

CLINICIAN NOTES

Summary notes for healthcare and nutritional professionals use only.

Important: Always refer back to your client's presenting case and symptoms. Remember our guidelines and suggestions do not replace medical advice.

The following is a summary of areas that may need your attention as a healthcare or nutritional professional. We do our best to help you prioritise areas to address, however, are limited in that capacity as the following suggestions are based purely on DNA results and your client's questionnaire answers. Depending on your client's symptoms, presenting issue, current health and goals, you may want to prioritise issues to address differently. The report can be a useful blueprint but it does not diagnose any health conditions or provide medical advice and should not be used in isolation to make any diagnosis or clinical decisions. Phenotype assessment by means of biomarker/functional assessment should be an iterative process that is layered on top of genetic data.

Poor sleep pattern

The overall score indicates that your client may be predisposed to experience poor sleep patterns. To determine the risk score, we have assessed their genetic variants (CLOCK) and sleep questionnaire results.

Sleep is when cell maintenance and repair occur, and when, for example, beta-amyloid plaque, one of the proteins responsible for blocking cell communications is cleared from the brain. Sleep is also important for gene expression, detoxification and methylation, and emerging evidence has assigned an important role to sleep as a modulator of metabolic homeostasis.

Nutrition and Lifestyle interventions: First, try to establish if your client is waking up in the middle of the night (stress and anxiety related) or struggling to fall asleep (melatonin, cortisol) and then discuss why their sleep patterns are disturbed (environmental issues, stress, anxiety, hormonal imbalances, etc.) and address the issue.

Consider additional nutrients that have a calming effect and/or support serotonin and melatonin production to help your client get into healthier sleeping patterns.

Appetite Regulation

According to the genetic variants as well as the cravings questionnaire result, your client has a risk for food cravings which can put you at risk of excessive weight gain.

They are also likely to have a reduced ability to feel full after meals, and can be overeating. Please be aware of this risk and limit their caloric intake to just 3 meals a day with no snacking in between. Daily exercise which can be a brisk walk, watching the diet and eating loads of leafy greens has been shown to help. For additional support, consider 5-HTP, chromium and magnesium. Please make your client aware of lifestyle triggers such as stress and poor sleep, and manage those as well.

Saturated Fat Balance (sensitivity)

Your client may also have a genetic predisposition to overabsorb certain fats making them potentially more sensitive to saturated fats in the diet. Unfortunately, the fatty acids that are absorbed are prone to being affected by oxidative stress.

Lifestyle/nutrition intervention: It is still important to include healthy polyunsaturated fatty acids and monounsaturated fats, an essential component of any diet as it helps the body to absorb nutrients as well as being a great source of energy. Reduce unhealthy fats, refined carbohydrates and add antioxidant phytonutrients. Exercise has also been shown to reduce risk gene expression, and should be encouraged.

Risk for omega 3/6 imbalance

If your client has a reduced D5D enzyme responsible for omega-3 metabolism (encoded by FADS1) this means that they have an impaired omega-3 pathway and a higher need for alpha linolenic acid and EPA/DHA. If your client has an increased D6D activity in omega-6 enzyme (encoded by FADS2) this indicates a decreased need for omega-6. Increased D6D activity has been correlated to inflammatory states. The EFA deficiency and fat dietary intake questionnaires will indicate if they are getting an appropriate amount of EFAs through their diet.

Lifestyle and nutritional support: Support genetic variants by reducing intake of omega 6 fats such as grain fed or non-free-range chicken and other meats and processed commercial fats. Ensure adequate intake of oily fish, green vegetables, nuts and seeds with anti-inflammatory properties through diet.

Functional test to consider: Fatty Acid Profile

Risk for inflammation and related conditions

We have assessed your client's genetic variants including IL6 Receptor (cytokine), TNF alpha (cytokine involved in systemic inflammation) and MnSOD. It is important to note that genetics alone do not affect response or susceptibility to inflammatory conditions, but also a person's environmental factors that also regulate gene transcription. These environmental factors can be diet, infection, pollution, sleep and stress.

Your client has the genetic predisposition for inflammation, and according to their inflammation questionnaire result, they may be experiencing symptoms of inflammation. This indicates your client's body is reacting or overreacting, to something.

Lifestyle/nutrition intervention: Try to avoid or limit foods that inflame as much as possible: shop-bought processed products, fried foods, and potential allergies or irritating substances such as alcohol. Replace with anti-inflammatory foods in their diet such as olive oil, green leafy vegetables (spinach, kale, collards etc.), nuts (like almonds and walnuts), fatty fish (like salmon, mackerel, tuna, and sardines) and colourful fruits (blueberries, cherries, oranges etc.). In addition, consider supportive nutrients such as omega-3, vitamin E, polyphenols (flavonoids), ascorbic acid (vitamin C) and curcumin.

Functional test to consider: Organic Acid Testing

Stress

According to the genetic variants your client may be more sensitive to stress and their stress questionnaire results indicate that they are experiencing levels of stress. Life stressors are among the risk factors for depression and increasingly research is evidencing links to upregulation of the key areas of the immune system involved in inflammation.

Nutrition and lifestyle interventions: Ensure that your client is managing stress and sleeping well and that their gut is healthy. For additional support, consider a digestive enzyme, support the methylation systems and ensure adequate intake of tryptophan rich foods for serotonin and melatonin conversion which help with mood and sleep. Good stomach acid is also required to stimulate absorption of B vitamins. Stress switches off stomach acid due to the fight or flight reaction.

Functional test to consider: Adrenal Function

Burnout

According to the genetic variants your client may be more sensitive to stress. Their burnout questionnaire result may indicate if they are experiencing levels of burnout due to prolonged stress, putting you at risk of potential adrenal fatigue.

Functional test to consider: Adrenal function

Propensity to higher BMI

The score indicates that your client may have a propensity to higher BMI. We are increasingly understanding that higher BMI and risk of obesity is a complex interplay between our genetics, lifestyle and environment. Consider focusing on reports rated as elevated risk and moving to any with a rating of a moderate risk.

Functional test to consider: Organic Acid Testing

Methylation Cycle - risk of an imbalance

Your client's result may indicate a susceptibility to an imbalance in the methylation process and potential low folate, low B12 and high homocysteine levels.

Nutritional and lifestyle modification recommendations:

- Sleep well, stress less, meditate, get moderate exercise and eat organic leafy greens and proteins to support the compromised genes well.
- Healthy foods that contain natural folate should be okay, as would be the active form of folate called methylfolate.
- If you need a supplement, look for 5-MTHF (5-methyltetrahydrofolate).
- If your client's serum B12 is also high, avoid the synthetic supplemental version of B12 called cyanocobalamin and instead favour the more useable methylcobalamin (methyl B12) or hydroxycobalamin (hydroxy B12).
- Another good B-vitamin is the methyl version of B6, called P-5-P.

You may need some groundwork before you start adding any methylated supplements.

1. Repairing the digestive system and optimising the flora should be one of the first steps in correcting methylation deficiency.
2. Avoiding exposure to toxins is important! Look at your client's household cleaning supplies and cosmetics, try opt for more natural, preservative free, non toxic products.
3. If you do start supplements, you may need to start low to avoid detox side effects like anxiety, fatigue, achiness and more. If adding methyl B's cause your client to over-methylate, taking Niacin (vitamin B3) 25-50 mg, can slow the cycle down and reduce the symptoms of over-methylation that can include muscle pain or headaches, fatigue, insomnia, irritability or anxiety.

Additional functional tests to consider:

You can investigate whether your client is methylating well by checking their Homocysteine and MCV (mean corpuscular volume of red blood cells) or Methylmalonate and FIGLU in a urinary organic acid test.

Methylation explained

Methylation is the attachment of a one-carbon methyl group (CH₃), onto a compound. This process is critical for proper DNA function, gene regulation, amino acid metabolism, and neurotransmitter (dopamine, serotonin, adrenaline, noradrenaline) synthesis.

Folate is a crucial molecule involved in these reactions. It can be derived from our diet but has to then be converted into a biologically active form of folate, 5-MTHF (5-methyltetrahydrofolate).

Methylenetetrahydrofolate reductase (MTHFR) is the enzyme which catalyses conversion of a folate intermediate (5,10-MTHF) to 5-MTHF, the biologically active form. 5-MTHF is required for converting homocysteine into methionine, a crucial step in the methionine cycle and the production of **S-adenosyl methionine (S-AdoMet)** a key methyl donor. S-AdoMet is able to donate its available methyl group to compounds such as DNA, RNA, proteins or lipids (using methyltransferase enzymes) becoming S-adenosylhomocysteine and then homocysteine.

Homocysteine can go on to become cysteine, taurine, glutathione (vitamin B6-dependent) or it can be converted back to **methionine**

by **methionine synthase (MTR)**, closing up the two metabolic cycles. MTR and its partner enzyme **MTRR (methionine synthase reductase)** work together in the methionine cycle. MTR works in the final step to regenerate homocysteine into methionine using methyl cobalamin (methyl-B12), and MTRR regenerates the methyl cobalamin for MTR to use.

The methylation cycles can be influenced by diet, as folate can be obtained from food. Low folate may translate to low 5-MTHF levels leading to homocysteine accumulation due to impaired ability to convert it back to methionine. High homocysteine is usually found in combination with low folate and B12, also low monoamine neurotransmitters (serotonin, epinephrine, dopamine). Folate and methionine cycle metabolisms are inter-linked, and low folate/high homocysteine levels have been associated with many diseases including various cardiovascular (CVD) complications, renal diseases, and neurodegenerative disorders. In CVD patients, research has established folate supplementation lowered homocysteine levels through improvements in methylation cycle efficiency.

MTHFR, MTR, and MTRR are three key enzymes with vital roles in the folate and methionine cycle metabolisms, which affect neurotransmitter synthesis, methylation capacity and gene expression, and homocysteine metabolism.

Risk for impaired detoxification

Your client may have impaired detoxification pathways and, according to the questionnaire results, they appear to be symptomatic for toxin overload. Make sure your client's lifestyle is supporting these risk variants as the pathway is under strain and contributing to their toxicity.

Lifestyle/nutrition intervention: Support in the form of dietary changes first and supplement only as a back up if necessary.

- [If CYP1A1 AG or GG variant] Reduce exposure to procarcinogens such as cigarette smoke, charred meats (including barbeque), vehicle fumes and wood smoke. In addition paying attention to and optimising Phase 2 detoxification pathways will help to remove reactive intermediates.
- [If CYP1A2 CC variant] CYP1A2 enzyme activity can be enhanced by eating more cruciferous vegetables such as broccoli and Brussel sprouts.
- [If GSTM1 or GSTT1 absent] The GST enzymes are induced in part by phytochemicals such as glucosinolates of cruciferous vegetables, curcumin from turmeric and allylic sulphides from allium vegetables. As part of your detoxification protocol support by adding a variety of these foods to your client's daily diet to increase activity of the other, functioning GST enzymes.
- [If GSTM1 or GSTT1 absent] Research has shown Vitamin C is metabolised by GSTs and those who have reduced activity of these enzymes may have difficulty in utilising this important vitamin. It is important to ensure intake of plenty of vitamin C rich food sources. Implement detoxification protocols such as a diet rich in antioxidants and minimised exposure to toxins.
- [If COMT AG or AA] Support for methylation includes nutrient cofactors and methyl donors such as methionine, Vitamins B12 & B6, betaine, magnesium and folate which can be found in a range of foods.
- [If NQO1 CT or TT] Consider regularly adding curcumin and lycopene rich foods to your diet in order to assist your ability to produce the NQO1 enzyme.

Additional functional tests to consider: Liver blood test such as total bilirubin, Albumin, Alkaline phosphatase (ALP), Aspartate aminotransferase (AST) and Alanine aminophosphatase (ALT) or Urinary Organic acid test

Oestrogen Balance - risk of an imbalance

The overall score indicates your client may be at risk. To determine the risk score, we have assessed their genetic variants including CYP1A1, CYP1B1, COMT, GSTM1 and GSTT1 alongside the toxicity and oestrogen questionnaires to determine if they may be symptomatic.

Nutritional and lifestyle support:

Support in the form of dietary and environmental changes.

- The brassica family contains several powerful nutrients (indole-3 acetate, indole-3 carbonyl, diindolylmethane, sulforaphane and phenyl isothiocyanates) to enhance liver detoxification processes. Broccoli and kale sprouts are especially potent. The alliums, including garlic, onions, scallions, chives and leeks, are rich in sulphur-containing amino acids and the flavone antioxidant quercetin. These compounds help the liver detoxify and reduce the production of oestrogen. Seaweed (a few grams a day) can influence hormonal pathways to help reduce sluggish metabolism and feed the endocrine system. Herbs such as oregano, thyme, rosemary, sage and turmeric also support liver hormone breakdown.
- Aim to support the COMT enzyme with methylation support (see methylation section).
- To reduce exposure of unstable DNA adducts optimise phase 2 detoxification routes via COMT and GSTs.
- The GST enzymes are induced in part by phytochemicals such as glucosinolates of cruciferous vegetables, curcumin from turmeric and allylic sulphides from allium vegetables.

Functional test to consider: Oestrogen profiling

Response to cholesterol lowering foods

GG allele is associated with some improvement in higher blood cholesterol profiles when plant sterol and/or beta-glucan foods are included in the diet. In addition, this genotype is at increased risk of increasing total and LDL-cholesterol blood levels with regular consumption of fat containing dairy products.

Caffeine

Your client is a slow metaboliser of caffeine and might consider reducing consumption or switching to caffeine-free drinks.

Risk for vitamin D deficiency

Your client has genetic variants which may predispose them to a vitamin D deficiency. In addition to bone health, emerging evidence from clinical studies has indicated that vitamin D deficiency is associated with several inflammatory diseases. Your client may therefore benefit from supplementing vitamin D3.

The **VDR gene** encodes the hormone receptor for vitamin D3, the active form of vitamin D in the body. Variants can lead to lower vitamin D levels and your client may have an increased requirement for vitamin D, especially during the winter months. You might want to get their vitamin D levels checked, if you feel that they might be symptomatic of vitamin D deficiency.

Functional test to consider: Vitamin D Serum