Because of the overwhelming volume of emails I have received asking about our research, I have pasted below a prepared message. Perhaps it will have some useful information for you. I am sorry that I can't directly reply to your message.

Disclaimer

Thank you for inquiring about the University of Canterbury research on micronutrient supplementation. The information in this document is not intended to be a substitute for professional medical advice, diagnosis or treatment. All information contained in this document is for general information purposes only. Individuals desiring to use micronutrients to treat mental health conditions should do so only with medical supervision. In addition, it is important that medications being used for a psychiatric condition not be stopped without physician oversight. Physicians should consult with the product manufacturer to determine how best to proceed in terms of dosing and use of micronutrient supplementation.

Conflict of Interest Statement

Research on these products has been funded by unrestricted grants and donations. The companies have provided pills and placebos, free of charge, for prior studies, without restriction on what is published.

Neither I nor my co-investigators are affiliated with any of these companies, nor do I or they receive any compensation, speakers' fees, consulting fees, or any other profit from their sales. I do not have any stock ownership or investment interest in them or any other company like this.

Three educational resources for the public:

- 1. Online course (MOOC) on mental health and nutrition (for the public and professionals alike)— free for audit or pay for a certificate. You can enrol and start anytime: https://www.edx.org/course/mental-health-and-nutrition
- 2. Microcredential certificate through UC Online: Nutrition and Wellbeing (uconline.ac.nz)
- 3. **The Better Brain,** a book that I co-authored for the public and contains much of the background for why we should consume micronutrients: It can be ordered at various locations: www.thebetterbrainbook.com

Current Studies

You can find out more about our studies and the work being conducted by the Mental Health and Nutrition Research Lab by going to Mental Health and Nutrition Research Lab. The best way to stay abreast of our research is to like our Facebook page www.facebook.com/mentalhealthandnutrition. We are currently recruiting for TWO studies in NZ: 1) A study on emotion dysregulation in kids 6-10 years using micronutrients and/or mindfulness, see: The M&M Trial | University of Canterbury, and 2) a study on diet and OCD, see: NUTRI OCD TRIAL | University of Canterbury

The range of the response to micronutrients from our research can vary from a small but noticeable improvement to a substantial and dramatic life changing improvement. Based on short-term controlled trials (8-10 weeks) with *medication-free* children and adults, about 50% show a meaningful and clinically important change across a number of different symptoms, such as anxiety, mood, aggression, and inattention. Others show a more modest improvement. A minority (about 20%) do not seem to respond at all (although this percent includes dropouts who we assume didn't like taking the pills). Our research shows that the number of people responding goes up the longer they stay on the micronutrients. One appealing aspect of the approach is that people report very few side effects and these side effects tend to be mild and transient. Other researchers report up to 80% of patients respond to micronutrients – these trials have not been blinded trials. Blinded trials tend to reduce the overall response rate as they control for the placebo effect and include anyone who expressed an interest in the study, regardless of whether they completed it or consumed the pills.

Many different psychiatric conditions and symptoms have been studied around the globe, ranging from ADHD, mood disorders, insomnia, anxiety and stress. Trials range from the gold standard randomized controlled trial (RCT) to case series, experimental designs, and case reports. Therefore, the information below may or may not

be related to your specific condition/symptoms. Please refer to the list of publications to see whether there is any research on the specific symptoms you are seeking help for. I have organized the list based on symptoms/conditions. Also read about medication-nutrient interactions to determine whether this is a viable approach for you.

I have divided the message into three parts:

- 1. Product information, because so many people want to know what multinutrient products have been researched.
- 2. Contact information for keeping up-to-date on this important topic.
- 3. A list of scientific publications on *all* products studied for the treatment of psychological problems.

PRODUCT INFORMATION

The Mental Health and Nutrition Research Lab, *Te Puna Toirora*, studies a number of different products but most of our earlier work was completed on a product available commercially as *EMPowerplus* (EMP). However, because of updates in the formula as well as a division of the company, most of our current research is on a product called *Daily Essential Nutrients* (DEN).

The various versions of this product are now the most studied formula in the world for reducing and managing symptoms associated with mental illness. The ingredients of these supplements are mostly ordinary minerals and vitamins. They are certainly not unusual or exotic: a normal everyday diet includes most of the nutrients, although not in such high amounts.

The ingredients are not a secret: they are listed on every bottle, on the websites mentioned, and in the published articles.

To find out more about the products, go to www.hardynutritionals.com for Daily Essential Nutrients or www.truehope.com for EMPowerplus Advanced. These websites would be the sources for purchasing if you live in Canada or USA. To purchase in the United Kingdom, there is a distributor there: www.naturalmentalhealth.co.uk – I believe this makes it cheaper as you wouldn't be paying VAT.

To purchase these supplements in **New Zealand or Australia**, the distributor in New Zealand is Straussherbs in Auckland (www.naturezonehealth.com). You can contact Eric Blankenbyl at straussherbs@xtra.co.nz, or 0800 1 24680. Hardy Nutritionals has a Product Specialist for New Zealand, her name is Jerry Oler, 001-403-381-1423, jerry.o@hardynutritionals.com. Truehope has a Product Specialist named Teresa: teresa@mmhforum.org. There are Product Specialists or Scientists available through the websites to assist. The companies have a system in place for talking with you and the relevant physicians about the use of the products. There are now naturopaths, functional doctors, and other health practitioners who sell DEN directly through their practices. You can find one near you: https://www.hardynutritionals.com/health_professional_locator

In NZ, you will need your physician to approve the purchase of the nutrients. This is because of possible interactions with medications you may be prescribed AND because some of the nutrients are above the limits set by the government on nutrient doses that are allowed to be sold over-the-counter. If you are not on medications, an email from the GP practice stating you are not currently taking any psychiatric medications will suffice.

The price of the micronutrients usually includes a support system offered by the company to assist someone (and their prescribing physician) in transitioning from medications to nutrients. This transition does need to be done carefully. You can book this training directly on the Hardy website.

Can I get them paid for?

In NZ, we have managed to get the micronutrients funded in some cases through WINZ or through a disability allowance and we are keen to try to find a way to get it funded more broadly although this will

be challenging. Straussherbs is a supplier for WINZ which makes it easier. You need a letter from your doctor to support your application to WINZ.

Recently, Pharmac has recommended that DEN be used as a treatment for ADHD if first line treatments don't work. However, they have not yet decided on funding. You can see the decision here:

2022-08-combined-PTAC-meeting-record.pdf (pharmac.govt.nz). The process for getting it funded will likely be slow but this decision is a momentous one in that it is the first time that Pharmac has recommended a nutrient treatment for a psychiatric condition outside of lithium. Watch this space!

The cost is lower if the micronutrients are being used for the management of mild symptoms (like stress or general wellbeing) given that a lower dose would likely be sufficient. There are variations of the products available, one version is called **Optimal Balance** (previously called Daily Self Defense) (www.hardynutritionals.com) that we have some data supporting its effectiveness for mild psychological symptoms like insomnia or stress.

What is the best daily dose?

A full daily dose for supporting <u>psychiatric</u> symptoms with DEN is 4 capsules three time a day (=12/day). Our research indicates titrating up to that dose over a week although for some people who tend to be sensitive to medications, this titration may need to be done more slowly. For those taking the *EMPowerplus Advanced* formula, the recommended dose on the bottle is 4 pills/day, although all research was conducted using higher doses than this. For example, in our PMS study, we used 8 pills a day to help alleviate PMS, with two thirds of women going into remission. We nor others have ever compared efficacy of the two products so we cannot recommend one over the other, it is best to look at the research and what product was used to obtain a clinical response.

For those using these products for **general health** and to assist with **managing stress**, as identified by our research after the earthquakes, the optimal dose may be lower, such as 4 a day.

You will notice that *if you buy DEN in NZ*, the recommended dose on the bottle is 4 capsules a day (or as recommended by a health practitioner), and this is because that dose represents what would be necessary for **maintaining good health. It is NOT the dose we have found to be therapeutic through research if using DEN to **treat psychiatric symptoms**. You may need to take *more* to obtain a therapeutic effect.

The dose we used for children with ADHD (7-12 years) ranged from 9 to 12 a day of DEN. Based on our published research with children, we started with equivalent of 9 (three 3X/day) and then increased to 12 if no response within a month. Our research on children with anxiety (8-12 years) showed that 8 a day was therapeutic. Our research experience is that as children enter the teenage years, the dose may need to be increased to maintain symptom control. We think this is because puberty is a metabolically active time and therefore the nutritional demands likely increase. Some women note that PMS symptoms are better managed with an additional dose during that time of the month. Our smoking cessation study found that 8 pills a day (4 twice a day) can help with reduction of cigarettes consumed. Taking antibiotics alongside micronutrients may result in an extra dose needing to be taken temporarily due to the impact the antibiotics have on the gut. These recommended doses are based on our research that has been conducted on people who were NOT taking any psychiatric medications (e.g. antidepressants, anxiolytics, stimulants).

It is recommended that you give this treatment at least 3 months before making a decision on whether it has been helpful for you. If you are transitioning from medications to nutrients, experience based on psychiatrists' reports indicate you should give it at least 6 months to a year as the transition can be challenging (see below). Being consistent and taking all doses is key to optimizing the chances of success.

Both DEN and EMP are available as a powder for those who cannot swallow pills. EMP is also now available as a powder that can be absorbed in the mouth via the oral mucosa which is an easier option for kids who cannot swallow pills and it comes in flavours that kids seem to like (tropical punch, banana, sour berry). We conducted one study using this delivery system with *no additional effect* of the nutrients over placebo in reducing stress in a university population; however, there was a group difference on irritability and anger in that those taking the micronutrients were less irritable and angry than those taking placebo. More trials are underway.

You can find the publication here:

 Katta, N. M., Blampied, N. M., Mulder, R. T., & Rucklidge, J. J. (2023). Micronutrients Absorbed via the Oral Mucosa Reduce Irritability and Anger but not Stress in University Students during COVID-19: A Randomized Placebo-Controlled Trial. *International Journal of Stress Management*. https://psycnet.apa.org/record/2023-65540-001

To buy the lightning sticks: can be purchased via this website: https://renovaworldwide.com . Please note that they come from the USA, so there might be a significant waiting period and shipping cost.

Are there any side effects?

The products, as studied to date, have not produced any serious adverse effects based on trials conducted with people <u>not concurrently taking medications</u>. The most common 'side effects' are relief from previously-experienced constipation and sleep improvement. Other side effects that may be reported are headaches and stomach aches, although they are typically mild and transitory. These difficulties can be avoided by taking capsules on a full stomach and with plenty of water. The nutrients have been evaluated for research which involves going through a very scrutinizing process with government agencies (e.g. FDA (USA), Health Canada, Medsafe (NZ)). No concerns have been raised.

Sometimes it is necessary to heal the gut to aid with absorption of nutrients. It may be advisable to take additional probiotics to assist with absorption. If the smell of the pills is a problem, try keeping them in the fridge or freezing them. This can also help if they make you feel too nauseous.

Are there nutrient-drug interactions?

Combining medication (especially psychiatric medications) with these micronutrients is probably one of the most challenging aspects of this work. This is because anecdotally, physicians report an increase in side effects when adding nutrients to a patient on psychiatric medications, a phenomenon which has sometimes been interpreted as the micronutrients amplifying the effect of the medications (Popper, 2014). This observation can be viewed as puzzling for some physicians given that their expectation is that nutrients should not interfere with the efficacy of a drug. This video explains one way in which micronutrients might exert an effect on the brain which may impact on the effect of medications.

Another way to understand this observed interaction is to be reminded of the problems of eating grapefruit with certain medications. Medications are processed in your liver and small intestine by a specialized group of proteins called cytochrome P450 (CYPs). CYPs break down medications, reducing the blood levels of many of them. Grapefruit interferes with this breakdown of medications. In fact, studies show that grapefruit and some other citrus fruits increase the blood levels of over <u>85 medications</u>. By slowing down the way in which CYPs normally break down medications in your gut and liver, grapefruit can increase the side effects of these drugs. With some drugs, even small amounts of grapefruit can cause severe side effects.

We have wondered whether a similar process might be occurring with this combination of nutrients in that the nutrients can change the metabolism of drugs, just like grapefruit. Two studies (<u>Gately and Kaplan</u>, <u>2009</u>; <u>Rucklidge et al.</u>, <u>2010</u>) have reported that patients tend to respond better to micronutrients if they also lower their dose of medications. However, more research is needed to best guide physicians on the drugnutrient interactions and the best way to cross taper. In the meantime, we advise extreme caution with combining nutrients with medications and warn that the recovery may be much slower and more difficult compared to our observations of recovery in people who are unmedicated.

It is important that you do not stop medications you are using for your psychiatric condition. Please first discuss options with your prescribing physician to see whether trying the micronutrients alongside medications is a viable option for you. You might find it helpful to bring along the list of scientific publications below as not all physicians are familiar with micronutrient treatment in people taking psychiatric medications. Your physician should consider discussing your case with the staff at Hardy Nutritionals/Truehope to determine how best to proceed in terms of dosing and use of medication. The companies are very familiar with how to cross taper so please use their expertise. *Please don't just stop your medications without adequate support and*

consultation. Likewise, please do not take the nutrients alongside medications without first discussing with your prescriber.

If you are a physician considering using these supplements for patients who are currently taking psychiatric medications, I urge you to read <u>Dr. Popper's commentary</u> and <u>review</u> carefully. The titration needs to be done carefully to minimize withdrawal and interaction effects – and the companies can assist you with this process. The companies may suggest amino acids to assist with reducing withdrawal symptoms. I have heard *anecdotally* that amino acids can be very helpful. Please note that regardless of nutrient supplementation, coming off of medications has been identified by research to cause withdrawal symptoms in some patients.

The more medications someone is on, the more challenging the transition can be. At this stage in the research, we are unable to satisfactorily assist with the best method for transition nor provide any locally trained physicians who can assist with the transition. The companies may be able to refer you to physicians who are familiar with this approach. Anecdotally, some patients have found the transition very difficult, while others have been able to switch to micronutrients without much difficulty and experience symptom relief, often for the first time. We cannot predict at this stage who will have problems and who won't as well as who will benefit from the micronutrients and who won't.

Why might this approach work?

At this stage in the research, we can only speculate about why this approach might work and we need much more research. It is possible that decreased nutrient density of food is a contributing factor in some cases as food has become less nourishing and nutrient-dense over time, for many reasons, including how we select crops, use of herbicides, and even increased carbon dioxide in the atmosphere. A diet high in ultra-processed food is typically calorie rich but nutrient poor. There are also individual factors like our genetics and the health of our microbiome (the bacteria that live inside of us). We wonder whether micronutrients at the doses we have researched can influence gene expression, aid with the manufacture of important neurotransmitters like serotonin and dopamine as well as influence the diversity of our bacteria. It is also possible that the micronutrients replete our bodies of chronic nutrient deficiencies. Many of the review articles listed below discuss the evidence behind these speculations and we will be publishing studies investigating some of these mechanisms of action over the next few years.

Can I get the nutrients from a one-a-day supermarket pill?

Some people ask if they can get these same nutrients from an over-the-counter supermarket pill or put various different formulas together to achieve the same dose and breadth of nutrients as those we have studied. This has been tried and as far as I know, generally unsuccessfully. In the early days of this work, Dr. Charles Popper, a psychiatrist at Harvard, showed that using EMP produced markedly better benefits than OTC pills purchased at a local health food store.

It is not just about dose and specific nutrients, but also the overall balance of nutrients, how well they are absorbed (which is influenced by how it is manufactured) and where the nutrients are sourced. DEN and EMP are the products that have been studied and so if you want to try to replicate our results, I suggest you use one of them at the dose used in the studies. <u>Do not buy a supermarket brand and then just double or triple etc the dose to attempt to achieve the same doses as DEN/EMP</u>. This could lead to consumption of nutrients in toxic levels. A publication that explains the challenges of dose and breadth is discussed here:

Rucklidge, J. J., Harris, A. L., & Shaw, I. C. (2014). Are the amounts of vitamins in commercially available dietary supplement formulations relevant for the management of psychiatric disorders in children? New Zealand Medical Journal, 127(1392), 73-85. Microsoft Word - content.doc (website-files.com)

Why are there so many pills?

The large number of pills does not imply that the micronutrient dosing is high. Many commercial products contain a broad spectrum of micronutrients in one or two capsules daily, but the nutrients are present in chemical forms that are poorly absorbed, even at higher doses. One way to enhance bioavailability of the minerals is to deliver them in chelated forms (chelation promotes passage from the gut into the blood stream, where the minerals dissociate from the chelates), but the chelated minerals are bulky and cannot be condensed into one or two capsules. Furthermore, some broad-spectrum formulations also provide macro-minerals, such

as calcium, magnesium, and phosphorus, which are often under-represented in diets and are required in much larger bulk quantities than micronutrients. Products containing chelated microminerals and bulky macrominerals require more pills each day, are more expensive, but will likely be more effective than regular formulations.

Should I get my nutrient levels checked?

Some people also ask about nutrient levels and whether they need to get theirs evaluated before trying micronutrients. We published a study that showed that nutrient levels were not very good at predicting who would respond and who wouldn't respond to the treatment. Also, many people can have "normal" nutrient levels and still benefit from this approach. We wonder if nutrient levels are only good to identify the nutritional needs of someone who is generally healthy. Perhaps those who are unwell physically or mentally have *higher nutritional needs* than the average person. If this is so, then nutritional levels will be of limited value to determine who might need more than what they can get out of their diet. Have a look at:

- Rucklidge, J. J., Johnstone, J., Gorman, B., & Boggis, A., & Frampton, C. (2014). Moderators of treatment response in adults with ADHD to micronutrients: demographics and biomarkers. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 50, 163–171. DOI: 10.1016/j.pnpbp.2013.12.014
- Rucklidge, J. J., Eggleston, M., Johnstone, J. M., Darling, K., Stevens, A. J., Kennedy, M. A., & Frampton, C. M. (2019). Can we predict treatment response in children with ADHD to a vitamin-mineral supplement? An investigation into pre-treatment nutrient serum levels, MTHFR status, clinical correlates and demographic variables. Progress in Neuropsychopharmacology & Biological Psychiatry, 89, 181-192. DOI: 10.1016/j.pnpbp.2018.09.007
- Rucklidge JJ, Eggleston MJF, Boggis A, Darling K, et al. (2019). Do Changes in Blood Nutrient Levels Mediate Treatment Response in Children and Adults With ADHD Consuming a Vitamin–Mineral Supplement? *Journal of Attention Disorders*. https://doi.org/10.1177/1087054719886363

I wrote a blog on this topic: https://blogs.canterbury.ac.nz/science/2018/11/30/should-i-get-my-nutrient-levels-checked-to-determine-if-i-need-to-take-a-supplement/

However, there are practitioners who do use specific single nutrients based on biochemistry results. This may be helpful if the broad-spectrum approach does not work for you. If you want to find such a practitioner, check out bio-balance http://www.biobalance.org.au/ as they list integrative medical doctors who follow Bill Walsh's individualized nutrient approach.

The main strict contraindications are uncommon metabolic conditions, such as Wilson's disease (copper), hemochromatosis (iron), phenylketonuria (phenylalanine), and trimethylaminuria (choline).

What about hair analysis?

Exploring mineral status via hair is generally seen as quite controversial but we did delve a little bit into it with the child ADHD study. Sadly, we didn't replicate any previous findings on identified deficiencies in children with ADHD. We only found 3 differences between kids with and without ADHD – germanium (Ge), chromium (Cr), and bismuth (Bi). Lower Ge and Cr and higher Bi in kids with ADHD. We explored whether mineral ratios might be more relevant and they appear to be more useful. However, given we were the first lab to extensively explore ratios, we have to be cautious in not over interpreting the findings too much. But our data support a broader spectrum nutrient approach to the treatment of ADHD, which at least aligns with our research!

Perham, J. C., Shaikh, N. I., Lee, A., Darling, K. A., & Rucklidge, J. J. (2020). Toward 'element balance' in ADHD: an exploratory case control study employing hair analysis. *Nutritional Neuroscience*, 1-11. doi:10.1080/1028415X.2019.1707395 https://doi.org/10.1080/1028415X.2019.1707395.

Are the nutrients synthetic?

If you want to read more about our hair analysis, you can find it here:

There seems to be an increasing trend to describe vitamins as either natural or synthetic, which seems to be accompanied by a lot of product promotion. When a vitamin is called synthetic, it is done to imply that it is artificial - that the ingredient is somehow simulated or manufactured in a test tube from unrelated chemicals (this certainly describes pharmaceutical drugs).

This description is not accurate, especially when synthetic and artificial are used interchangeably in the process. When it comes to vitamins there is only one meaning for the word synthetic and it does not mean artificial.

Manufacturers, scientists, and regulators (FDA and Health Canada) use the term synthetic with a very different meaning and purpose. In nature, vitamins exist in a cellular environment. They are inside plant cells performing the functions that make them essential. This means that there are proteins, carbohydrates, lipids, other vitamins, minerals, enzymes, and phytochemicals, etc. all mixed together (i.e. the whole food chemical environment).

Of course, it is best to get your essential nutrients from whole foods. However, there is research to suggest that even whole foods don't always have optimum levels of essential nutrients, which means that we are left short in our diets. That means we need to add a supplement, not a replacement.

When a vitamin is extracted from its whole food environment it is considered synthetic for the purpose of manufacturing, regulation (identification) and research, not because it has become artificial. It is still plant based. Even though some minor aspects of the physical environment change, they do not become artificial. All the health benefits that we have researched for more than a decade have been imparted by these 'kinds' of supplemental vitamins.

The vitamin mineral formulations we have studied are not a whole food product. They are designed to be added to a balanced diet, taken with meals, to increase nutrient density.

Can I achieve these changes with diet manipulation alone?

The nutrients should be consumed with a healthy diet and the less processed food in the diet the better. We don't yet know whether someone can achieve the results we have documented though dietary manipulation alone or whether they need the additional nutrients from supplementation to achieve the benefits. The diet that has been studied the most for showing beneficial effects for mental health is the Mediterranean diet. A healthy diet pattern includes fresh foods, high in vegetables and fruits, nuts, healthy fats, fish, whole grains and low in processed foods.

CONTACT INFORMATION, BOOKS, RESOURCES, VIDEOS AND BLOGS

We have a Facebook page where we post information about new studies. Please like our page and you will receive updates on our research: www.facebook.com/mentalhealthandnutrition

This video tells you a bit about my research journey: https://www.youtube.com/watch?v=5YXEQ-m- dc

Many of the research studies mentioned below can be found on Research Gate: https://www.researchgate.net/profile/Julia Rucklidge/publications

Please follow me on twitter and you can find out more about upcoming research: @JuliaRucklidge

Instagram: www.instagram.com/ucmentalhealthandnutrition

If you are interested in learning more about the research on micronutrients, please watch a TEDx talk I delivered on November 1st 2014 in Christchurch (only 18 minutes): https://www.youtube.com/watch?v=3dqXHHCc5IA

Bonnie and I wrote this piece for *The Conversation*: Junk food and the brain: how modern diets lacking in micronutrients may contribute to angry rhetoric. Read the full article here.

Jehan Casinader wrote this excellent piece on the Drained Brain: https://www.stuff.co.nz/life-style/food-wine/124427998/drained-brains-why-nutrition-could-help-to-solve-our-mental-health-crisis

This article published in the Press outlines the benefit achieved for one family. https://www.stuff.co.nz/national/health/97446699/micronutrients-help-children-with-adhd-new-research-shows

Or, one of these hour long talks I have delivered at the University of Canterbury on the field and the rationale behind using nutrients to treat mental illness:

What if Nutrition could treat mental illness 2014: http://www.youtube.com/watch?v=FrxdoIn6DQQ What if Nutrition could treat mental illness 2015: https://www.youtube.com/watch?v=Ji7ExrqV1x8 Feeding the brain: exploring nutrition's role in mental health. 2019.

https://www.youtube.com/watch?v=WNLbFztA9Us&list=PL1D0DE06F56864BA4&index=4&t=2057s Building a better brain with Nutrition 2021: https://www.youtube.com/watch?v=kucDDgyqSxl

An excellent opinion piece by Bonnie Kaplan in the Calgary Herald on December 31, 2018: https://tinyurl.com/y4gg5r4p

Alternatively, follow a blog that Prof Bonnie Kaplan and I wrote together: https://www.madinamerica.com/author/jrucklidge/

Naomi Arnold wrote an excellent piece highlighting the challenges of getting nutrients funded: https://www.stuff.co.nz/life-style/well-good/teach-me/94727527/are-micronutrients-the-answer-to-nzs-mental-health-crisis

Our work was also featured on our Changing World, NZ National Radio. http://www.radionz.co.nz/national/programmes/ourchangingworld/audio/201853940/optimal-nutrition-the-answer-to-treating-adhd

An article outlining some of the challenges we have faced related to this work: www.magazinestoday.co.nz/mental-health-crusader/

And for those professionals out there wanting to stay abreast of this field of research, consider joining ISNPR (international Society for Nutritional Psychiatry Research): http://www.isnpr.org/

Those wanting to learn a new, very effective method for swallowing pills should take a look at a training video that Prof Kaplan produced following four studies to develop this new method: https://www.youtube.com/watch?v=Zxqs7flHJQc

PUBLICATIONS ON EMP/DEN

I have divided the research into categories and listed them chronologically; however, there will be some overlap as some of the studies have broader implications than just for that one disorder.

Mood disorders/emotional dysregulation:

- Kaplan, B. J., Simpson, J. S. A., Ferre, R. C., Gorman, C. P., McMullen, D. M., & Crawford, S. G. (2001). Effective mood stabilization with a chelated mineral supplement: An open-label trial in bipolar disorder. *Journal of Clinical Psychiatry*, 62(12), 936-944.
- Popper, C. W. (2001). Do vitamins or minerals (apart from lithium) have mood-stabilising effects?
 Journal of Clinical Psychiatry, 62(12), 933-935.
 https://www.psychiatrist.com/jcp/article/pages/2001/v62n12/v62n1203.aspx
- Kaplan, B. J., Crawford, S. G., Gardner, B., & Farrelly, G. (2002). Treatment of mood lability and explosive rage with minerals and vitamins: two case studies in children. *Journal of Child and Adolescent Psychopharmacology*, 12(3), 205-219. https://doi.org/10.1089/104454602760386897
- Kaplan, B. J., Fisher, J. E., Crawford, S. G., Field, C. J., & Kolb, B. (2004). Improved mood and behavior during treatment with a mineral-vitamin supplement: an open-label case series of children. *Journal of Child and Adolescent Psychopharmacology*, 14(1), 115-122. https://doi.org/10.1089/104454604773840553

- Simmons, M. (2003). Nutritional approach to bipolar disorder. *Journal of Clinical Psychiatry*, 64(3), 338.
- Gately, D., Kaplan, B.J. (2009). Database analysis of adults with bipolar disorder consuming a micronutrient formula. *Clinical Medicine: Psychiatry*. https://doi.org/10.4137/CMPsy.S2278
- Frazier, E.A., Fristad, M., Arnold, L.E. (2009). Multinutrient Supplement as Treatment: Literature Review and Case Report of a 12-year-old Boy with Bipolar Disorder. *Journal of Child and Adolescent Psychopharmacology*. 19:453-460. https://doi.org/10.1089/cap.2008.0157
- Rucklidge, J. J., & Harrison, R. (2010). Successful treatment of Bipolar Disorder II and ADHD with a micronutrient formula: A case study. CNS Spectrums, 15(5):289-295. https://doi.org/10.1017/S1092852900027516
- Rucklidge, J. J., Gately, D., & Kaplan, B. J. (2010). Database Analysis of Children and Adolescents with Bipolar Disorder Consuming a Micronutrient Formula. *BMC Psychiatry*, 10, 17. http://www.biomedcentral.com/1471-244X/10/74
- Frazier, E.A., Fristad, M.A. & Arnold, L.E. (2012). Feasibility of a nutritional supplement as treatment for pediatric bipolar spectrum disorders. *Journal of Complementary and Alternative Medicine*, 18:678-85. https://doi.org/10.1089/acm.2011.0270
- Frazier, E. A., Gracious, B., Arnold, L. E., Failla, M., Chitchumroonchokchai, C., Habash, D., & Fristad, M. A. (2013). Nutritional and safety outcomes from an open-label micronutrient intervention for pediatric bipolar spectrum disorders. Journal of Child and Adolescent Psychopharmacology, 23(8), 558-567. doi:10.1089/cap.2012.0098. https://doi.org/10.1089/cap.2012.0098
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- Retallick-Brown, H., Rucklidge, J. J., & Blampied, N. (2016). Study protocol for a randomised double blind, treatment control trial comparing the efficacy of a micronutrient formula to a single vitamin supplement in the treatment of premenstrual syndrome. *Medicines*, 3, 32. http://www.mdpi.com/2305-6320/3/4/32
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 Medicine, 27(3), 14-18. https://www.ncbi.nlm.nih.gov/pubmed/23784606
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Addictions:

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Insomnia:

Lothian, J. A, Blampied, N., & Rucklidge, J. J. (2016). Effect of Micronutrients on Insomnia in Adults: A
Multiple-Baseline Design. Clinical Psychological Science. https://doi.org/10.1177/2167702616631740

Brain injury:

 Kaplan BJ, Leaney C, Tsatsko E (2016). Micronutrient treatment of emotional dyscontrol following traumatic brain injury: A case study. *Annals of Psychiatry and Mental Health*, 4(5): 1078. https://www.jscimedcentral.com/Psychiatry/psychiatry-4-1078.pdf

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- Bradley, H. A., Campbell, S. A., Mulder, R. T., Henderson, J. M. T., Dixon, L., Boden, J. M., & Rucklidge, J. J. (2020). Can broad-spectrum multinutrients treat symptoms of antenatal depression and anxiety and improve infant development? Study protocol of a double blind, randomized, controlled trial (the 'NUTRIMUM' trial). BMC Pregnancy and Childbirth, 20(1), 488. https://doi.org/10.1186/s12884-020-03143-z
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- Carr AC, Bradley HA, Vlasiuk E, Pierard H, Beddow J, Rucklidge JJ. Inflammation and Vitamin C in Women with Prenatal Depression and Anxiety: Effect of Multinutrient Supplementation. *Antioxidants* (Basel). 2023 Apr 17;12(4):941. https://doi.org/10.3390/antiox12040941

Three studies investigating the **safety and toxicity** of these two products show that, as studied to date, they have not produced any serious adverse effects:

- Simpson, J. S. A., Crawford, S. G., Goldstein, E. T., Field, C., Burgess, E., & Kaplan, B. J. (2011).
 Systematic review of safety and tolerability of a complex micronutrient formula used in mental health.
 BMC Psychiatry, 11(62). http://www.biomedcentral.com/1471-244X/11/62
- Rucklidge, J. J., Eggleston, M. J. F., Ealam, B., Beaglehole, B., & Mulder, R. T. (2019). An
 Observational Preliminary Study on the Safety of Long-Term Consumption of Micronutrients for the
 Treatment of Psychiatric Symptoms. *Journal of Alternative and Complementary Medicine*.
 doi:10.1089/acm.2018.0352 https://www.liebertpub.com/doi/10.1089/acm.2018.0352
- Leung, B. M. Y., Srikanth, P., Gracious, B., Hatsu, I. E., Tost, G., Conrad, V., Johnstone, J. M., & Arnold, L. E. (2022). Paediatric adverse event rating scale: a measure of safety or efficacy? Novel analysis from the MADDY study. *Current Medical Research and Opinion*, 38(9), 1595-1602. https://doi.org/10.1080/03007995.2022.2096333

HAVE ANY OTHER NUTRIENT FORMULAS BEEN STUDIED?

Other micronutrient products have been studied by other scientists from around the world, and some of these have been shown to be beneficial in some situations <u>at the recommended dose on the label</u> (stress, aggression in prisoners, anxiety, autism, low mood). Other nutrients, like omega 3s, have also been studied but as that literature is huge, I recommend you contact an omega 3 specialist for details on the use of these nutrients on brain health. The micronutrient formulas that have been shown to be efficacious (based on at least ONE randomized controlled trial) include:

 Brain Child Spectrum Support/ANRC Essentials (autism): http://www.brainchildnutritionals.com/spectrum-support-vitamins.html/ or http://www.autismnrc.org/anrc-essentials

Professor Jim Adams at Arizona State University has conducted a number of studies using nutrients for the treatment of autism, using three products: Spectrum Support II/IIITM, SyndionTM, and ANRC Essentials PlusTM (a revised version of SyndionTM). Spectrum Support comes as a capsule or colloidal suspension--the standard dose is two capsules (or two teaspoons) twice a day. For ANRC Essentials PlusTM, the company provides information on how to gradually increase to the optimal dose based on body weight. The formula comes either as capsules or a powder to mix with your favorite juice (they suggest orange, mango, or cranberry).

- Adams, J. B., & Holloway, C. (2004). Pilot study of a moderate dose multivitamin/mineral supplement for children with autism spectrum disorder. *Journal of Alternative and Complementary Medicine*, 10(6), 1033-1039. http://online.liebertpub.com/doi/abs/10.1089/acm.2004.10.1033
- Adams, J. B., Audhya, T., McDonough-Means, S., Rubin, R. A., Quig, D., Geis, E., Gehn, E., Loresto, M., Mitchell, J., Atwood, S., Barnhouse, S., & Lee, W. (2011). Effect of a vitamin/mineral supplement on children and adults with autism. *BMC Pediatrics*, 11, 111. https://doi.org/10.1186/1471-2431-11-111
- Adams, J. B., Audhya, T., Geis, E., Gehn, E., Fimbres, V., Pollard, E., Mitchell, J., Ingram, J., Hellmers, R., Laake, D., Matthews, J., Li, K., Naviaux, J., Naviaux, R., Adams, R., Coleman, D., & Quig, D. (2018). Comprehensive Nutritional and Dietary Intervention for Autism Spectrum Disorder—A Randomized, Controlled 12-Month Trial. *Nutrients*, 10(3), 369. http://www.mdpi.com/2072-6643/10/3/369
- 2. Forceval (aggression in prisoners): http://www.forceval.co.uk

Forceval is available in a capsule or in effervescent tablets and is a licensed medicine in the UK. The recommended dose is one capsule daily. The main target for the formula is to combat malnutrition. However, Forceval has been used along with fish oil for omega 3s to successfully reduce aggression in people incarcerated in prisons. There were no adverse reactions.

- Gesch CB, Hammond SM, Hampson SE, et al. (2002). Influence of supplementary vitamins, minerals
 and essential fatty acids on the antisocial behaviour of young adult prisoners. The British Journal of
 Psychiatry, 181(1) 22-28; https://doi.org/10.1192/bjp.181.1.22
- 3. Bayer's Berocca (stress/anxiety): http://www.berocca.com

Berocca is the most studied B-complex formula for reduction of stress. It can be taken as a capsule or an effervescent tablet that you add to water. It has been studied primarily in people drawn from the general population. No concerning side effects have been reported.

Carroll, D., Ring, C., Suter, M., & Willemsen, G. (2000). The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: a double-blind placebo-controlled trial. *Psychopharmacology*, 150(2), 220-225. https://doi.org/doi:10.1007/s002130000406

- Schlebusch, L., Bosch, B. A., Polglase, G., Kleinschmidt, I., Pillay, B. J., & Cassimjee, M. H. (2000). A double-blind, placebo-controlled, double-centre study of the effects of an oral multivitamin-mineral combination on stress. South African Medical Journal, 90(12), 1216-1223. https://www.ncbi.nlm.nih.gov/pubmed/11234653
- Kennedy, D. O., Haskell, C. F., Robertson, B., Reay, J., Brewster-Maund, C., Luedemann, J., Maggini, S., Ruf, M., Zangara, A., & Scholey, A. B. (2008). Improved cognitive performance and mental fatigue following a multi-vitamin and mineral supplement with added guarana (Paullinia cupana). *Appetite*, 50(2-3), 506-513. https://doi.org/10.1016/j.appet.2007.10.007
- Kennedy, D., Veasey, R., Watson, A., Dodd, F., Jones, E., Maggini, S., & Haskell, C. (2010). Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. *Psychopharmacology*, 211(1), 55-68. https://doi.org/doi:10.1007/s00213-010-1870-3
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- Scholey, A., Bauer, I., Neale, C., Savage, K., Camfield, D., White, D., Maggini, S., Pipingas, A., Stough, C., & Hughes, M. (2013). Acute effects of different multivitamin mineral preparations with and without Guarana on mood, cognitive performance and functional brain activation. *Nutrients*, 5(9), 3589-3604. https://doi.org/10.3390/nu5093589
- White, D., Cox, K., Peters, R., Pipingas, A., & Scholey, A. (2015). Effects of Four-Week Supplementation with a Multi-Vitamin/Mineral Preparation on Mood and Blood Biomarkers in Young Adults: A Randomised, Double-Blind, Placebo-Controlled Trial. *Nutrients*, 7(11), 5451. http://www.mdpi.com/2072-6643/7/11/5451
- 4. Swisse Ultivite (stress): Search results for: 'ultivite' | Swisse Wellness

Swisse UltiviteTM is available in both a women and men's version and is taken as one capsule daily with a meal. Several studies support its use for reduction of stress in otherwise healthy people. No side effects were reported.

- Harris, E., Kirk, J., Rowsell, R., Vitetta, L., Sali, A., Scholey, A., & Pipingas, A. (2011). The effect of multivitamin supplementation on mood and stress in healthy older men. *Human Psychopharmacology*, 26(8), 560-567. https://doi.org/10.1002/hup.1245
- Harris, E., Macpherson, H., Vitetta, L., Kirk, J., Sali, A., & Pipingas, A. (2012). Effects of a multivitamin, mineral and herbal supplement on cognition and blood biomarkers in older men: A randomised, placebo-controlled trial. *Human Psychopharmacology: Clinical and Experimental*, 27(4), 370-377. https://doi.org/10.1002/hup.2236
- Sarris J, Cox, KH M, Camfield DA, et al. (2012). Participant experiences from chronic administration of a multivitamin versus placebo on subjective health and wellbeing: A double-blind qualitative analysis of a randomized controlled trial. *Nutrition Journal*, 11, 110. http://doi.org/10.1186/1475-2891-11-110
- Pipingas, A., Camfield, D. A., Stough, C., Cox, K. H., Fogg, E., Tiplady, B., Sarris, J., White, D. J., Sali, A., Wetherell, M. A., & Scholey, A. B. (2013). The effects of multivitamin supplementation on mood and general well-being in healthy young adults. A laboratory and at-home mobile phone assessment.
 Appetite, 69, 123-136. https://doi.org/10.1016/j.appet.2013.05.016
- Camfield, D. A., Wetherell, M. A., Scholey, A. B., Cox, K. H., Fogg, E., White, D. J., Sarris, J., Kras, M., Stough, C., Sali, A., & Pipingas, A. (2013). The effects of multivitamin supplementation on diurnal cortisol secretion and perceived stress. *Nutrients*, 5(11), 4429-4450. https://doi.org/10.3390/nu5114429
- Macpherson, H., Rowsell, R., Cox, K. H., Scholey, A., & Pipingas, A. (2015). Acute mood but not cognitive improvements following administration of a single multivitamin and mineral supplement in healthy women aged 50 and above: a randomised controlled trial. *Age (Dordr)*, 37(3), 9782. https://doi.org/10.1007/s11357-015-9782-0
- 5. Blackmores Executive B (stress): http://www.blackmores.com.au/products/executive-b-stress-formula

Blackmores is taken as one capsule twice a day with meals. One study showed improved work-related stress. It is also available as an immediate-release and sustained-release capsule. No side effects have been reported.

- Stough, C., Scholey, A., Lloyd, J., Spong, J., Myers, S., & Downey, L. A. (2011). The effect of 90 day administration of a high dose vitamin B-complex on work stress. *Human Psychopharmacology: Clinical and Experimental*, 26(7), 470-476. https://doi.org/10.1002/hup.1229
- 6. **Enlyte** (depression): https://www.enlyterx.com/

There has been one study using Enlyte to treat people with a variant of the *MTHFR* gene who also had major depression. The treatment consists of one capsule taken on an empty stomach. It is available by prescription and may be covered by insurance in the US. No reported side effects.

- Mech A, Farah A. Correlation of clinical response with homocysteine reduction during therapy with reduced B vitamins in patients with MDD who are positive for MTHFR C677T or A1298C polymorphism: a randomized, double-blind, placebo-controlled study. *Journal of Clinical Psychiatry*. 2016 May;77(5):668-71. https://doi.org/10.4088/JCP.15m10166
- 7. **Optivite** (premenstrual symptoms): www.optimox.com

Optivite was first studied in the 1980s and as far as I am aware, there have been no new studies for the last two decades. The product is still available for purchase. The studies suggested between six and twelve capsules a day. The bottle recommends two-to-six tablets daily with meals. The main concern raised about taking a dose above ten capsules is that it delivers vitamin B6 in a range that can produce some neurological side effects, including tingling of limbs. Fortunately, the side effect is reversible once you stop taking the pills.

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Internationally, there are over 50 randomized placebo-controlled trials (RCTs; including some of the ones listed above and below) conducted on various micronutrient formulas. RCTs are the gold standard design used to make clinical decisions. These trials have shown the benefits of micronutrients for reducing aggression in prisoners; slowing cognitive decline in the elderly; helping people overcome addictions; treating symptoms of depression, stress, anxiety, autism and ADHD. The only trials that found no benefits studied people who did not have any psychiatric symptoms to begin with or that used a select few nutrients, not the full array of nutrients in combination. Taken together, over 80% of these trials have shown benefit of active over placebo. Please email me if you want a list of these studies.

8. **Centrum Silver** (cognition): https://www.centrum.com/products/multivitamins/centrum-silver-adults-50-plus/

This product was used in one study looking at improving cognition in older people, finding that Centrum Silver led to improved cognition, memory, executive function.

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How can I support this work?

If this method has been of benefit to you or your family, please tell people! Tell your GP, psychiatrist, psychologist, local MP, etc. The only way we can try to gain some financial support for the cost of nutrients is to bring the benefits to the attention of those who can influence the public funding system in NZ and other places.

If you are interested in donating to our research programme, please donate through the University of Canterbury Foundation: https://www.canterbury.ac.nz/uc-foundation/ and in the designation, choose other and in the comment box write: For Julia Rucklidge's Mental Health and Nutrition Research.

Thank you for your interest in our work. Please let me know how it goes if you do choose to go down this route.

Prof Julia Rucklidge