The Australasian Association
and Register of Practicing
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To: The Hon. Members of the Committee,

The House of Representatives,
Standing Committee on Health, Aged Care and Sport,
PO Box 6021, Canberra ACT 2600

RE: Precision nutrition for the prevention and remitting of Type 2 Diabetes via targeted engagement with the evidence based Nutritional Medicine (Clinical Nutrition) paradigm.

N.B. AARPN member contributors to this document include: Natasha Radcliffe (Director), Dr. Mansi Dass-Singh (Director), Joshua Sutherland (Director), Petra Hooyenga, Nicole James (Director), Benedict Freudenmann, Maryanne Ireland, Melinda Overall, and Megan van Genderen. The AARPN directors prepared and are responsible for the final document.

Dear Committee,

We are grateful for the opportunity to provide a submission to the Parliamentary Inquiry into Diabetes in Australia. We begin this submission by introducing you to The Australasian Association and Register of Practicing Nutritionists (AARPN). AARPN is a full ordinary member of Allied Health Professions Australia (AHPA) and is Australia's only single-profession association that exclusively represents degree qualified professional Nutritionists that are clinically trained in Clinical Nutrition (also termed Nutritional medicine due to its origins in the merging of medicine and nutrition science in the 1950's (Cardenas, 2016)) and whom AARPN accredits as Certified Practicing Nutritionists (CPN) through its trademarked professional accreditation program.

CPN Certified Practicing Nutritionist
AARPN
TM 2063292 The Australasian Association and Register of Practicing Nutritionists (AARPN) LTD

The purpose of the AARPN CPN program is to afford Government, employers, other health professionals, and consumers, the ability to clearly distinguish in a transparent manner, degree qualified clinically trained Nutritionists (Practicing Nutritionists) from those of lesser training - or from those whose scope of practice does not include Clinical Nutrition/Nutritional Medicine, who may also engage the term Nutritionist in the context of a non-clinical Nutrition Scientist. The CPN program is accompanied by AARPN prescribed professional development and a comprehensive set of competencies that reflect the scope of practice of 'Certified Practicing Nutritionist'.

Our profession is synonymous with the delivery of personalised nutrition through evidence informed engagement with the scientific evidence based Clinical Nutrition/Nutritional Medicine paradigm. We are unique in the allied health dietary services space, as we have a legislatively underpinned nutritional therapeutic prescribing and nutritional supplement compounding capacity, as per the exemptions afforded to qualified clinically trained Nutritionists (also termed Nutritional Medicine Practitioners) under Section 42AA (Australian Therapeutic Goods Act 1989) and Schedule 5 Item 6 (Therapeutic Goods Administration, 2018) of the [Australian] Therapeutic Goods Act and Regulations, and which also function to provide formal confirmation and acknowledgement of our status as both health professionals and health practitioners, respectively.

A primary directive of AARPN is to advocate for Certified Practicing Nutritionists and expand public access to high quality personalised nutritional interventions for the betterment of public health at the individual, group, and population level. In this capacity, and as per the Australian National Diabetes Strategy 2021-2030, we seek to put forward that the allied health services provided by Certified Practicing Nutritionists (CPNs) represent an opportunity for the Australian Government to complement and enhance the effectiveness of its current objectives to prevent, diagnose and manage diabetes, in a unique way, that no other allied health dietary services profession can provide. The increasing numbers of individuals living with diabetes is suggestive of a critical need for change in approach to the risk assessment and clinical management of diabetes in Australia. In this submission we focus on terms of reference 1, 2 and 5 and include novel strategies designed to capture (and enact upon in a clinical capacity) metabolic risk in the community (i.e, targeting the 'low hanging fruit' opportunities) - with the intention of preventing disease progression and remediating established type 2 diabetes via a personalised Nutritional Medicine (Clinical Nutrition) approach.

Terms of Reference (the *AARPN submission is focussing on numbers 1, 2 and 5*)

1. ***The causes of diabetes (type 1, type 2 and gestational) in Australia, including risk factors such as genetics, family history, age, physical inactivity, other medical conditions and medications used***
2. ***New evidence-based advances in the prevention, diagnosis and management of diabetes, in Australia and internationally***
3. The broader impacts of diabetes on Australia's health system and economy;
4. Any interrelated health issues between diabetes and obesity in Australia, including the relationship between type 2 and gestational diabetes and obesity, the causes of obesity and the evidence-base in the prevention, diagnosis and management of obesity; and
5. ***The effectiveness of current Australian Government policies and programs to prevent, diagnose and manage diabetes.***

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Abbreviations:
AUC: Area under the curve, CI: confidence interval, Cr: Chromium, DB: Double-blinded, DI: Disposition index, FBG: Fasting blood glucose, FI: Fasting insulin, IR: insulin resistance, I^2: Heterogeneity, MD: Mean difference, MTD: Mediterranean Type Diet, N: number, NHMRC: National Health and Medical Research Council, DB: Double-blinded, RCT: Randomised placebo-controlled clinical trial, HOMA-IR- Homeostatic model assessment of insulin resistance, Hb1Ac: Glycated hemoglobin $A_{1c,}$ VDR: Vitamin D receptors, WMD: weighted mean difference, SMD: standardized mean difference SMD, SD: standard deviation.

Background

The World Health Organization (WHO, 2023) recognises that approximately 422 million people worldwide have diabetes. A logistic regression of 255 high-quality data sources, (published between 1990 and 2018, from 138 countries, with adults aged 20-79 years) has estimated (adjusting for age related factors) the prevalence of diabetes (including previously undiagnosed diabetes) to rise to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 (Saeedi et al. 2019). In an already overburdened public health system, an estimated expenditure of AUD $3.1 billion was attributed to diabetes for 2019–20, with $2.0 billion of this expenditure attributed to type 2 diabetes, and hospital services accounting for 42% ($838.5 million) of this figure (AIHW, 2023).

Diabetes may have any of the following clinical representations (RACGP, 2023):

1. Type 1 diabetes – develops owing to the destruction of β -cell destruction mainly due to an autoimmune aetiology that translates into insulin deficiency and deranged glucose homeostasis.
2. Type 2 diabetes – develops owing to a progressive defect in insulin signalling that translates into long-standing insulin resistance.
3. Young-onset T2DM - There is emerging data indicating that T2DM in younger people (aged <40 years), has a more rapid deterioration of β-cell function, relative to that seen in later-onset T2DM (Magliano et al., 2020, Fan et al., 2022).
4. Gestational diabetes mellitus (GDM) – defined as glucose intolerance with onset or first recognition during pregnancy.
5. Other specific types of diabetes – for example, monogenic diabetes and diabetes secondary to other causes.

Diabetes mellitus Type 2 (T2DM) is a chronic and progressive metabolic disorder characterized by persistent hyperglycaemia (World Health Organization (WHO), 2023). In Australia, the number of people living with T2DM has increased almost 3-fold between 2000 and 2021, from around 400,000 to almost 1.2 million and is the 10th leading cause of death in Australia (Australian Institute of Health and Welfare (AIHW), 2023)). Almost 4.6% of Australians were registered with the National Diabetes Services Scheme (NDSS) and Australasian Paediatric Endocrine Group (APEG) state-based registers in 2021. An

estimated 10.7% (51,900) of Aboriginal and Torres Strait Islander people are diagnosed with T2DM (2018-19). According to NDSS and APEG data, every day, an average of 165 are newly diagnosed with T2DM. The prevalence of this morbidity evidently increases with the level of remoteness and socioeconomic disadvantage (AIHW, 2023). Type 2 diabetes is associated with various complications, including ketosis and electrolyte imbalance, cardiovascular disease, kidney damage, nerve damage (neuropathy), retinopathy (eye damage), reduced bone turnover and creation, and dementia (Lam, 2022; Thomas, Cooper, & Zimmet, 2016; Di Stasi, Maseroli & Vignozzi, 2022; Leon, & Maddox, 2015; Deshpande, Harris-Hayes, & Schootman, 2008; Calimag et al. 2023; Fayfman, Pasquel, & Umpierrez, 2017; Compston, 2018; Singh et al. 2022).
There are multi-systemic drivers and causes for the Type 2 Diabetes epidemic (and the Obesity epidemic associated with Type 2 diabetes). Key factors that have been identified include the shift in food consumption to mass produced processed foods that are frequently energy rich and nutrient poor - and advancements in transport and technology leading to more sedentary lifestyles, leading to both overweight and obesity, as well as nutrient deficiencies. Other factors can include diabetes risk genes as individuals with single/both parents with diabetes have a 40%/70% chance of developing T2DM (Ali, 2013).

Type 2 Diabetes as a preventable and remittable disease

Type 2 diabetes develops along a spectrum of insulin resistance and impaired insulin production (Weir & Bonner-Weir, 2004) that presents the opportunity for prevention through early detection and intervention, and for remission of the established disease.

Pathway from insulin resistance to Type 2 diabetes

Insulin is a hormone produced by the beta cells of the pancreas that plays a crucial role in regulating blood glucose levels. It facilitates the entry of glucose into skeletal muscle cells, where it is used for energy or stored as glycogen. Chronic insulin resistance (IR) refers to a metabolic state when a given concentration of insulin yields a lower biological effect than expected due to a reduced response of target tissues (such as muscle and liver) to the effects of insulin. It is also the common pathology in impaired glucose tolerance (IGT) and Impaired fasting glucose (IFG), noting that almost one in six adults are affected by IGT or IFG (RACGP, 2023) both of which reflect increased risk of developing diabetes in the future (Perreault et al. 2021).

Chronic insulin resistance (herein referred to simply as insulin resistance) is synonymous with metabolic syndrome (MetS), of which the often concurrently presenting obesity is a significant risk factor for both insulin resistance and type 2 diabetes. Metabolic syndrome (MetS) is a cluster of conditions including abdominal obesity, high blood pressure, high triglycerides, low HDL cholesterol, and elevated fasting glucose. Excess adipose tissue, especially abdominal fat (as indicative of MetS), contributes to insulin resistance by releasing inflammatory cytokines that promote insulin resistance such as TNF alpha (Plomgaard et al. 2017).

Stages of progression

Initial compensation: When the body becomes resistant to the effects of insulin over a chronic period of time, the cells (particularly those GLUT4 receptors in the muscles) do not take up glucose efficiently. As the breakdown in effective insulin signalling worsens, the pancreas increases insulin production to compensate, which initially maintains normal blood sugar levels, with the individual becoming normoglycemic upon blood glucose testing. As the pancreas produces more and more insulin to compensate for insulin resistance, the levels of insulin in the bloodstream become elevated, a state referred to as hyperinsulinemia.

Glucose build-up: Despite the elevated insulin levels, glucose uptake by muscle cells remains impaired due to insulin resistance and this leads to higher levels of glucose in the bloodstream. This will begin to be detectable via HbA1c testing.

Beta-Cell dysfunction: The constant demand for increased insulin production can lead to dysfunction and exhaustion of the insulin-producing beta cells in the pancreas causing a gradual decline in the pancreas' ability to produce sufficient insulin. As a result of insufficient insulin, blood sugar levels start to rise above normal levels because cells cannot effectively take up glucose from the bloodstream, a state referred to as hyperglycaemia. Beta-Cell dysfunction contributes to the transition from insulin resistance to overt type 2 diabetes and if left untreated, from Type 2 diabetes to Type 1 diabetes.

Diagnosis of diabetes: At this point, blood sugar levels are consistently higher than normal, and the individual may experience symptoms such as increased thirst, frequent urination, fatigue, and blurred vision. Specific diagnostic criteria include: HbA1c ≥6.5% (48 mmol/mol) on two separate occasions or FBG ≥7.0 mmol/L or random blood glucose ≥11.1 mmol/L confirmed by a second abnormal FBG on a separate day, or oral glucose tolerance test (OGTT) before (fasting) and two hours

after an oral 75 g glucose load is taken. Diabetes is diagnosed as FBG ≥7.0 mmol/L or two-hour post-challenge blood glucose ≥11.1 mmol/L (RACGP, 2023).

Prevention through early detection of insulin resistance and/or compromised blood glucose control

Current medical recommendations are that individuals who are not at high risk of type 2 diabetes should be screened for risk of diabetes every three years from 40 years of age using the Australian type 2 diabetes risk assessment tool (AUSDRISK) (RACGP, 2023). While not part of the existing standard medical screening protocol for the assessment of asymptomatic individuals for diabetes risk, insulin resistance is the most powerful predictor of future development of type 2 diabetes (Taylor, 2012). Testing of HbA1c and/or random and fasting blood glucose levels represent detection of disease risk at a potentially more advanced stage of progression, whereby reduced insulin response or availability, has already compromised blood glucose regulation. In terms of the capacity to detect diabetes risk, the earliest detector is elevated fasting insulin, followed by HbA1c, followed by fasting and random blood glucose measurement. HbA1c is an important indicator of cumulative (preceding 2 to 3 months) glycaemic history (Sherwani et al. 2016) and can indicate impaired glycaemic regulation prior to the returning of abnormal fasting or random blood glucose results which are themselves, indicative of the presence of the actual disease - albeit potentially still mild enough to remain outwardly asymptomatic. It is logical then that the earlier the risk is detected, then the less biochemical and physiological distance must be covered to return the individual back to a state of metabolic health.

Type 2 diabetes remission

Type 2 diabetes remission has been defined as an HbA1c of under 6.5% (48 mmol/mol) for at least three months without the need for glucose-lowering medications (Diabetes Australia, 2023). Where obesity has been a factor in the development of Type 2 diabetes, substantial weight loss can lead to diabetes remission (Lean et al. 2018; El-Eshmawy, 2023). Improvements in metabolic markers of glycaemic control that contribute to remission of the disease can also be achieved via targeted Clinical Nutrition/Nutritional Medicine interventions (as per the evidence presented below) and this is particularly necessary where the Type 2 diabetes is not accompanied by obesity, or when weight has been lost but metabolic markers have not sufficiently improved for the disease to be classified as in remission - or where preventative intervention is desired prior to progression to hyperglycemia.

Evidence for Clinical Nutrition/Nutritional Medicine interventions

Genetics, diet, physical activity levels, obesity, and other factors, can all influence the development and progression of insulin resistance to Type 2 diabetes. Regarding the regaining of glucose control - early detection, personalised Nutritional Medicine interventions, appropriate physical activity, and medical interventions as required, can be combined to improve glucose control, and reduce risk of progression to Type 2 diabetes as well as aid in the remediation of Type 2 diabetes and its precursor stages.

Dietary Modification:

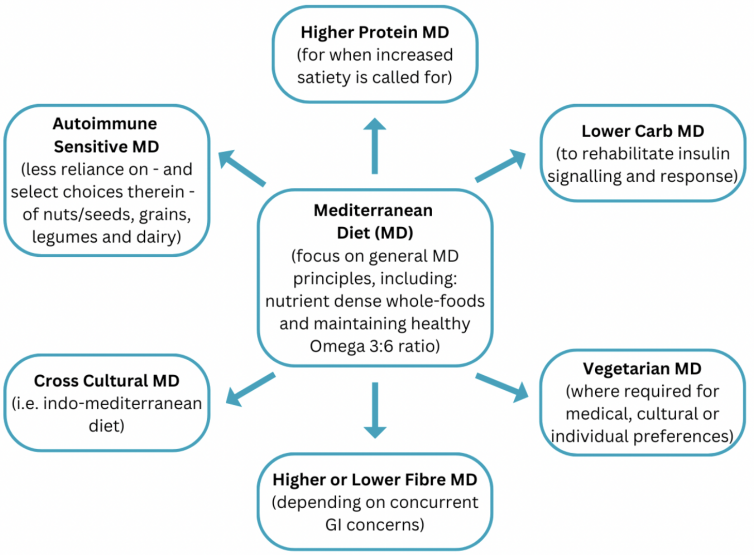
Mediterranean Type diet (and nutrients contained therein of particular interest - Omega 3 fatty acids and B vitamins)

In obese individuals with or without diabetes, the Mediterranean Type diet (MTD) has been demonstrated to facilitate weight loss and to improve metabolic markers of both insulin sensitivity and of inflammation and metabolic syndrome (Martín-Peláez, Fito & Castaner, 2020; Trico et al. 2021; Mirabelli et al. 2020; Sood et al. 2022; Dayi & Ozgoren 2022; Esposito et al. 2015). It is a dietary approach that puts focus on monounsaturated fats, polyphenols and antioxidants, fibre, Omega-3 fatty acids, protein, and micronutrients. The diet is centered around foods such as fruits, vegetables, whole grains, legumes (beans, lentils, chickpeas), nuts and seeds, and omega 3 rich protein sources, such as fatty fish (like salmon, mackerel, and sardines) - with encouragement for additional moderate consumption of poultry, eggs, dairy products, and some fresh unprocessed red meats (with processed meats consumed only in small moderation if traditionally prepared and if culturally important). These foods provide a rich source of vitamins, minerals, fibre, antioxidants, and Omega 3 fatty acids which can aid in achieving a healthier metabolic environment.

See overview of evidence below:

MedTypeDiet Nutritional biochemical pathways targeted: insulin sensitivity, hyperinsulinemia, hyperglycaemia, insulin resistance.	
1. Type of Study: Cross-sectional secondary analysis of baseline data from an interventional study (RCT, de Courten et a. 2015) NHMRC Level of Evidence: III2 Participants' characteristics: N=65 [(overweight and obese, BMI ≥ 25 and <30 kg/m^2) healthy non-diabetic adults aged between 18 and 57 years] Form of nutrient: MTD, (validated by Panagiotakos et al 2006)modified and mapping against the Australian Guide to Healthy Eating [2023] to adjust the score to suit the Australian cohort Primary outcome dietary inflammatory index, Mediterranean diet score, hyperinsulinemic euglycemic clamps, glucose tolerance test. Results: Higher adherence to MTD (MD scores) was associated significantly with greater insulin sensitivity (β = 0.179; 95%CI: 0.39, 0.318) and lower levels of some inflammatory markers with no significant improvement in blood glucose. Reference: Sood, S., Feehan, J., Itsiopoulos, C., Wilson, K., Plebanski, M., Scott, D., Hebert, J. R., Shivappa, N., Mousa, A., George, E. S., & Courten, B. (2022). Higher Adherence to a Mediterranean Diet Is Associated with Improved Insulin Sensitivity and Selected Markers of Inflammation in Individuals Who Are Overweight and Obese without Diabetes. *Nutrients*, *14*(20), 4437. https://doi.org/10.3390/nu14204437	2.Type of Study: Systematic review and a de-novo meta-analysis NHMRC Level of Evidence: I Participants' characteristics: 8 meta-analyses and 5 RCTs (published between 2011-14) N=65 [(overweight and obese, BMI ≥ 25 and <30 kg/m^2) healthy non-diabetic adults aged between 18 and 57 years, intervention-94, control=91)] Duration of study: 12 months Form of nutrient: MTD, (validated by Panagiotakos et al 2006) modified and mapping against the Australian Guide to Healthy Eating [2023] to adjust the score to suit the Australian cohort Primary outcome: Glycosylated haemoglobin (HbA1c) in type 2 diabetes, and another assessed the probability of remission from the metabolic syndrome. Results: Meta-analysis of long-term clinical trials (n=3) demonstrated an overall effect estimate [−0.47% (95% CI −0.56 to −0.38) favouring the MTD for HbA1c when compared with the usual diet (I^2=3.5%). Subgroup analysis: Patients with Metabolic syndrome (Mets) and adhering to MTD (data from two RCTs) were observed to have a 49% (95% CI 14% to 96%) increased probability of remission from Met syndrome when compared with the control group. Prevention of diabetes: A greater adherence to MTD caused a significant reduction (from 19% to 23%,) of new diabetes (based on two meta-analysis data interpretation). Convergence analysis confidently showed that MTD can prevent type 2 diabetes by reducing HbA1c levels in Quality assessment: The Cochrane risk of bias tool indicated low heterogeneity and bias was noted. Convergence analysis graded the level of evidence high. Reference: Esposito, K., Maiorino, M. I., Bellastella, G., Chiodini, P., Panagiotakos, D., & Giugliano, D. (2015). A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. *BMJ open*, *5*(8), e008222. https://doi.org/10.1136/bmjopen-2015-008222

Pivoting Mediterranean Type Diet for personalised nutrition



Above: Example visualisation of the pivoting Mediterranean Type Diet being applied to real-word clinical requirements for diverse personalised, precision-nutrition, applied within the Nutritional Medicine paradigm.

The Mediterranean Type diet is very versatile and lends itself well to adaptation, which is often necessitated in real-world clinical settings (with adaptation for personalised intervention being a key skill set of the Certified Practicing Nutritionist - and with adaptation also supporting the key evidence-based-practice principle of *patient preference*. The Mediterranean Type diet can adapt to approaches ranging from vegetarian, low carbohydrate, higher protein, or autoimmune sensitive - and this makes it ideal as a pivoting tool for personalised, precision-nutrition dietary modification. It is possible, in the course of their health journey, that an individual may engage an initial approach (focusing on immediate health concerns) and then pivot to forms of the diet that promotes long term adherence and wellbeing. The principles of the diet can also be applied to non-western cultural ways of eating (i.e., indo-mediterranean diet).

The Mediterranean Type diet provides a variety of vitamins and minerals from its diverse and nutrient dense food sources, and these nutrients play roles in various cellular processes that impact insulin sensitivity, such as vitamin D, magnesium, chromium, omega 3 fatty acids. Also important to note is the Mediterranean diet's rich supply of B vitamins, due to its nutrient dense, wholefoods focus. While a range of nutrients (outlined further in this document) have robust clinical intervention evidence for their role as therapeutic nutraceuticals, there is reliable observational data that deficiencies in some B vitamins are associated with type 2 diabetes etiology, and therefore diet modification in the direction of replete B

vitamin consumption is desirable. For example, vitamin B6 (pyridoxine) via the effects of xanthurenic acid (Mascolo & Vernì, 2020) and vitamin B12 (cobalamin) via the effects of homocysteine on insulin signalling and sensitivity (Varela-Moreiras, Murphy Scott, 2009; Zhang et al. 2013; Zhang et al. 2021). It is worth noting that dimethylbiguanide, one of the most commonly prescribed medications for Type 2 diabetes, has been associated with vitamin B12 deficiency and that supplementation may be beneficial to ongoing/optimal glycaemic control (Kim et al. 2019; Kakarlapudi et al. 2022).

B6 Nutritional biochemical pathways targeted: Oxidative stress and inflammation via xanthurenic acid (XA) induced hyperglycaemia and deficiency of vitamin B6. Experimental data demonstrate the diabetogenic effects of the kynurenine pathway (Kyn) [of tryptophan (try) metabolism)]. Stress hormones (e.g., cortisol) might cause a deficiency of the active form of vitamin B6-Pyridoxal phosphate (coenzyme form) (owing to increased demand to support numerous enzymes in stress or inflammation-induced enzymes). This state progresses to the overproduction of diabetogenic metabolites such as xanthurenic acid (via the kynurenine pathway).

B6 1. Type of Study: Case-control study (clinical observational)
NHMRC Level of Evidence: III2
Participants' characteristics: N=(54), T2DM=30 (18F, 12 M), taking metformin; Control=24 (12 F, 12 M).
Form of nutrient: NA
Duration of intervention: NA
Primary outcome Tryptophan and kynurenine pathway metabolites
Results: Trp levels were not significantly different between the two groups [(T2DM =80.37 ± 22.50) vs Control= 68.9± 12.21) µM/L]. Kyn levels were significantly higher in the T2DM group (2.32 ± 0.84) than in the control group (1.76 ± 0.48) (p=0.01).
The Kyn/Trp ratio was higher in the T2D (2.88) subjects when compared with the control subject (2.51), but the difference was not statistically significant. Diabetogenic KP metabolites, induced by chronic stress or chronic low-grade inflammation, are one of the mechanisms promoting the development of T2D from pre-diabetes.
Reference: Oxenkrug, G. F. (2015). Increased Plasma Levels of Xanthurenic and Kynurenic Acids in Type 2 Diabetes. *Molecular Neurobiology*, 52(2), 805–810. https://doi.org/10.1007/s12035-015-9232-0

Vitamin B12 Nutritional biochemical pathways targeted: glycaemic control and insulin resistance
1. Type of Study:randomised, multi-arm, open-label clinical trial
NHMRC Level of Evidence: II
Participants' characteristics: N= (80) patients with type 2 diabetes and on stable oral antidiabetics and N= (20) patients - each were randomly allocated to one of the four groups.
Form of nutrient: Group A: add-on Folic acid @ 5mg/day; Group B: add-on Methylcobalamin @ 500mg/day; Group C: add-on Folic acid + Methylcobalamin @ 5mg/day + 500mg/day; Group D: Standard oral anti-diabetic drugs
Duration: Patients were followed up after 8 weeks.
Primary outcome: Vitamin B12 improved glycaemic control and insulin resistance in patients with type 2 diabetes mellitus.
Results: HbA1c improved in Groups B and C [median changes from baseline – 1.2 % (– 13 mmol/mol) and – 1.5 % (– 16 mmol/mol) respectively, p values 0.04 and 0.02 respectively] compared to Group D. Groups B and C also showed significant improvements in plasma insulin, insulin resistance and serum adiponectin compared to Group D. Serum homocysteine declined significantly in all three groups with add-on supplementation compared to standard treatment.
Reference: Satapathy, S., Bandyopadhyay, D., Patro, B. K., Khan, S., & Naik, S. (2020). Folic acid and vitamin B12 supplementation in subjects with type 2 diabetes mellitus: A multi-arm randomized controlled clinical trial. Complementary therapies in medicine, 53, 102526. https://doi.org/10.1016/j.ctim.2020.102526

B6 2. Type of Study: Case-control study (clinical observational data) nested in PREDIMED study
NHMRC Level of Evidence: III2
Participants' characteristics: N= (641) non-diabetic, 251 incident cases diagnosed during 3.8 years of median follow up.
Form of nutrient: NA
Duration: 1 year and 3.8 years follow-up (median)
Primary outcome Trp and kyn pathway metabolites (tryptophan, kynurenine, kynurenic acid, quinolinic acid, 3-hydroxyanthranilic acid) were measured and associated with the development of Diabetes (FBG) and HOMA-IR.
Results: Baseline Trp was prospectively associated with a slightly higher risk of T2D (P trend 0.045, fully adjusted models). Continuous 1-year changes in quinolinic acid (hazard ratio per SD 1.39; 95% CI, 1.09–1.77; P 0.047) showed a positive association with T2D incidence (All potential confounders were adjusted). Baseline trp was associated with a higher risk of incident T2D (hazard ratio 1.29; 95% CI, 1.04–1.61 per SD). Baseline Trp and Kyn acid [Baseline try (MD per SD 0.67; 95% CI, 0.46–0.88) and kyn (MD per SD 0.35; 95% CI, 0.23– 0.47)] were directly associated with changes in HOMA-IR in fully adjusted models from baseline to 1 year.
Reference: Yu, E., Razquin, C., Lapetra, J., Estruch, R., Ros, E., Cofán, M., Arós, F.,
Toledo, E., Serra-Majem, L., Sorlí, J., Hu, F. B., Papandreou, C., Martinez-Gonzalez, M., Salas-Salvado, J., Ruiz-Canela, M., Guasch-Ferre, M., Clish, C. B., Dennis, C.,
Liang, L., . . . Fitó, M. (2018). Association of Tryptophan Metabolites with Incident Type 2 Diabetes in the PREDIMED Trial: A Case–Cohort Study. *Clinical Chemistry, 64*(8), 1211-1220. https://doi.org/10.1373/clinchem.2018.288720

B6 3. Type of Study: Cohort study
NHMRC Level of Evidence: III2
Participants' characteristics: N= (171) diabetic, elderly >60 years
Form of nutrient: NA
Duration: NA
Primary outcome: PLP and XA were measured , HOMA-IR
Results: Plasma PLP associated significantly with XA concentrations (β=0.001, p<0.03); plasma XA was correlated with HOMA-IR (β=0.19, p<0.002) and with the odds of having T2DM (OR: 1.15, 95% CI: 1.03 – 1.27).
Reference: Reginaldo, C., Jacques, P., Scott, T., Oxenkrug, G., Selhub, J., and Paul, L. (2015). Xanthurenic acid is associated with higher insulin resistance and higher odds of diabetes. *Nutrition-The FASEB journal.* 29 (S1). https://doi.org/10.1096/fasebj.29.1_supplement.919.20

Omega 3 fatty acids

Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), play a role in modulating cellular signaling pathways involved in glucose metabolism and insulin response through mechanisms that include anti-Inflammatory effects via reducing inflammatory cytokine production (Malekshahi Moghadam et al. 2012), promoting the release from adipose tissue of the insulin sensitising adipokine adiponectin (Bahreini et al. 2018), and G Protein-Coupled Receptor Signaling of which the functional ω-3 FA receptor/sensor GPR120 has been demonstrated to mediate potent insulin sensitizing and antidiabetic effects by repressing macrophage-induced tissue inflammation (Oh et al. 2010).

Omega 3 Nutritional biochemical pathways targeted: fasting blood glucose, insulin resistance, and glycated hemoglobin
Type of Study: Systematic review and meta-analysis
NHMRC Level of Evidence: I
Participants' characteristics: N= 30 RCTs, 19 RCTs had diabetic participants (N= 920 intervention group, and 901 control group)
Form of nutrient: omega 3
Duration: varied
Primary outcome: Effect of omega-3 on fasting blood glucose, insulin resistance, and glycated hemoglobin.
Results: A significant effect of omega 3 on reducing FBG [SMD: -0.48; CI95%: -0.76, -0.19; p = 0.01; I2 = 88%] and insulin resistance [SMD: -0.61; CI95%: -0.98, -0.24; p = 0.01; I2 = 90%].
For glycated hemoglobin, there was no significant effect in the meta-analysis
Risk of bias: Cochrane scale
Reference: Delpino, F. M., Figueiredo, L. M., da Silva, B. G. C., da Silva, T. G., Mintem, G. C., Bielemann, R. M., & Gigante, D. P. (2022). Omega-3 supplementation and diabetes: A systematic review and meta-analysis. *Critical Reviews in Food Science and Nutrition,* 62(16), 4435–4448. https://doi.org/10.1080/10408398.2021.1875977.

Nutritional Supplementation Prescribing for complex Nutritional Medicine purposes

The following nutrients have excellent to good quality scientific evidence for their use as a Nutritional Medicine (Clinical Nutrition) intervention to disrupt the etiology of Type 2 diabetes. Singularly and/or collectively, they provide evidence in support of the efficacy of the Nutritional Medicine approach to Type 2 diabetes prevention and remission. Dosages are personalised and sit within the existing therapeutic guidelines for efficacy and safety, as per the training of, and the legislative exemptions accessed by, the Certified Practicing Nutritionist.

Vitamin D
Nutritional biochemical pathways targeted: beta cell apoptosis and function, insulin secretion, insulin resistance, insulin signalling cascade and gene expression of circadian clock-related genes via VDR. As per the evidence presented below, vitamin D represents both a risk parameter and an effective Nutritional Medicine intervention for the prevention and remitting of Type 2 diabetes in persons who do not have vitamin D sufficiency.

1. Type of study: A single centre, DB, RCT
NHMRC Level of Evidence: II
Participants' characteristics: N=307 infertile men [intervention (150), placebo group (156)
Form of nutrient: Cholecalciferol
Duration of intervention: 150 days
Primary outcome: insulin resistance measured by fasting plasma glucose, Hb1Ac, fasting serum insulin, HOMA-IR
Results: The intervention group was observed to have decreased fasting serum insulin (13%) compared to the placebo group (65 vs 74 pmol/L, P = .018) and a fall in HOMA-IR (19%) (2.2 vs 2.7, P = .025).
Power of the study: The study was statistically powered (80%) to detect significance at p=0.05.
Reference: Holt, R., Petersen, J. H., Dinsdale, E., Knop, F. K., Juul, A., Jørgensen, N., & Blomberg Jensen, M. (2022). Vitamin D supplementation improves fasting insulin levels and HDL cholesterol in infertile men. *The Journal of Clinical Endocrinology & Metabolism*, 107(1), 98-108.

2. Type of Study: Secondary analysis of the Vitamin D and Type 2 Diabetes study (DB, RCT)
NHMRC Level of Evidence: II
Participants' characteristics: Prediabetic, obese [N=1774, 44% women,56% men, 60% Caucasian) [intervention (888), placebo group (886)
Form of nutrient: Cholecalciferol
Duration of intervention: 365 days
Primary outcome: Disposition index (DI) and risk of developing diabetes
Results: The rate of diabetes incidence was significantly lower in the vitamin D group during the two years follow up period. Out of 275 (15.5%) participants who progressed to a diabetic state (within 12 - 24 months follow-up), 116 (13.1%) were in the vitamin D vs 159 (18.0%) in the placebo group (hazard ratio 0.70; 95% CI, 0.54-0.91).
Though no statistical difference was noted in the DI [The area under the curve of receiver operating characteristic for DI was 0.70 (95% CI, 0.66-0.74) for the vitamin D group and 0.69 (95% CI, 0.66-0.72) for the

3. Type of Study: Parallel design DB RCTs
NHMRC Level of Evidence: II
Participants' characteristics: Adults with prediabetes, low VD (<30ng/ml) (N= 162), 83 completed 6 months follow up (VD group=44, placebo=39)
Form of nutrient: Cholecalciferol
Duration of intervention-90 days plus follow-up of another 90 days
Primary outcome HOMA-IR, Progression (or regression) of glucose tolerance
Results: Improved insulin sensitivity and decreased risk of progression toward diabetes.
Significant fall in HOMA-IR score in the vitamin D group (2.6 vs. 3.1; P value = 0.04) at 6 months. The rate of progression toward diabetes was significantly lower in the intervention group (28% vs. 3%; P value = 0.002)

2.continued - placebo group], vitamin D improved β-cell function among those with baseline 25(OH)D levels less than 12 ng/mL. Reference: Rasouli, N., Brodsky, I. G., Chatterjee, R., Kim, S. H., Pratley, R. E., Staten, M. A., Pittas, A. G., & D2d Research Group (2022). Effects of Vitamin D Supplementation on Insulin Sensitivity and Secretion in Prediabetes. *The Journal of clinical endocrinology and metabolism*, *107*(1), 230–240. https://doi.org/10.1210/clinem/dgab649	3.continued - Reference: Niroomand, M., Fotouhi, A., Irannejad, N., & Hosseinpanah, F. (2019). Does high-dose vitamin D supplementation impact insulin resistance and risk of development of diabetes in patients with pre-diabetes? A double-blind randomized clinical trial. *Diabetes research and clinical practice*, *148*, 1–9. https://doi.org/10.1016/j.diabres.2018.12.008
4. Type of Study: Systematic review and meta-analysis of DB RCTs NHMRC Level of Evidence: I Participants' characteristics: 20 RCTs (N= 2703), subjects 48-67 years old Form of nutrient: Cholecalciferol Duration of intervention 2-6 months (median=3 months) Primary outcome HOMA-IR, FBG, Fasting serum insulin, Hb1Ac Results: VD supplementation resulted in a significant improvement in HOMA-IR (SMD = −0.57; 95%CI: −1.09~−0.04), but not in other outcomes. The review highlighted notable changes in subgroups-vitamin D supplementation produced different effects among various ethnicities with a similar trend: Middle Easterners showed the biggest reduction, the other Asians the second, and other ethnicities had the smallest preferred changes. And short-term (WMD_{FBG} = −8.44; 95%CI: −12.72~−4.15), high dose (WMD_{FBG} = −8.70; 95%CI: −12.96~−4.44), non-obese ($SMD_{Fasting\ insulin}$ = −1.80; 95%CI: −2.66~−0.95). Publication bias: low Reference: Li, X., Liu, Y., Zheng, Y., Wang, P., & Zhang, Y. (2018). The Effect of Vitamin D Supplementation on Glycemic Control in Type 2 Diabetes Patients: A Systematic Review and Meta-Analysis. *Nutrients*, *10*(3), 375. https://doi.org/10.3390/nu10030375	

Magnesium

Nutritional biochemical pathways targeted: Insulin resistance and beta cell function. Intracellular Mg deficiency is observed among people with long-standing diabetes and insulin resistance. In a state of hyperglycemia and hyperinsulinemia urinary Mg excretion increases. Mg supports insulin receptor function by moderating intracellular calcium concentration and influences insulin-mediated glucose uptake (tyrosine kinase activity). Mg improves the ability of beta-cells to compensate for variations in insulin sensitivity with significant hypomagnesaemia.

1. Type of Study: RCT NHMRC Level of Evidence: II Participants' characteristics: non-diabetic adults with hypomagnesia and decreased insulin sensitivity (N=97, intervention group=49, placebo=48). Form of nutrient: Magnesium chloride Duration of intervention: 90 days Primary outcome Belfiore's and HOMA-ß indices as measures of insulin sensitivity and beta-cell function- change in the AUC of the hyperbolic model of beta-cell function (HMbCF) derived from the fasting state. Results: Improved the ability of pancreatic beta-cells to compensate for decreases in insulin sensitivity as evident from changes in the hyperbolic distribution (AUC = 18.855 cm^2), in the Mg supplemented group compared to the placebo group, which had no changes (AUC = 7.631 cm^2). Significant decrease FBG in the post-intervention group [(4.6 ± 0.4mM) compared to placebo (4.9±0.5) (p = 0.01); FI significantly reduced (87.6 ± 20.4) vs 100.8 ± 42.6 (p=0.02) Power of the study: Adequately powered (80%) with p<0.05 to detect a difference of 30% between the groups that represents a clinically significant effect, (expected SD in the AUC of 3.51). Reference: Guerrero-Romero, F., & Rodríguez-Morán, M. (2011). Magnesium improves the beta-cell function to compensate variation of insulin sensitivity: a double-blind, randomized clinical trial. *European Journal of Clinical Investigation,* 41(4), 405–410. https://doi.org/10.1111/j.1365-2362.2010.02422.x	2. Type of study: Meta-analysis of RCTs NHMRC Level of Evidence: I Participants' characteristics: RCTs (N=9, parallel design-5, cross over-4), diabetic participants (on diet or medications) =370 Form of nutrient: Elemental magnesium Duration of intervention: 90 days Primary outcome Hb1Ac, FBG Results: FBG reduced significantly in the treatment groups compared to placebo [−0.56 mmol/l (95% CI, −1.10 to −0.01); *P* for heterogeneity = 0.02] with non-significant differences in HbA_{1c} [−0.31% (95% CI, −0.81 to 0.19); *P* for heterogeneity = 0.10]. Publication bias: No evidence of publication bias for meta-analyses of HbA_{1c} and fasting glucose levels as assessed by Begg's modified funnel plot, Reference: Song, Y., He, K., Levitan, E. B., Manson, J. E., & Liu, S. (2006). Effects of oral magnesium supplementation on glycaemic control in Type 2 diabetes: a meta-analysis of randomized double-blind controlled trials. *Diabetic Medicine*, 23(10), 1050–1056. https://doi.org/10.1111/j.1464-5491.2006.01852.x

Chromium

Nutritional biochemical pathways targeted: Insulin signalling, insulin receptor function, endoplasmic reticulum stress. Chromium in its activated form (chromodulin or as a trivalent complex known as glucose tolerance factor) up-regulates insulin signalling by increasing the activity of downstream effectors of insulin signalling PI3-kinase and protein kinase B (Akt); upregulates Glut4 translocation independent of the insulin signalling proteins by increasing the fluidity of the membrane; downregulates protein tyrosine phosphatases-1B (PTP1B), the negative regulator of insulin signalling; and alleviates endoplasmic reticulum stress within the cells, saving insulin receptor substrate from Jun NH(2)-terminal kinase (JNK) mediated serine phosphorylation and subsequent ubiquitination.

1. Type of Study: Systematic review and meta-analysis NHMRC Level of Evidence: I Participants' characteristics: 28 RCTs (before 2020) Form of nutrient: Variable [(chromium yeast (6), Cr picolinate (10), Cr chloride (4), Cr nicotinate (1), trivalent Cr (1), Cr pidolate (1) and Cr dinicocysteinate (1)] Duration of intervention: 4-25 weeks Primary outcome FBG, Hb1Ac and HOMA-IR Results: significant reduction in all glycemic control indices such as FPG, insulin, HbA1C and HOMA-IR levels after chromium supplementation. Furthermore, long term intervention (≥12 weeks) contributed to a greater reduction of all mentioned indices. Reference: Asbaghi, O., Naeini, F., Ashtary-Larky, D., Moradi, S., Zakeri, N., Eslampour, E., Kelishadi, M. R., & Naeini, A. A. (2021). Effects of chromium supplementation on lipid profile in patients with type 2 diabetes: A systematic review and dose-response meta-analysis of randomized controlled trials. *Journal of Trace Elements in Medicine and Biology*, 66, 126741–126741. https://doi.org/10.1016/j.jtemb.2021.126741	2. Type of Study: Systematic review and meta-analysis NHMRC Level of Evidence: I Participants' characteristics: 10 RCTs (n=509 patients, 269 intervention group and 240 control) Form of nutrient: Variable [(Cr containing milk powder (2) Cr enriched yeast (2), brewer's yeast (2), Cr picolinate (3), Cr nicotinate (1)] (Patients were also taking hypoglycaemic drugs) Duration of intervention: 90 days to 25 weeks Primary outcome FBG, and Hb1Ac Results: Hb1Ac decreased significantly in the intervention group compared to the control group, [Mean difference (MD) = −0.54, 95% CI = −0.98 to −0.09, P = 0.02). (I^2 = 84%); non-significant decrease in FBG in the intervention group compared to control [−29.65 mg/dL (95% CI = −68.62 to 9.31, P = 0.14, (I^2 = 97%)] Risk of bias: Cochrane Risk of Bias Tool: low Reference: Zhao, F., Pan, D., Wang, N., Xia, H., Zhang, H., Wang, S., & Sun, G. (2022). Effect of Chromium Supplementation on Blood Glucose and Lipid Levels in Patients with Type 2 Diabetes Mellitus: a Systematic Review and Meta-analysis. *Biological Trace Element Research,* 200(2), 516–525. https://doi.org/10.1007/s12011-021-02693-3

Myo-inositol

Nutritional biochemical pathways targeted: Insulin signalling. Acts like an insulin mediator, secondary messenger of insulin, improves insulin sensitivity via potentiating insulin signalling cascade through activation of P13kinase (metabolism and generation of PIP3 which acts as a second messenger for the activation of PI3K/AKT).

1. Type of Study: Systematic review of RCTs and case-control studies NHMRC Level of Evidence: II[3] Participants' characteristics: N=7 human [3 case-control, 1 RCT, 1 DB, RCT, 1 cohort, 1 pilot] Form of nutrient: Myo-inositol, D-chiro inositol Duration of intervention: 90 days Primary outcome insulin resistance measured by fasting blood glucose, Hb1Ac, fasting serum insulin decreased, no publication bias assessed, no meta-analysis conducted. Results: Narrative synthesis-inositol may be effective in prophylaxis and treatment of diabetes Reference: Özturan, A., Arslan, S., Kocaadam, B., Elibol, E., İmamoğlu, İ., & Karadağ, M. G. (2019). Effect of inositol and its derivatives on diabetes: a systematic review. *Critical reviews in food science and nutrition*, *59*(7), 1124–1136. https://doi.org/10.1080/10408398.2017.1392926	2. Type of study: Systematic review of RCTs NHMRC Level of Evidence: I Participants' characteristics: N=20 RCTs [1999 to 2013, subjects: T2DM (7, n=285) PCOS (6, n=202), GDM (4, n=576), metabolic syndrome (2, n=160, postmenopausal), elderly (1, n=16))] Form of nutrient: Myo-inositol, D-chiro inositol, pinitol Duration of intervention: 28 days to 365 days Primary outcome insulin resistance measured by fasting blood glucose, Hb1Ac, HOMA-IR Results: Inositol supplementation decreased FBG through an improvement in insulin sensitivity that is independent of weight as evidenced by reduction in FBG (MD=-0.44mmol/l, 95% CI: -0.65, -0.23); HOMA-IR (MD: -1.96 mmol mUI/l, 95% CI -2.62, -1.30); abnormal glucose tolerance [RR: 0.28, 95% CI:0.12, 0.66), fasting insulin (MD: -38.49 pmol/l, 95% CI: -52.63, -24.36), though no significant change in Hb1Ac was reported. Bias assessment: Funnel plots displayed symmetrical distributions for all the outcomes with the exception of fasting insulin and HOMA-IR Reference: Miñambres, I., Cuixart, G., Gonçalves, A., & Corcoy, R. (2019). Effects of inositol on glucose homeostasis: Systematic review and meta-analysis of randomized controlled trials. Clinical Nutrition (Edinburgh, Scotland), 38(3), 1146–1152. https://doirg/10.1016/j.clnu.2018.06.957

Principal elements of the Certified Practicing Nutritionist (CPN) Approach to pre and Type 2 diabetes

The following diagram outlines an example scenario of a client interacting with the Certified Practicing Nutritionist (CPN) process, in the context of dealing with pre and Type 2 diabetes. The diagram uses an example scenario of an individual presenting with obesity, and outlines (as examples) the differential assessment process of determining the source of weight gain, and how this informs subsequent clinical steps. The diagram details the interaction between the CPN process and a multidisciplinary team approach. This example can be used to inform and support the subsequent (page 11) Diabetes Prevention and Remission Pilot Study Design - which is concordant with the submission made by the Star Pharmacy Group, entitled: **Star Pharmacy Group Pilot Study Proposal in Collaboration with Australasian Association and Register of Practicing Nutritionists.**

Principal elements of the Certified Practicing Nutritionist (CPN) Approach to pre and Type 2 diabetes

1. Client Presentation to CPN – direct client initiated OR via referral from other health care professional

2. Detailed Case History Take & initial risk assessment with integration of existing medical evidence such as but not limited to, current medications, pathology results such as fasting blood glucose, HbA1c, metabolic markers, & referral notes from other health professionals. Biometric & physical activity assessment & preliminary nutritional assessment via 24-hour recall, AUSDRISK via online tool (if not already completed & known), TGA approved HbA1c kit test (if unknown/as needs basis).

3. Differential assessment of signs & symptoms including: analysis of all evidence & information gathered in Step 2 & differential assessment of likely primary factors. **Example: Obesity related pre or Type 2 diabetes** – Determine source of weight gain, as this defines approach required i.e., **Possibility 1)** ***excess energy intake*** → energy intake restriction via modified Mediterranean Type diet **&** nutritional medicine support of insulin signalling; or **(2)** ***peri or menopausal weight gain*** → hormonal testing & complex nutritional medicine intervention in conjunction with personalised dietary modification; or **(3) possible** ***hypothyroid*** for medical investigation & support in conjunction with targeted dietary modification and complex nutritional medicine, as likely multi-disciplinary care.

Multi-disciplinary team approach

Referral to other health care professionals as appropriate e.g., medical practitioner, psychologist, exercise physiologist OR with client's consent, engagement with health care professionals involved in the client's case such as the referring practitioner or members of the multi-disciplinary care team

4. Evidenced based translation to nutritional biochemical paradigm – identification of the primary nutritional biochemical drivers and optimal target points for intervention.

5. Further CPN initiated investigations as warranted i.e., dietary intake recording, pathology testing e.g., fasting insulin, thyroid profiling, hormones (oestrogen, progesterone, testosterone, androgens).

Information sharing where multi-disciplinary team approach has been engaged & client has consented to information sharing.

6. Formulation of personalised therapy goals/outcomes with client. E.g., to improve glucose handling/insulin sensitivity as evidenced by reduction in HbA1c levels → i.e., (in the context of the obesity example) better food choices to promote weight loss, 20 minutes walking per day to increase physical activity.

7. Formulation of personalised nutritional medicine intervention plan to address specific health needs in a manner respectful of client preferences, needs, barriers & enablers, such as literacy, cost, cultural.

8. Implementation of evidence based personalised modification of diet to support therapeutic treatment goals/outcomes & accompanied by evidence based targeted prescribing of therapeutic nutritional supplements (including customised nutritional supplement compounding when appropriate) for nutrient repletion & complex nutritional medicine purposes (*as per exemptions under Section 42AA & Schedule 5 Item 6 of the Therapeutic Goods Act & Regulations*). E.g., prescribed interventions, such as vitamin D to address a known deficiency, &/or compounded myo-inositol/magnesium to support insulin signalling.

9. Consultation based follow-up of client progress against treatment goals & therapeutic outcomes e.g., review of weight loss & metabolic markers.

10. Review & adjustment of treatment goals, & nutritional therapeutic interventions, incorporating any new information received such as pathology results, & additionally referral for further pathology testing &/or referral to other health care professionals (when appropriate).

Diabetes Prevention and Remission Pilot Study - Design

This following is a pilot study design, in collaboration with the Star Pharmacy Group and is concordant with their submission entitled: **Star Pharmacy Group Pilot Study Proposal in Collaboration with Australasian Association and Register of Practicing Nutritionists.** *See the next page (below the diagram) for the study hypothesis and further contextual information.*

1. Pharmacy clientele from multiple stores owned by Pharmacist collaborator/research partner

2a. Receipt of communication from pharmacy advising of the pilot study and their invitation to express interest in being selected for participation if they meet the stated inclusion criteria

2b. In store advertising of the pilot study

3. Pharmacy client expresses interest to the pharmacy in participation via email or in-store. Nomination includes basic demographic data, contact information, and statement of which part of the inclusion criteria they meet: overweight/obesity, medicated for high blood pressure, medicated for elevated cholesterol, medicated for or have current medical diagnosis of type 2 diabetes, or previous blood test result showing elevated fasting insulin, elevated fasting HBA1c or elevated glucose (either fasting or non-fasting).

4. Pharmacy clientele who have expressed interest in the pilot study are randomly selected for participation in the pilot study

5. Dispensing of Case Take form via either collection in store or via email. Video will be available to participants to watch that explains how to complete the Case Take form.

6. Participant returns the Case Take Form in store and is booked for appointment with CPN.

7. Prior to appointment, CPN reviews Case Take form with particular attention to diabetes risk factors.

8. Participant attends CPN appointment (in fasting state) where baseline readings are taken for blood glucose and HBA1c and referral given for testing of fasting insulin. Participant meets with the CPN and works through completed Case Take form with the participant to ensure all information is complete. Participant is given food intake diary and instruction on how to complete (3 week-days and 1 weekend day). Food intake diary to be returned to Pharmacy of issue within two weeks. The next (second) appointment is booked for review of fasting insulin result on return of food intake diary. [Participant's returning elevated blood glucose, elevated HBA1c or elevated fasting insulin will be follow-up to ensure a second appointment is made.]

9. CPN reviews Case Take form and analyses food intake diary with particular attention to diabetes factors and identifies key nutritional intervention areas for improvement. In line with ethical obligations, this report will be provided to the participant regardless of their fasting insulin result.

10a. Second appointment: No existing diabetes diagnosis, normal blood glucose and normal HBA1c, and normal fasting insulin. Participant will receive report on nutritional issues and basic dietary advice – end of participation in the study but participant is able to continue as a non-study client of the CPN or be referred to another CPN for support should they seek to do so.

10b. Second appointment: pre-existing diagnosis of type 2 diabetes, or elevated blood glucose, or elevated HBA1c or elevated fasting insulin. Participant will receive report on nutritional issues and CPN will work with them to identify personalised type 2 diabetes prevention/remediation treatment goals and prescribe personalised dietary modifications and appropriate personalised therapeutic nutritional medicine supplements (including the prescription and preparation of nutritional supplement compounds when appropriate, as per exemptions provided under Section 42AA and Schedule 5 Item 6 of the Therapeutic Goods Act and Regulations). Third appointment with CPN is booked for 8 weeks' time and referral given for second fasting insulin test for 7 weeks' time. Sharing of results with participants medical practitioner (upon client consent)

11. Third appointment, follow-up of progress, testing of fasting glucose and HBA1c and review of second fasting insulin result. Adjustment of Nutritional Medicine therapeutic interventions as appropriate. Fourth and final appointment made for 8 weeks' time and third and referral given for third and final fasting insulin test for 7 weeks' time.

12. Fourth appointment, follow-up of progress, testing of fasting glucose and HBA1c and review of third fasting insulin result. Maintenance program formulated with ongoing goals for the completing participant. Referral to CPN or medical practitioner for ongoing care.

13. Compilation and analysis of results.

14. Production of report and publication of summary results.

Hypothesis: Within a community pharmacy setting, a personalised precision nutrition approach can disrupt the aetiology of Type 2 Diabetes. This pilot study, to be conducted in collaboration with *Star Pharmacy Group,* is envisaged to involve between 200 and not more than 500 participants whose progress will be tracked for 6 months. Objectively, the endpoint of this study is anticipated to be *improvement in Type 2 diabetes related risk factors and metabolic markers, such as overweight/obesity, HBA1C, fasting insulin, fasting glucose, reduction in medication reliance*. Subjectively, the endpoint is anticipated to show that *improvements have occurred in the overall health and wellbeing of individuals with metabolic dysfunction, pre-diabetes and Type 2 diabetes*.

In reference to the pilot study, we are seeking to ascertain the appetite of the Government to engage with and support this pilot study which also represents a viable commercial model (upon the removal of the random selection component) should government support not be available, or at the conclusion of the study period. The Academy of Sciences current decadal plan for Nutrition has recognised the need for focus on personalised nutrition (in balance with the prevailing focus on broader public health nutrition) and there is an enormous gap to fill in the provision of personalised precision nutrition services for diabetes prevention and care. We are also aware that the Federal Government is investing funds to explore allied health professions working to the limit of their respective qualifications and scope of practice - and and while we respect the current government position on encouraging such matters, we seek to point out that an important aspect of such investigation is highlighting where an existing profession is already purpose built to fit a need, but as yet, has not realised the level of Commonwealth support necessary to maximise its reach. We respectfully put forth to the Government that we are a resource ready and available to be engaged to fill that gap - i.e., personalised Nutritional Medicine intervention for pre and Type 2 diabetes - which sits entirely within our scope of practice in reference to qualification and legislative exemptions that underpin our nutritional therapeutic prescribing capacity. While private health insurance rebates (and when applicable, NDIS funds) are available to subsidise the cost to the client for such services, fundamentally, the Clinical Nutrition/Nutritional Medicine services (and therein access to the knowledge and independent nutritional therapeutic prescribing and compounding capacity that is unique to clinically trained Nutritionists/Nutritional Medicine practitioners) are currently only accessible to people who can afford to pay (as Medicare funding for dietary services has not been extended to include Certified Practicing Nutritionists). Sadly, this user-pays system discriminates against the economically/socially and culturally vulnerable people who are especially affected by diabetes due to these demographic risk factors.

Conclusions

The challenges presented by the Type 2 diabetes epidemic are complex and need to be addressed from multiple angles, including public health, education, industry regulation of products and advertising as well as health care. With regards to health care, we recommend the following:

1. Increase low cost, easy access opportunities for early detection of diabetes risk (GP, pharmacy, community centres etc.)
2. Provide non-pharmacological pathways for personalised Nutritional Medicine treatment focused on diet and lifestyle.
3. Provide Medicare support for personalised nutritional medicine health care.

We are a workforce with the skills and potential to be mobilised to address the current pandemic of diabetes and related obesity - and the tremendous health, societal and economical costs associated with it. We look forward to the opportunity to actively engage with this process and contribute towards tangible and sustainable health outcomes for Australians affected by pre- and Type 2 diabetes.

Yours sincerely,

The Australasian Association and Register of Practicing Nutritionists (AARPN)

www.aarpn.com
https://ahpa.com.au/allied-health-professions/certified-practicing-nutritionist/
https://ahpa.com.au/our-members/australasian-association-and-register-of-practicing-nutritionists/

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THERAPEUTIC GOODS ACT 1989 - SECT 42AA

42AA This Part not to apply to advertisements directed at health professionals etc.

(1) This Part does not apply to advertisements directed exclusively to:

(a) medical practitioners, psychologists, dentists, pharmacists, optometrists, chiropractors, physiotherapists, nurses, midwives, dental hygienists, dental prosthetists, dental therapists or osteopaths; or

(b) persons who are:

(i) engaged in the business of wholesaling therapeutic goods; or

(ii) purchasing officers in hospitals; or

(c) herbalists, homoeopathic practitioners, naturopaths, nutritionists, practitioners of traditional Chinese medicine or podiatrists registered under a law of a State or Territory; or

(d) a class of persons specified under subsection (1A).

(1A) The Minister may, by legislative instrument, specify a class of persons for the purposes of paragraph (1)(d).

(2) This Part does not apply to advertisements directed exclusively to persons who are members of an Australian branch (however described) of one of the bodies prescribed for the purposes of this subsection.

(3) For the purposes of subsection (2), a person is taken to be a member of an Australian branch of one of those bodies if, and only if, the person has the qualifications and training that are necessary or appropriate for membership of the relevant body.

(4) This Part does not apply to advice or information given directly to a patient by a person referred to in paragraph (1)(a) or (c) or subsection (2) in the course of treatment of that patient.

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