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Guidelines Review for Malaysian Recommendation on Omega-3 Intake in Type 2 Diabetes Mellitus

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Abstract

This review highlighted a fundamental dietary recommendation of ω-3 intake for Malaysian T2DM patients through assessment of previous T2DM guidelines. Any adult T2DM evidence-based guideline or CPG was considered for this review. Title and abstracts were screened based on the inclusion/exclusion criteria and the descriptive data were extracted. From 392 records, 30 were shortlisted; but only twelve were included. Six guidelines suggested fatty fish consumption, with three guidelines recommended at least two/three fatty fish serving weekly, others proposed the plant source of ω-3, like the daily consumption of 2g-3g of plant sterol, 10g daily flaxseed intake and plant-based fats/oil, nuts, seeds. Another three guidelines mentioned a general recommendation of PUFAs. In conclusion, incorporating ω-3 in T2DM management is beneficial and a recommendation of weekly serving of at least two/three local fatty fish and daily intake of plant-based ω-3, seeds, legumes and enriched vegetable oil were suggested for Malaysian T2DM patients.

Keywords: omega-3, T2DM, ALA, EPA, DHA, diabetes mellitus type 2

Introduction

The rapid upsurge in the global prevalence of Diabetes Mellitus (DM) brings a significant concern in healthcare. In fact, according to International Diabetes Federation[1], DM is confirmed to be the fastest growing health emergency of the 21st century. Approximately 10.5% (537 million) of the world population is living with DM in 2021 and this percentage is expected to project to 12.2% (783 million) in the next 24 years[1]. As for Malaysia, 1 in every 5 people was diagnosed with DM, summing up to almost 19% (4.4 million) of the Malaysian population, making it the leading country in the Western Pacific region with the highest DM cases[2]. This percentage is predicted to increase to 19.6% (6.5 million) by 2045[2]. DM is a global health burden in which it is responsible for USD699 million of the total global health

expenditure in 2021[3]. Correspondingly, the estimated total cost of DM in Malaysia is USD600 million[4, 5]. Given its substantial health and economic burden, identifying an optimal therapy to abrogate the development of T2DM is essential. While there are several types of DM (e.g., type 1 DM (T1DM), type 2 DM (T2DM), and gestational DM (GDM))[6], this systematic review will emphasize primarily on T2DM. This is because T2DM is very common with 95% of the diagnosis in worldwide including Malaysia[4]. Characterized by hyperglycemia, T2DM is a metabolic disorder resulting from defects in insulin secretion by the pancreatic β-cell, insulin resistance or inadequate response to insulin[7]. The exact cause of T2DM remained debatable with several pathophysiological theories including peripheral insulin resistance, impaired regulation of hepatic glucose production or declining β-cell function and failure[8]. The risk factors for T2DM are strong family histories, ethnicity, physical inactivity, overweight or obesity, social economy status and eating pattern[9]. Uncontrolled or untreated T2DM can lead to several health problems such as blindness, kidney failure, heart attack, stroke and lower limb amputation[3]. Several approaches of T2DM treatment include pharmacological and lifestyle modifications. Despite being successful, the pharmacological approach of T2DM has adverse effects such as gastrointestinal and musculoskeletal symptoms[10]. Lifestyle intervention that includes increased physical activity, better stress management and improved eating pattern has proved to be as successful as pharmacological intervention but with less or no side effects[11]. However, the ability of patients to adhere to lifestyle changes remained the biggest challenge in this approach[12]. Hence, the need for auxiliary treatment for T2DM led to the venture of omega-3 (ω-3), given its substantial benefits to health[13]. ω-3 Polyunsaturated Fatty Acid (PUFA) is a diet-obtained essential fatty acid that can be acquired from two sources which are fish/seafood-derived eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and plants derived alpha-linoleic acid (ALA)[13]. To date, the efficacy of ω-3 in managing T2DM has been tremendously discussed[14, 15]; however, its practical use has remained controversial. To date there is no recommendation for ω-3 intake in the recent 6th Diabetes Clinical Practice Guidelines (CPG) in Malaysia[16]. Therefore, the primary purpose of this systematic review is to highlight a fundamental dietary recommendation of ω-3 intake for T2DM patients in Malaysia by assessing previous T2DM guidelines and exploring the evidence of ω-3 as one of the additional approaches for T2DM treatment.

Materials and Method

This systematic review was conducted based on PRISMA guidelines[17].

Inclusion and Exclusion Criteria

Any evidence-based guideline or CPG on the management of adult T2DM was considered for this systematic review. The guideline or CPG must have been published in the last ten years, ranging from 2014 to 2023, by any professional society, government body or national/ international diabetes association. CPGs that focused only on prevention and other types of DM (e.g., T1DM or GDM), other age groups (e.g., adolescent, pediatric and elderly) and specifically on DM comorbidities only (e.g., non-alcoholic liver failure disease, chronic kidney disease, cardiovascular disease were excluded. Furthermore, all outdated CPG (published before 2014), clinical trials, unpublished, drafts, conference papers, discussion papers, the subtopic of guideline reports and reviews of CPG were also excluded. Also, CPGs written in languages other than English were not considered. The primary purpose of this review is to recommend the ω-3 intakes for T2DM patients, hence any CPGs without ω-3 recommendation will also be excluded.

Search Strategy

Filters were set to English language and publications date from 2014 to 2023. Four guideline databases (Medical Guideline Clearinghouse and Library, Guideline International Network (GIN), National Institute for Health and Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN)) were searched from October 2022 to March 2023 using the term "Type 2 Diabetes". Other databases (PubMed and Cochrane Library) were also searched using the keywords such as ω-3, T2DM, Diabetes Mellitus type 2, Guidelines, Clinical Practice Guideline, CPGs, MNT Guidelines, nutrition guideline. Furthermore, diabetes societies and other websites were also manually searched to find any eligible guidelines.

Studies Screening and Selection

Duplicates were removed using Endnote, then further hand-checked to remove additional copies. The titles and abstracts screening were done by one independent reviewer, based-on the inclusion and exclusion criteria.

Data Extraction

Two reviewers extracted the descriptive data from all the included CPGs: Organization name/ author/ year of publication/ country of origin/ guideline name/ ω-3 recommendations.

Results

392 records were identified through a systematic searched, where 111 records were obtained from the guidelines databases such as GIN (n=20), NICE (n=17), SIGN (n=75) and Medical Guideline Clearinghouse and Library (n=74). Another 200 records were found through the electronic databases search of PubMed (n=140) and Cochrane Library (n=60). A further hand-search was conducted on other websites and diabetes society websites in which 5 records were identified. A total of 370 records (after the removal of duplicates) were then screened through the title and abstracts and 340 records were removed, resulting in only 30 records that were further assessed for eligibility. 18 records were excluded based on the pre-specific criteria (Figure 1), which included Malaysia diabetes CPG[16].Finally, 12 guidelines were finalized to be included in the qualitative synthesis. The details of each guideline were summarized in Table 1 along with their ω-3 intake recommendation for T2DM patients. These guidelines were published within ten years (2014 to 2023) and consisted of two diabetes CPGs from the Ministry of Health[18, 19], four CPGs from the diabetes association or society[20-23], two nutrition guidelines[24, 25], a standard care[26], two diabetes recommendations [27, 28] and a management guideline[29], all from various diabetes societies and association. These guidelines were from various countries including Singapore, Japan, India, the United States (US), the United Kingdom (UK), Canada, Colombia, Qatar and Saudi Arabia. In recommending ω-3 intake, six of the guidelines suggested fatty fish consumption [19-21, 24-26], in which 3 guidelines stated the recommended amount of at least two or three fatty fish serving per week[19, 21, 25]. Also, some guidelines proposed on the plant source of ω-3 such as the daily consumption of 2 to 3g of plant sterol[25], 10g daily flaxseed intake[29] and plant-based fats/oil, nuts and seeds[20, 23, 24, 26]. Other than that, three guidelines mentioned a non-specific recommendation of PUFA and Monosaturated Fatty Acid (MUFA)[18, 22, 28]. Respectively, four guidelines[20, 21, 25, 26] suggested a Mediterranean diet, two [21, 25] suggested Dietary Approach to Stop Hypertension (DASH) diet and a guideline [21] suggested Nordic-style diet as a way to achieve the ω-3 intake among T2DM

patients. Most of the ω-3 recommendations were associated with cardioprotective effects and protection against dyslipidemia[22, 26, 29].

Discussion

The general ω-3 recommendation for the Malaysian population has been established in the Malaysian Dietary Guidelines 2020[30]. However, up until now, there is still no T2DM-specific nor conclusive recommendation of ω-3 intake suggested by the Malaysian diabetes CPG for the T2DM patients in Malaysia[16]. This systematic review is the first to highlight a general dietary recommendation of ω-3 intake for T2DM patients in Malaysia. Six out of twelve guidelines for the management of T2DM recommended consuming fatty fish as a strategy to increase ω-3 intake[19-21, 24-26]. They recommended at least two or three fatty fish serving per week[19, 21, 25]. Incorporating ω-3 recommendation in T2DM management is beneficial as it has advantageous effects on glycemic control, triglyceride (TG) levels, and inflammation[31]. Basically, ω-3 PUFA is a diet-obtained essential fatty acid that can be acquired from two sources which are fish/ seafood derived; EPA and DHA and plants derived ALA[13]. ω-3 PUFA has multiple actions but the complete explanation is still unknown[32]. Some theories include the influence of ω-3 on metabolite and/or hormone concentrations that in turn influence cell and tissue behavior, the influence of ω-3 PUFA on other factors (e.g., oxidation of low-density lipoprotein (LDL); oxidative stress) that in turn influence cell and tissue behavior, direct effects of ω-3 PUFA on cell behavior via surface or intracellular fatty acid “receptors” or “sensors” or effects of ω-3 PUFA on cell behavior mediated via changes in the composition of cell membrane phospholipids[33]. Fish with high-fat content such as salmon, cod, herring, tuna and sardine, is the most common source of ω-3 due to its high EPA and DHA content[34]. Usually, fatty fish is defined into two groups, lean fish and oily fish. Lean fish such as cod, typically store fat in their liver, unlike oily fish that store fat in the flesh[33]. Different fish have a different EPA:DHA ratio; therefore, eating various fatty fish is more beneficial[35]. Examples of fish with high ω-3 in Malaysia are kerapu (six bar grouper), siakap (barramundi), terubok, kembung, bilis, patin, keli and haruan[36].

The effectiveness of EPA and DHA in T2DM management has been studied widely in both *in–vivo* and clinical studies, usually in the form of fish oil. However, there were also studies that investigated the ω-3 effect on T2DM by incorporating fatty fish into the subject’s diet. For instance, in the study by Wallin et al, they found that the consumption of fish among T2DM patients was associated with a lower risk of myocardial infarction but not stroke[37]. Besides that, they also observed that fish consumption is inversely related to heart disease-related mortality[37]. Similarly, [38]reported a significant ($p<0.05$) improvement of very low-density lipoprotein (LDL) and high-density lipoprotein (HDL) among the T2DM patients that were given ω-3 diet compared to the group that received ω-6 diet for two consecutive 3.5 weeks. However, a significant ($p<0.05$) fasting plasma glucose (FPG) reduction was observed in the ω-6 diet group rather than ω-3 diet group of T2DM patients[38]. Interestingly, a study with fish oil supplementation also recorded an important finding of significant reduction of pro-inflammatory cytokines (i.e., Tumor Necrosis Factor-α (TNF- α), Interleukin 1-β (IL-1β) and Interleukin-6 (IL-6)), reduced blood glucose level, improved insulin sensitivity, increased HDL level and reduced TG level and atherogenic index plasma among the overweight/obese T2DM patients that were supplemented with 2.4g/day of fish oil for 8 weeks compared to the control group. However, no significant ($p>0.05$) changes were observed in fasting insulin level, total cholesterol level and LDL level[39]. As for *in–vivo* study, [40]recorded that there were significant ($p<0.05$) decreased in glucose level, improved glucose tolerance as well as reduced

concentrations of liver cholesterol, cholesteryl ester, and triacylglycerol among the wild-type male mice that were fed with fish oil for 30 weeks. Hence, [40]concluded that mice fed a high-fat diet supplemented with fish oil improved metabolic features associated with type 2 diabetes such as impaired glucose tolerance and hepatic steatosis. Another study reported the neuroprotective effect of ω-3 that was observed on the *db/db* mice that were fed with the ω-3 diet for 26 weeks compared to the other mice group that were fed with the ω-6 diet. The ω-3 fed mice were also found to have better glucose tolerance along with slower progress of diabetic retinopathy compared to the other group; therefore, suggested that dietary ω-3 might confer a protective systemic effect against the early onset of T2DM[41].

ALA, on the other hand, is rising in popularity as this plant-derived ω-3 serves as an excellent alternative source for vegetarians or those who don't eat fish[42]. ALA is an essential precursor in synthesizing both EPA and DHA[43]. The information on the synthesizing process was debatable and the efficacy of its absorption in the human gut remained unknown, yet the animal study revealed that the process occurred in the liver[38, 44]. In our systematic review, six guidelines recommended the intake of plant-based ω-3 [20, 23, 24, 26, 29]and plant sterol[25]. Plant sterol is a natural cholesterol-lowering compound found in plants. The various health benefit of plant sterol remained under substantial revision [45] and will not be discussed further in this review. Among the example of dietary sources of ALA are vegetable oils (i.e., canola oil), seeds (i.e., flaxseed), nuts (i.e., walnuts) and green leafy vegetables (i.e., spinach and kale)[42, 43]. The amount of ALA recommended for a healthy woman is 1.1g/day and for a man is 1.6g/day[43]. However, no recommended value of ALA has been established for T2DM patients. Despite that, one of the included guidelines proposed daily consumption of 10g of flaxseed as a strategy to achieve the daily ω-3 requirement for T2DM[29]. Malaysian ALA sources include, soybean products ("taufu", "fucok", beansprouts and soybean drinks), seeds, legumes and enriched vegetable oil (i.e., canola oil) and oil blend[33]. Mixed responses were reported in the study of ALA efficacies in T2DM management. A study by [46]reported the significant ($p<0.05$) reduction of serum insulin and serum high-sensitivity C-reactive protein (hs-CRP) along with the increased total plasma nitrite level and plasma total antioxidant capacity among 30 T2DM patients who received 12 weeks supplementation of 1000mg of flaxseed oil twice daily compared to the placebo group. Fascinatingly, this study also investigated the effect of fish oil intake on T2DM patients and concluded that both flaxseed and fish oil have a similar capability in treating T2DM[46]. In another study, daily consumption of 10g baked flaxseed cookies for 12 weeks resulted in a significant ($p<0.05$) decrease in constipation symptom score, FPG level, cholesterol level, TG level, LDL level, cholesterol/HDL ratio and improved body mass index among the constipated T2DM patients compared to the placebo group. This study concluded that flaxseed consumption might be valuable in preventing and treating T2DM[47]. Despite all the significant results, studies were also reported on the non-effective impact of plant-based ω-3. [48]stated that the high doses of flaxseed oil have no effect on glycemic control in T2DM patients, which he investigated through 10g/day flaxseed oil supplements to 18 T2DM patients for 6 months. They found out that there were no significant ($p>0.05$) changes in insulin, FPG and even HbA1c among the treatment group compared to the placebo group. Likewise, evidence from the animal studies was also reported with mixed responses, as seen in the study by [49] that reported the significant ($p<0.05$)reduction of FPG, HbA1c, blood lipid, plasma lipopolysaccharide, IL-1β, TNF-α, IL-6, IL-17A and malondialdehyde (MDA) in the Male Sprague-Dawley Streptozotocin-nicotinamide induced diabetic rat that was fed with flaxseed oil for 5 weeks compared to the control group of the rat. Also, a study reported that the ALA-supplemented diet in diabetic retinopathy rats helped to reduce IL-6, returned vascular endothelial growth factor level to control value and reduced brain-derived neurotrophic

factor, which summarized that ALA is beneficial in the prevention of diabetic retinopathy[50]. On the contrary, a study by [51] reported that the 4-week intake of the ALA diet among diabetic rats did not change the myocardial function and injury; however, it helped to reduce IL-6, TNF-α, superoxide and MDA.

Mediterranean diet, DASH diet and Nordic-style diet are the diets recommended by the guidelines included in this review[20, 21, 25, 26]. Basically, the Mediterranean and Nordic diets are both the traditional living habits of people who live in the Mediterranean Sea and Nordic countries[52], while DASH is the diet specifically designed to lower blood pressure[53]. All these diets promoted ω-3 rich food, encouraged "plant-based" eating patterns, and higher intake of fruits, vegetables, grains (especially whole grains), legumes, nuts, and seeds, while limiting consumption of red and processed meat nutrient-rich[52, 54]. The Mediterranean diet has been extensively studied and associated with many health benefits[54]. An integral part of the Mediterranean diet is the high intake of olive oil, believed to be due to olive cultivation in the Mediterranean region. This diet consists of the intake of local produce goods that are usually unprocessed or minimally refined, having fresh fruits as a typical dessert, with sweets containing sugars or honey a few times per week, fish and poultry consumed in low to moderate amounts; red meat consumed in low amounts; and wine in moderation, consumed with meals, and high intake of nuts, olive oil[54]. [55] reported that an intensive 12 months intervention of a low carbohydrate Mediterranean diet, traditional Mediterranean diet and American Diabetes Association recommended diet resulted in a significant reduction of HbA1c, blood lipid, HOMA-IR, LDL, TG and increased of HDL (only for low carbohydrate Mediterranean diet) among 259 T2DM patients. DASH diet, on the other hand, originated in the 1990s by the National Institute of Health as an effort to treat hypertension[56]. The distinguishing criteria of the DASH diet are the reduction of sodium to about 1500mg/day. DASH diet specifically encourages the intake of food rich in good fats such as olive oil, avocados, nuts, hemp seeds, flaxseeds and fish rich in ω-3 fatty acids[56]. The efficacy of the DASH diet was discussed in a study by[57], which investigated the effectiveness of the DASH diet on T2DM patients and reported on the reduction of FPG, HbA1c, LDL and increased HDL levels after adapting to DASH diet for 8 weeks among 31 T2DM patients compared to the control group in Iran. This study ruled out that the beneficial effect of the DASH diet was accredited to its high intake of legumes and soy. Similarly, another study reported the reduction of FPG, insulin, LDL, HOMA-IR, and total cholesterol in both groups of T2DM patients that were subjected to 16 weeks of the DASH diet and legume-based DASH diet[58]. The Nordic diet is a diet formed by five Nordic countries that have a similar public health issue[59]. This diet is almost similar to the Mediterranean diet except that the main fat source for the Nordic diet is canola/rapeseed oil and the range of fatty fish intake due to their marine-rich archipelago[52]. A few studies investigated the health benefits of the Nordic diet on T2DM patients. For instance, Ohlsson [60]reported a significant ($p<0.05$) impact of the endocrine profile, which correlated with anthropometric and metabolic improvements, demonstrated through the decline of cholecystokinin, C-peptide, glucagon, leptin, glucagon-like peptide 1, and polypeptide YY among the group of T2DM patients that adapted the Okinawan based-Nordic diet for 28 weeks compared to the control group. Another interesting cross-sectional study by Daneshzad [61]reported similar findings of significantly lower levels of aspartate aminotransferase ($p<0.0001$), reduction of LDL ($p<0.05$), 65% lower risk for being hypertensive among the T2DM patients who were subjected to Nordic diet from 2014 to 2016. Therefore, this study summarized that the Nordic diet is associated with reductions in the prevalence of obesity, LDL levels and blood pressure among T2DM patients. As for Malaysian, although the eating pattern has improved and changed over time, our population still remain consistently in excess of average

calorie needs by a minimum of 30%, with decreased plant/animal protein ratio over time, deficiencies in fruit, vegetable, legumes, and dairy intake along with excessive meat, salt, and sugar intake. However, the diet quality remained multifactorial and was associated greatly with higher education levels, maternal years of schooling, being a female, not working, and higher household and personal income[62]. On the other hand, the prevalence of non-communicable diseases and associated risk factors has increased rapidly, some as high as 170%[62, 63]. Therefore, a tremendous effort needs to be made to educate the Malaysian population to eat better and healthier. To our best knowledge, this review, is the first one in Malaysia to highlight a fundamental dietary recommendation of ω-3 intake for T2DM patients in Malaysia by assessing previous T2DM guidelines and exploring the evidence of ω-3and also to help promote omega-3 evidence-based practice in CPG of Diabetes in Malaysia. This review was designed using the PRISMA guideline as its major reference to ensure a top-notch quality. Therefore, it might provide a good insight for the clinicians and dietitians who manage T2DM patient, allowing them to suggest a good supplementary treatment for the patients. Also, it is encouraged for healthcare professionals to refer to this document to support/complement the recommendations provided in the present CPG of Diabetes in Malaysia. The results of this work should be used in clinical practice guideline development, to ultimately guide evidence-based practice in personalized nutrition and move this emerging field forward. Despite that, although we made effort to include everything, no guideline from grey literature were included. Also, this review focused only on T2DM therefore it cannot be applied to other type of diabetes. Finally, no quality assessment was done on the included guidelines nor did any quantitative analysis.

Conclusion

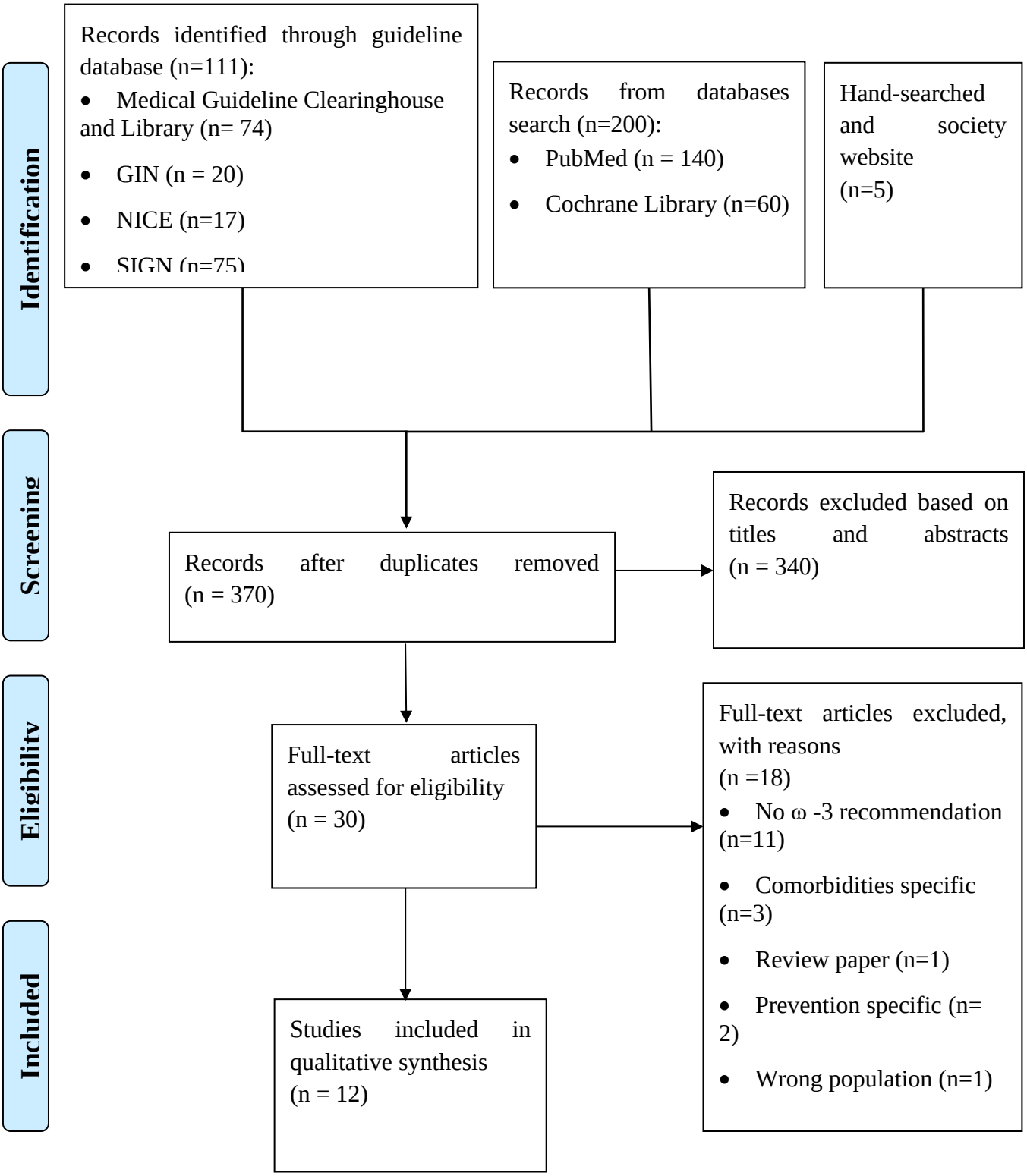
Studies on the health benefits of ω-3 PUFA go back to the 1970s, ever since, it has caused an outburst in the research world[64]. To date, the efficacy of ω-3 in managing T2DM has been tremendously discussed; however, its practical use has remained controversial. Even in Malaysia, there is no recommendation for ω-3 intake in the recent 6th Diabetes CPG[16]. Despite being controversial, ω-3 exerts many potential health benefits, especially in cardio-related diseases[31]. So, to address that study gap, we highlight a general dietary recommendation of ω-3 intake for T2DM patients in Malaysia, which was obtained by summarizing the twelve selected guidelines and CPGs. A weekly serving of at least two or three fatty fish like “kerapu” (sixbar grouper), “siakap” (barramundi), “terubok”, “kembung”, “bilis”, “patin”, “keli”, “jelawat”, sardine, tuna, and “haruan” [35, 36, 65]provides a good basis of ω-3 intake (and cardioprotective effect for T2DM patients)[37, 38]. Besides that, daily intake of plant-based ω-3 (i.e. soybean products (“taufu”, “fucok”, beansprouts and soybean drinks), seeds, legumes and enriched vegetable oil (i.e. canola oil) and oil blend) is also recommended in managing T2DM given its diverse benefits besides being a good alternative source for vegetarians or those who don’t eat fish[43]. Also, educating Malaysian T2DM patients on the benefits of fresh food consumption is equally important as well as promoting a balance diet and encouraging low salt intake in their daily diet.

Table 1 Diabetes Guidelines for ω-3 Recommendation Summary

Author/ Guideline Organisation or society	Guideline Name		Year Published	Country of Origin	ω-3 Recommendation
[19]	MOH Clinical Practice Guideline 2014: Diabetes Mellitus		2014	Singapore	Recommend consumption of fish rich in ω-3 PUFAs is encouraged at least twice a week.
[27]	Type 2 diabetes in adults: management		2015	United Kingdom (UK)	Eat oily fish.
[23]	Clinical practice guideline for the prevention, early detection, diagnosis, management and follow up of type 2 diabetes mellitus in adults		2016	Colombia	Reduce saturated and trans fats consumption, replace with fat from fish and vegetable, preferably mainly MUFAs such as canola and olive oils.
[22] (The Japan Diabetes Society)	Japanese Clinical Practice Guideline for Diabetes 2016		2018	Japan	The intake of PUFA is recommended for T2DM patient with dyslipidaemia.
[25]	Evidence-based nutrition guidelines for the prevention and management of diabetes		2018	United Kingdom (UK)	Recommend Mediterranean and DASH diets; encourage two portions of oily fish weekly and intake of products with 2 to 3g of plant sterols daily.
[24]	Clinical Nutrition Guideline for Overweight and Obese Adults with Type 2 Diabetes (T2D) or Prediabetes, or Those at High Risk for Developing T2D		2018	United States (US)	Recommend plant fats rich in MUFA and PUFAs and oily fish rich in ω-3 fatty acids.

Author/ Guideline Organisation or society	Guideline Name		Year Published	Country of Origin	ω-3 Recommendation
[29]	ICMR Guidelines for Management of Type 2 Diabetes 2018		2018	India	Recommend flaxseed (10g/ day) and fish intake for cardio protective effect.
[18]	National Clinical Guidelines: The Diagnosis and Management of Type 2 Diabetes Mellitus in Adults & The Elderly		2021	Qatar	Recommend fat intake less than 35%, preferably MUFAs and PUFAs.
[20]	Saudi Diabetes Clinical Practice Guidelines (SDCPG)		2021	Saudi Arabia	Recommend Mediterranean diet, emphasizing on the intake of foods rich in long chain ω-3 fatty acids like fatty fish, nuts and seeds.
[28] (Research Society for the Study of Diabetes in India (RSSDI))	RSSDI Clinical Practice Recommendations for the Management of Type2 Diabetes Mellitus 2022		2022	India	Recommend a diet rich in ω-3 fatty acids.
[21]	Diabetes Canada Clinical Practice Guidelines		2022 (updated version)	Canada	Recommend unsaturated fat as preferred fat type, encourage Mediterranean diet, DASH diet, Nordic-style diet that suggest more than three fatty fish servings per week.
[26]	Standards of Care in Diabetes		2023	United States (US)	Suggest Mediterranean diet rich with MUFAs and PUFAs and eat food with high ω-3 fatty acids such as fatty fish, nuts and seeds for cardio protective effect.

Figure 1-PRISMA Flowchart



References

1. *International Diabetes Federation*, in *IDF Diabetes Atlas 2022*. 2022.
2. *IDF Diabetes Atlas: 10th edition 2021*, in *Malaysia Diabetes Report 2000-2045*. 2021.
3. *Diabetes*. 2021.
4. Akhtar, S., et al., *Prevalence of type-2 diabetes and prediabetes in Malaysia: A systematic review and*

meta-analysis. Plos One, 2022.
5. Ganasegeran, K., et al., *A Systematic Review of the Economic Burden of Type 2 Diabetes in Malaysia.* International Journal of Environmental Research and Public Health, 2020.
6. *National Diabetes Statistics Report*. 2022.
7. Galicia-Garcia, U., et al., *Pathophysiology of Type 2 Diabetes Mellitus.* International Journal of Molecular Sciences, 2020.
8. Mahler, R.J. and M.L. and Adler, *Type 2 Diabetes Mellitus: Update on Diagnosis, Pathophysiology, and Treatment.* The Journal of Clinical Endocrinology & Metabolism, 1999: p. 1165-1171.
9. Fletcher, B., M. Gulanick, and C. and Lamendola, *Risk Factors for Type 2 Diabetes Mellitus.* Journal of Cardiovascular Nursing, 2002: p. 17-23.
10. *Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.* New England Journal of Medicine, 2002: p. 17-23.
11. Chen, L., et al., *Effect of lifestyle intervention in patients with type 2 diabetes: a meta-analysis.* Metabolism, 2015: p. 338-347.
12. Gupta, L., et al., *Factors Determining the Success of Therapeutic Lifestyle Interventions in Diabetes - Role of Partner and Family Support.* European Journal of Endocrinology, 2019: p. 18-24.
13. Shahidi, F. and P. and Ambigaipalan, *Omega-3 Polyunsaturated Fatty Acids and Their Health Benefits.* Annual Review of Food Science and Technology, 2018: p. 345-381.
14. Hartweg, J., et al., *Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus.* Cochrane Database of Systematic Review, 2008.
15. Delpino, F.M., et al., *Omega-3 supplementation and diabetes: A systematic review and meta-analysis.* Critical Reviews in Food Science and Nutrition, 2022: p. 4435-4448.
16. *Clinical Practice Guidelines: Management of Type 2 Diabetes Mellitus, 6th. Edition*. 2020, Ministry of Health Malaysia.
17. Page, M.J., et al., *The PRISMA 2020 statement: an updated guideline for reporting systematic reviews.* British Medical Journal, 2021: p. 71.
18. *Ministry of Public Health Qatar National Clinical Guidelines: The Diagnosis and Management of Type 2 Diabetes Mellitus in Adults & The Elderly.* 2021, Ministry of Public Health Qatar.
19. *MOH Clinical Practice Guideline 2014: Diabetes Mellitus.* 2014, Ministry of Health Singapore.
20. *Saudi National Diabetes Centre Saudi Diabetes Clinical Practice Guidelines (SDCPG)*. 2021, Saudi National Diabetes Centre Saudi Diabetes.
21. *Diabetes Canada Clinical Practice Guidelines*. 2022, Diabetes Canada.
22. Haneda, M., et al., *Japanese Clinical Practice Guideline for Diabetes 2016.* Journal of Diabetes Investigation, 2018: p. 1-45.
23. Aschner, P.M., et al., *Clinical practice guideline for the prevention, early detection, diagnosis, management and follow up of type 2 diabetes mellitus in adults.* Colombia Médica, 2016.
24. *Clinical Nutrition Guideline for Overweight and Obese Adults With Type 2 Diabetes (T2D) or Prediabetes, or Those at High Risk for Developing T2D.* American Journal of Managed Care, 2018.
25. *Evidence-based nutrition guidelines for the prevention and management of diabetes. 2018*. 2018, DiabetesUK.
26. *Standards of Care in Diabetes.* Journal of Clinical and Applied Research and Education, 2023.
27. *Type 2 diabetes in adults: management.* 2015, National Institute for Health and Care Excellence (NICE).

28. Makkar, B.M., et al., *RSSDI Clinical Practice Recommendations for the Management of Type 2 Diabetes Mellitus 2022.* International Journal of Diabetes in Developing Countries, 2022: p. 1-143.
29. *ICMR Guidelines for Management of Type 2 Diabetes 2018*. 2018, Indian Council of Medical Research(ICMR).
30. *Malaysian Dietary Guidlines 2020*. 2021, Ministry of Health Malaysia.
31. Xiao, Y., et al., *The effects of omega-3 fatty acids in type 2 diabetes: A systematic review and meta-analysis.* Prostaglandins, Leukotrienes & Essential Fatty Acids, 2022.
32. Leng, X., et al., *All n-3 PUFA are not the same: MD simulations reveal differences in membrane organization for EPA, DHA and DPA.* Biochimica et Biophysica Acta (BBA), 2018.
33. Calder, P.C., *Mechanisms of Action of (n-3) Fatty Acids.* The Journal of Nutrition,, 2012: p. 592S-599S.
34. Bowen, K.J., W.S. Harris, and a. Kris-Etherton, *Omega-3 Fatty Acids and Cardiovascular Disease: Are There Benefits?* Current Treatment Options in Cardiovascular Medicine, 2016: p. 69.
35. Ng, K.W., *Omega-3 Fatty Acids: Potential Sources in the Malaysian Diet with the Goal Towards Achieving Recommended Nutrient Intake.* Malaysian Journal of Nutrition, 2006.
36. Nur Airina, M. and J. Muhammad, *Fatty Acid Composition of Selected Malaysian Fishes.* Sains Malaysiana, 2012.
37. Wallin, A., N. Orsini, Forouhi,Nita G, and A. and Wolk, *Fish consumption in relation to myocardial infarction, stroke and mortality among women and men with type 2 diabetes: A prospective cohort study.* Clinical Nutrition, 2018.
38. Karlström, B.E., et al., *Fatty fish in the diet of patients with type 2 diabetes: comparison of the metabolic effects of foods rich in n-3 and n-6 fatty acids.* The American Journal of Clinical Nutrition, 2011.
39. de Souza, D., et al., *Fish oil reduces subclinical inflammation, insulin resistance, and atherogenic factors in overweight/obese type 2 diabetes mellitus patients: A pre-post pilot study.* Journal of Diabetic Complications, 2020.
40. Jelinek, D., et al., *A high-fat diet supplemented with fish oil improves metabolic features associated with type 2 diabetes.* Nutrition, 2013.
41. Burdge, G.C., *Metabolism of α-linolenic acid in humans.* Prostaglandins, Leukotrienes and Essential Fatty Acids., 2006: p. 161-168.
42. Rajaram, S., *Health benefits of plant-derived α-linolenic acid.* The American Journal of Clinical Nutrition, 2014.
43. *Omega-3 Fatty Acids: Factsheet for Health Professionals*. National Institute of Health: Office for Dietary Supplements, 2022.
44. Sapieha, P., et al., *Omega-3 polyunsaturated fatty acids preserve retinal function in type 2 diabetic mice.* Nutrition and Diabetes, 2012.
45. Kopylov, A.T., et al., *Diversity of Plant Sterols Metabolism: The Impact on Human Health, Sport, and Accumulation of Contaminating Sterols.* . Nutrients, 2021.: p. 1623.
46. Raygan, F., et al., *A comparison between the effects of flaxseed oil and fish oil supplementation on cardiovascular health in type 2 diabetic patients with coronary heart disease: A randomized, double-blinded, placebo-controlled trial.* Phytotherapy Research, 2019.
47. Soltanian, N. and M. and Janghorbani, *A randomized trial of the effects of flaxseed to manage constipation, weight, glycemia, and lipids in constipated patients with type 2 diabetes.* Nutrition &

Metabolism, 2018: p. 36.
48. Barre, D.E., et al., *High dose flaxseed oil supplementation may affect fasting blood serum glucose management in human type 2 diabetics.* Journal of Oleo Science, 2008.
49. Zhu, L., et al., *Dietary flaxseed oil rich in omega-3 suppresses severity of type 2 diabetes mellitus via anti-inflammation and modulating gut microbiota in rats.* Lipids in Health and Disease 2020.
50. Shen, J.-h., et al., *Effect of α-linolenic acid on streptozotocin-induced diabetic retinopathy indices in vivo.* Archives of Medical Research, 2013.
51. Xie, N., et al., *α-Linolenic acid intake attenuates myocardial ischemia/reperfusion injury through anti-inflammatory and anti-oxidative stress effects in diabetic but not normal rats.* Archives of Medical Research 2011.
52. Krznarić, Ž., et al., *The Mediterranean and Nordic Diet: A Review of Differences and Similarities of Two Sustainable, Health-Promoting Dietary Patterns.* Frontiers in Nutrition, 2021.
53. Benson, G. and J. Hayes, *An Update on the Mediterranean, Vegetarian, and DASH Eating Patterns in People With Type 2 Diabetes.* Diabetes Spectrum, 2020: p. 125-132.
54. Guasch-Ferré, M. and W.C. Willett, *The Mediterranean diet and health: a comprehensive overview.* Journal of Internal Medicine, 2021: p. 549-566.
55. Elhayany, A., et al., *A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study.* Diabetes, Obesity and Metabolism, 2010.
56. Challa, H.J., M.A. Ameer, and K.R. Uppaluri, *DASH Diet To Stop Hypertension*. 2023: StatPearls Publishing.
57. Azadbakht, L., et al., *Effects of the Dietary Approaches to Stop Hypertension (DASH) Eating Plan on Cardiovascular Risks Among Type 2 Diabetic Patients: A randomized crossover clinical trial.* Diabetes Care, 2011: p. 55-57.
58. Hosseinpour-Niazi, S., et al., *Improvement of glycemic indices by a hypocaloric legume-based DASH diet in adults with type 2 diabetes: a randomized controlled trial.* European Journal of Nutrition, 2022.
59. Meltzer, H.M., et al., *Environmental Sustainability Perspectives of the Nordic Diet.* Nutrients, 2019.
60. Ohlsson, B., et al., *Alignments of endocrine, anthropometric, and metabolic parameters in type 2 diabetes after intervention with an Okinawa-based Nordic diet.* Food & Nutrition Research, 2018.
61. Daneshzad, E., et al., *Association of modified Nordic diet with cardiovascular risk factors among type 2 diabetes patients: a cross-sectional study.* Journal of Cardiovascular and Thoracic Research, 2018.
62. Ramadas, A., et al., *Diet Quality of Malaysians across Lifespan: A Scoping Review of Evidence in a Multi-Ethnic Population.* Nutrients, 2021.
63. Goh, E.V., et al., *The nutrition transition in Malaysia; key drivers and recommendations for improved health outcomes.* BMC Nutrition, 2020.
64. Harris, W.A., *Omega-3 Fatty Acids and Health.* . 1995.
65. WanRosli, W.I., et al., *Fat content and EPA and DHA levels of selected marine, freshwater fish and shellfish species from the east coast of Peninsular Malaysia.* International Food Research Journal, 2012.