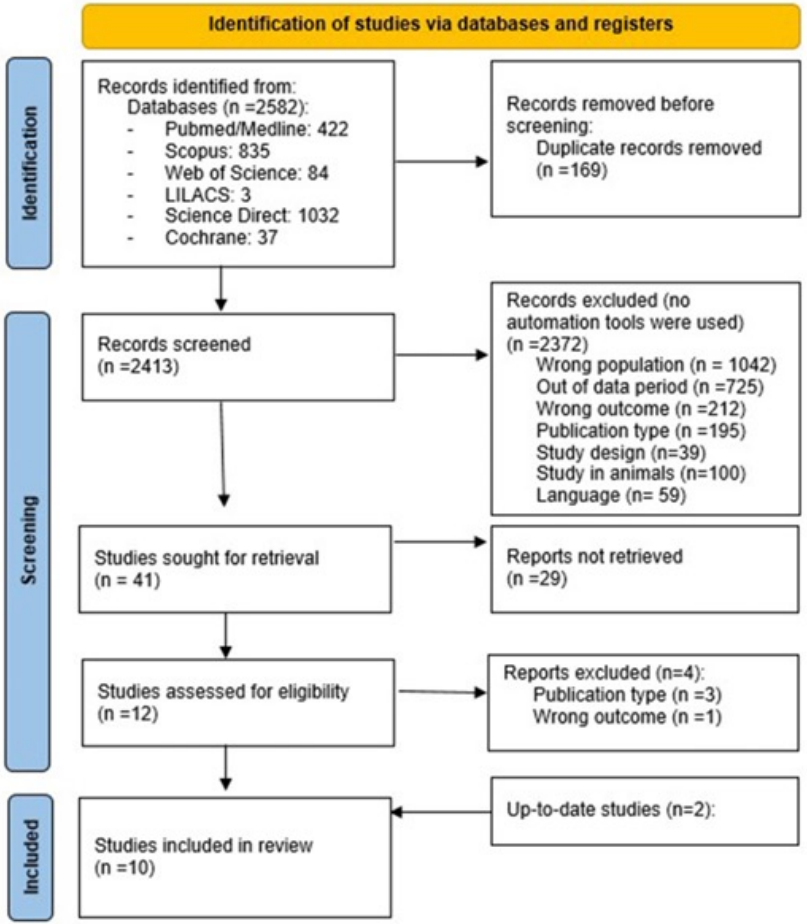
Authors/year/country	Sample size	Study design	Mean age (SD)	Gender (% females)	Intervention	Placebo	Duration of study (weeks)	Measured outcome(s)
Amer et al., 2014 [23] USA	I (n = 198) C (n = 192)	RCT (crossover)	48 (10)	B (57)	DASH diet	Control diet	12	Occurrence and severity of headache
Di Lorenzo et al., 2019 [24] Italy	I (n = 18) C (n = 17)	RCT (crossover)	43.5 (9.5)	B (82.9)	VLCKD	VLnCKD	12	Frequency and severity of headache Change in BMI
Arab et al., 2021a [26] Iran	I (n = 51) C (n = 51)	RCT (parallel)	34.54 (0.99)	F (100)	DASH diet	Dietary advice	12	Headache frequency, duration, severity, and quality of life Mental health measures
Arab et al., 2021b [25] Iran	I (n = 51) C (n = 51)	RCT (parallel)	34.54 (0.99)	F (100)	DASH diet	Dietary advice	12	Parameters of oxidative stress status and Headache frequency, duration, and severity
Haslam et al., 2021 [27] Australia	I (n = 11) C (n = 5)	RCT (crossover)	42.6 (11.2)	B (87.5)	Ketogenic diet	"Anti-headache" dietary pattern	12	Migraine Frequency, Severity and Duration Days to reach ketosis Change in body weight and composition Change in physical activity

I, intervention; *C*, control; *RCT*, randomized control trial; *B*, both gender; *DASH*, Dietary Approaches to Stop Hypertension; *VLCKD*, very low-calorie ketogenic diet; *VLnCKD*, very low-calorie non-ketogenic diet; *F*, females only

- **The DASH diet** is high in fiber and minerals such as calcium, magnesium, and potassium, and these nutrients may promote DASH's anti-inflammatory effects in different ways.
- High-fiber diets reduce inflammation by slowing glucose absorption, altering the gut microbiota, and thus lowering inflammatory cytokine production
- **KDs** have been reported to improve migraine status mechanistically by inducing an increase in brain dopaminergic activity via ketogenesis. Moreover, ketone bodies have been shown in an animal model to increase the activity of gamma amino butyric acid, which appears to play a protective role in migraines.

Jibril, A.T., Shab-Bidar, S., Djafarian, K. et al. Effect of Major Dietary Interventions on Migraine: a Systematic Review of Randomized Control Trials. SN Compr. Clin. Med. 4, 185 (2022)

PICOS criteria	Inclusion criteria	Exclusion criteria
Population	Children, adolescents, and adults with a diagnosis of migraine	Individuals without migraine
Intervention	Achievement of ketosis by: —production of endogenous ketone bodies induced by ketogenic dietary therapies (CKD, MCT, LGI, MAD, or VLCKD) OR —administration of exogenous ketone bodies (EK)	Ketosis unrelated to ketogenic diets or exogenous ketone body administration (e.g., ketosis in diabetes)
Comparison	Comparison patients who remained on their usual diet, on placebo treatment, or on pharmacologic treatment; other interventions; without a comparator	Not applicable
Outcomes	Reduction in the frequency and intensity of migraine episodes	Unrelated to migraine episodes
Types of studies included	Randomized controlled trials; uncontrolled observational studies	Full text not available; without the outcomes of interest; not human studies; reviews, opinion articles, guidelines, letters, editorials, comments, case reports and case series, news, conference abstracts, theses, and dissertations; and *in vitro* or animal studies
Research question	What is the efficacy of the ketosis for the prevention or attenuation of migraine?	



Neri LCL, Ferraris C, Catalano G, Guglielmetti M, Pasca L, Pezzotti E, Carpani A, Tagliabue A. ***Ketosis and migraine: a systematic review of the literature and meta-analysis****. Front Nutr. 2023 Jun 12;10:1204700.*

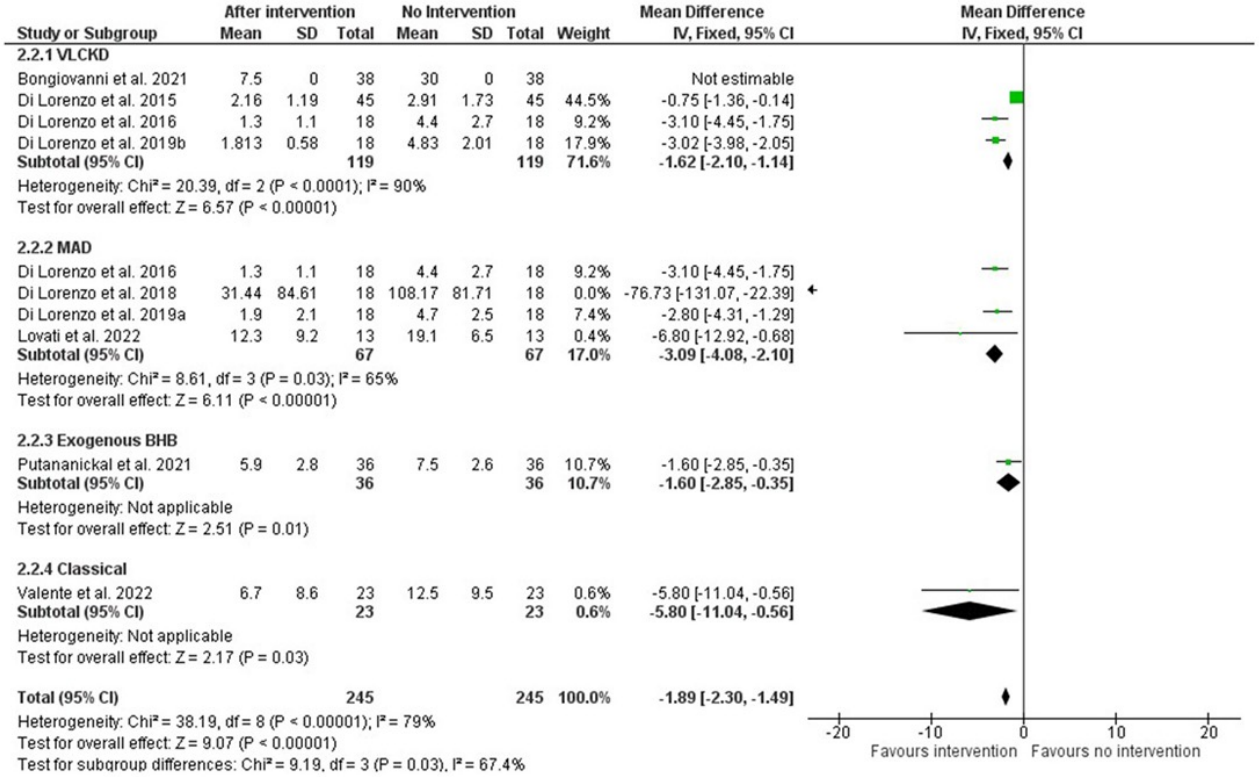
frontiers | Frontiers in Nutrition

TYPE Systematic Review
PUBLISHED 12 June 2023
DOI 10.3389/fnut.2023.1204700

Ketosis and migraine: a systematic review of the literature and meta-analysis

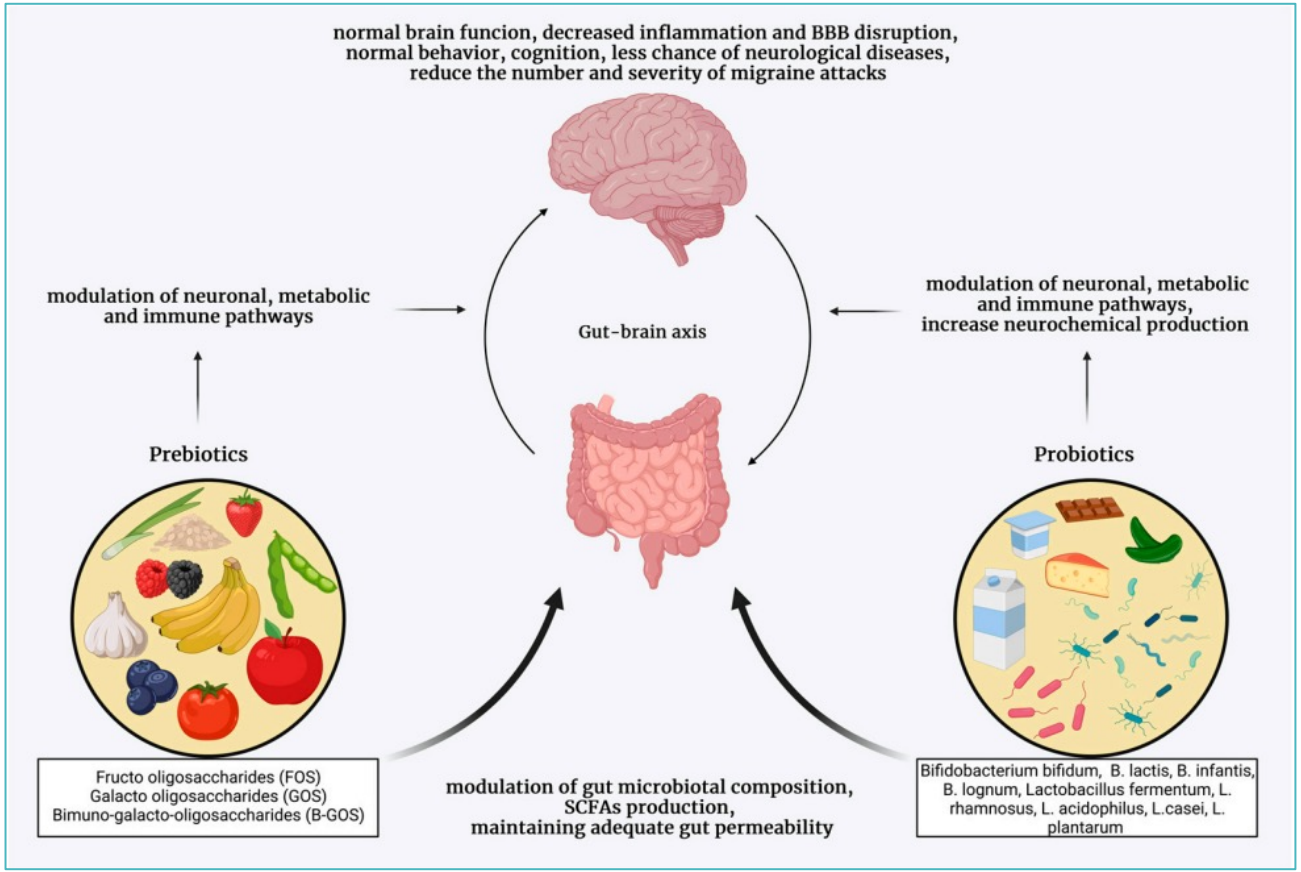
ketogenic therapy, which replaces the brain's glucose fuel source with ketone bodies, potentially reduces the frequency or severity of headaches.

Meta-analysis of different types of ketosis-inducing interventions on migraine frequency attacks (number per month)



Neri LCL, Ferraris C, Catalano G, Guglielmetti M, Pasca L, Pezzotti E, Carpani A, Tagliabue A. Ketosis and migraine: a systematic review of the literature and meta-analysis. Front Nutr. 2023 Jun 12;10:1204700.

The gut microbiome is altered in patients with migraine and the gut-brain axis in migraine has attracted a high attention



Importance of the Microbiota and Diet in Migraine. Neurol. Int. 2023, 15, 1174–1190

Gazerani P. A Bidirectional View of Migraine and Diet Relationship. Neuropsychiatr Dis Treat. 2021;17:435-451

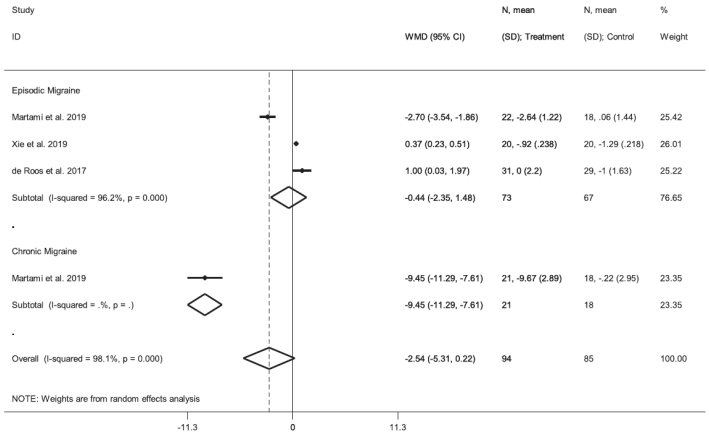


Figure 2. Forest plot of randomized controlled trials investigating the effects of Probiotic supplementation on the frequency of migraine attacks.

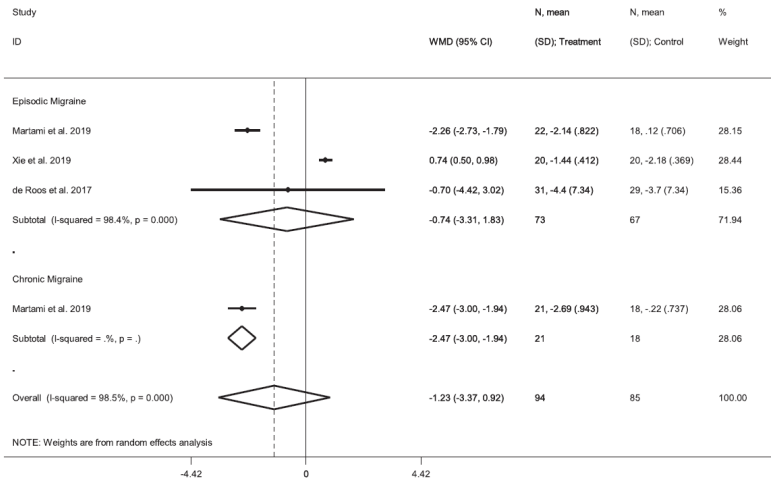


Figure 3. Forest plot of randomized controlled trials investigating the effects of Probiotic supplementation on the severity of migraine attacks.

NUTRITIONAL NEUROSCIENCE
2022, VOL. 25, NO. 3, 511–518
https://doi.org/10.1080/1028415X.2020.1764292

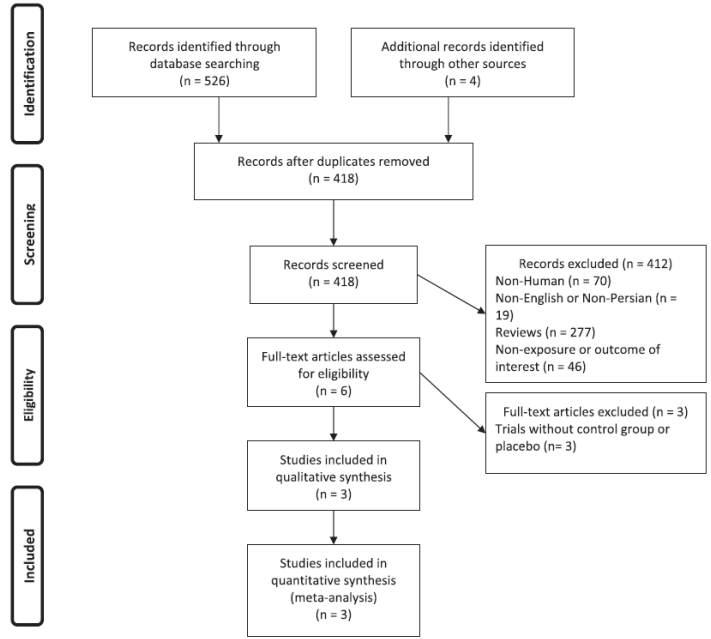
Taylor & Francis
Taylor & Francis Group

REVIEW

Check for updates

Effect of probiotic supplementation on migraine prophylaxis: a systematic review and meta-analysis of randomized controlled trials

Nutritional Neuroscience, 25:3, 511-518, 2022



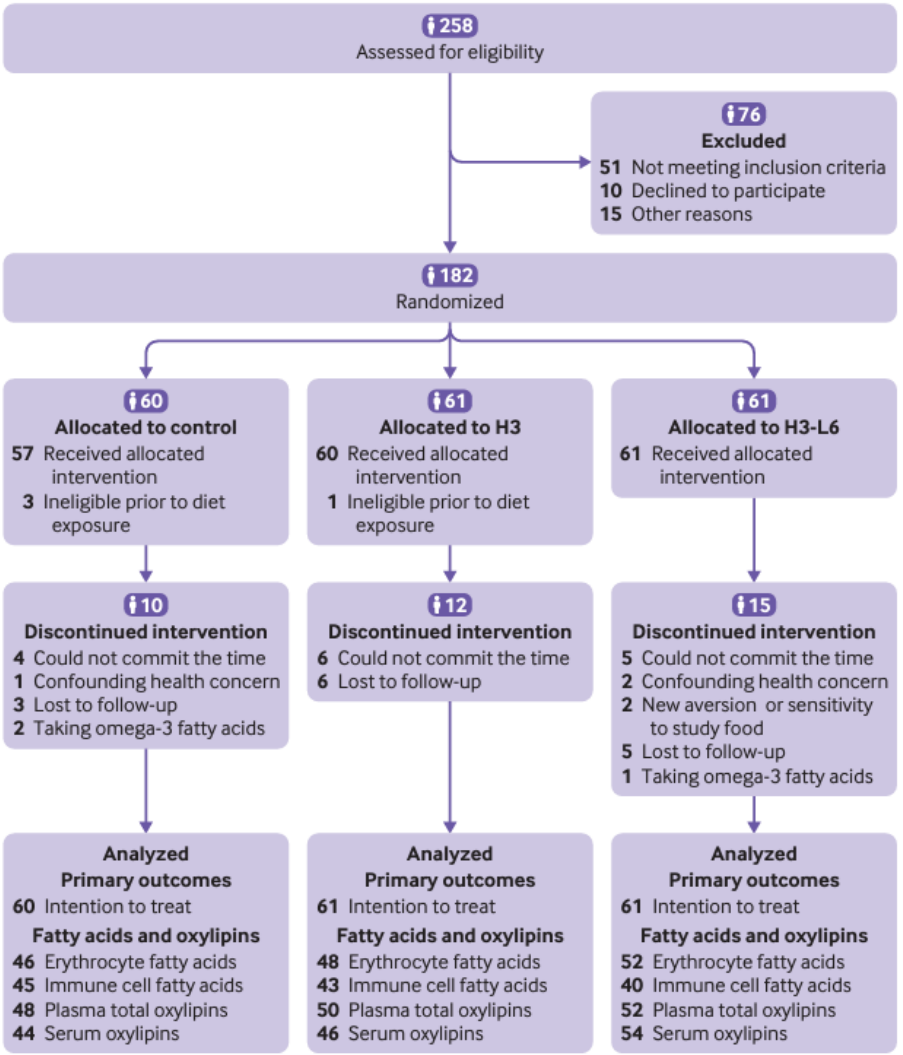
The main results showed that probiotic supplementation had no significant effect on the frequency and severity of migraine headaches.

Dietary fatty acids for migraine

- These fatty acids are precursors to oxylipins that are proposed to contribute to pain and inflammation.
- Omega-3 derivatives exert analgesic and anti-inflammatory properties, and omega-6 derivatives are algesic.
- In a recent randomized controlled trial, 182 participants were divided to consume one of the three diets:

1. control diet (typical levels of omega-3 and omega-6)
2. interventional diet with higher omega-3 + omega-6 levels the same as the control diet
3. interventional diet with higher omega-3 + lower omega-6.

In both intervention diets, the frequency of headaches was lower with shorter headaches.



BMJ 2021;374:n1448

British Journal of Nutrition (2023), 129, 947–954 doi:10.1017/S0007114522000046
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The relationship between dietary nutrients patterns and intensity and duration of migraine headaches

Table 3. Principal factor loading of nutrients intake

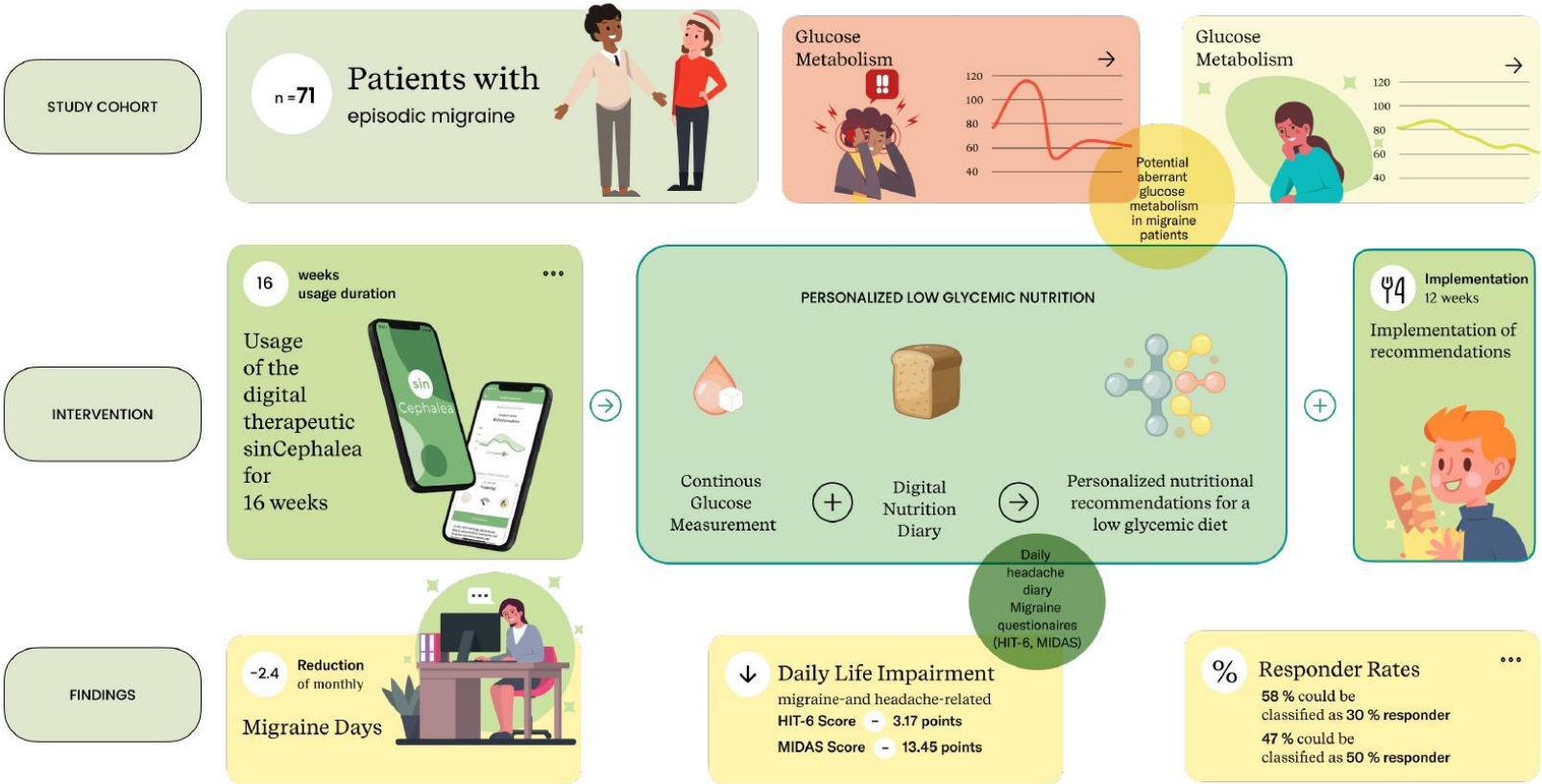
Nutrients	Pattern 1	Pattern 2	Pattern 3
Ca (mg)	0·91		
Vitamin A (RAE)	0·90		
Vitamin K (μg/d)	0·90		
Vitamin C (mg/d)	0·85		
Vitamin B_6 (mg/d)	0·78		
Vitamin B_2 (mg/d)	0·77		
Mg (mg/d)	0·65		
Vitamin B_1 (mg/d)		0·96	
Carbohydrate (g/d)		0·88	
Vitamin B_3 (mg/d)		0·85	
Vitamin B_9 (μg/d)		0·80	
Protein (g/d)		0·79	
Total fibre (g/d)		0·65	
Vitamin B_{12} (μg/d)			0·91
Vitamin D (μg/d)			0·86
Percent of variance explained	49·88	22·06	12·72

RAE, retinol activity equivalents.
Factor loadings of < 0·5 have been removed to simplify the table. Extraction method: principal component analysis. Rotation method: Varimax with Kaiser Normalization. a. Rotation converged in four iterations.

Conclusion

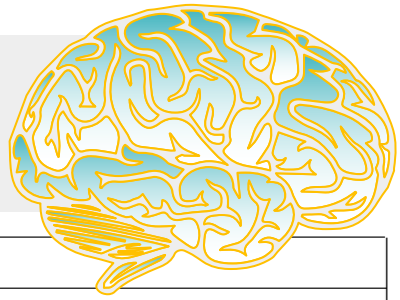
Our study found a significant relationship between the second identified dietary pattern, which included vitamin B_1, carbohydrate, vitamin B_3, vitamin B_9, protein, and total fibre and VAS and pain duration. Furthermore, we found a relationship between MIDAS and the first nutrient pattern, characterised by Ca, vitamin A, vitamin K, vitamin C, vitamin B_6, vitamin B_2 and Mg, among women. Additionally, there was a significant association between the third nutrient pattern (vitamin D and B_{12}) and pain duration. Overall, this research demonstrates that dietary nutrients patterns should be monitored closely in individuals suffering with migraine.

sinCephalea is a non-pharmacological, digital migraine prophylaxis that is, firstly, used by patients regularly and according to the instructions, and secondly, induces a therapeutic effect that is within the range of pharmacological interventions. To date, no unexpected side effects have been reported from the use of sinCephalea.



Nutrients. 2022 Jul 17;14(14):2927.

Migraine Affects Diet Choice



Migraine Affects Dietary Choices

Element	Observation	Level of Evidence	Reference(s)	Future Considerations
Food Intake and Food Avoidance Behavior • Choice of diet • Nutritional metrics (diet quality, composition, meal schedule, and amount)	**Epidemiological Studies** • A migraine-specific pattern of food intake in migraine patients • Aura influences choice of food	Low	21,23,50,124,127,128	• Age, sex, race, genetic predisposition, and environmental factors, geographical locations • Proper control groups, proper study design and length • Longitudinal studies, cofactorial designs (eg, sleep, exercise) • Neurotransmitters, hormones, and adipocytokines levels • Role of the hypothalamus • Type of migraine (episodic, chronic, with or without aura) • Comorbid conditions • Microbiome analysis

Notes: Please note that selected elements, mainly are based on the findings of the systematic reviews and meta-analyses in the literature (see references) and future considerations are selected points for inspiration.

- **Dietary quality and dietary patterns are two important aspects.**
- **The DDS (dietary diversity score) is used to evaluate if adequate nutrient is included and what the overall quality of the diet is.**

Neuropsychiatric Disease and Treatment 2021:17 435–451

Neurological Sciences (2021) 42:3403–3410
https://doi.org/10.1007/s10072-020-04982-6

ORIGINAL ARTICLE

Association of dietary diversity score (DDS) and migraine headache severity among women

Neurol Sci 42, 3403–3410 (2021)

Diet and migraine: what is proven?

Parisa Gazerani[a,b,c]

Curr Opin Neurol. 2023 Sep 20

KEY POINTS

- Dietary triggers of migraine attacks must be identified and differentiated from prodromal symptoms.
- Elimination diets for the omission of dietary triggers must be personalized with the aid of a dietician to ensure diet quality.
- The ketogenic diet and Dietary Approaches to Stop Hypertension diets are found effective in reducing the frequency, duration, and severity of migraine headaches in adult patients.
- Microbiome research in migraine is emerging, and the use of pre or probiotics is being studied.
- Digital health can be used in monitoring, education, and patient adherence purposes in migraine care.

Future perspectives

- Dietary recommendations may aid in immediate control, slow progression, or prevention of diet-related comorbidities. Apply patient-centric model.
- Consider comorbidities and a broader lifestyle modification, including sleep hygiene, stress management, regular exercise, or smoking cessation.
- Consider the effect of migraine or its evolution over age and among the genders on dietary choices, Pay attention to dietary patterns, quality, and amount

Thanks

Sunrise Over Hamnoy in the Lofoten Islands – Credit to photographer Colby Brown