The Role of Kiwifruit in Supporting Psychological Health and Wellbeing

Michael Billows

Faculty of Health and Medical Sciences

School of Psychology

The University of Adelaide

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List of Abbreviations

ACST	Australian central standard time
ANZCTR	Australian and New Zealand Clinical Trial Registry
AUD	Australian dollars
BP	Blood pressure
BDNF	Brain-derived neurotrophic factor
CBT	Cognitive behaviour therapy
CHMHREC	CSIRO Health and Medical Research Ethics Committee
CNS	Central nervous system
CSBM	Complete spontaneous bowel movement
CSIRO	Commonwealth Scientific and Industrial Research Organisation
CVD	Cardiovascular disease
DALY	Disability adjusted life years
DASH	Dietary approaches to stop hypertension
DASS	Depression Anxiety Stress Scale
DASS-21	Depression Anxiety Stress Scale – 21 item version
ECT	Electro-convulsive therapy
EMA	Ecological momentary assessment
EU	European Union
FC	Functional constipation
GSRS	Gastrointestinal Symptom Rating Scale
GoKiPH	Gold Kiwifruit and Psychological Health
GP	General Practitioner
HDIvC	Habitual dietary intake of vitamin C questionnaire
IBS	Irritable bowel syndrome

iPhD	Industry-sponsored Doctor of Philosophy
JBI	Joanna Briggs Institute
JD	Japanese diet
KD	Ketogenic diet
MDD	Major depressive disorder
MDP	Mediterranean dietary pattern
MFSI	Multi-dimensional Fatigue Symptom Inventory
ND	Nordic diet
NRT	Nicotine replacement therapy
PICO	Population intervention comparisons and outcome
POMS	Profile of Mood States
POMS-B	Profile of Mood States - Brief
POMS-SF	Profile of Mood States - Short Form
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PUFAs	Polyunsaturated fatty acids
RCT	Randomised controlled trial
RDI	Recommended dietary intake
SVS	Subjective Vitality Scale
TMD	Total mood disturbance
WEMWBS	Warwick-Edinburgh Mental Well-being Scale
WHO	World Health Organisation
YLD	Years of healthy life lost to disability

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Fly, be free.

"Come to the edge," he said.

"We can't, we're afraid!" they responded.

"Come to the edge," he said.

"We can't, We will fall!" they responded.

"Come to the edge," he said.

And so they came.

And he pushed them.

And they flew."

Guillaume Apollinaire

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree. The author acknowledges that copyright of published works contained within this thesis resides with the copyright holder(s) of those works. I give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time. I acknowledge the support I have received for my research through the provision of an Australian Government Research Training Program Scholarship.

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Abstract

Mental health disorders, including depression, contribute significantly to the individual, societal and global burden of disease. Increasingly, diet quality is seen as a modifiable risk factor for mental health. There is preliminary support for healthy dietary intake to confer benefits to mental health in clinical populations through the delivery of vitamins and nutrients associated with mood. This thesis presents the results of a rapid review of the literature and two intervention trials that examined the potential for gold kiwifruit, a nutrient-dense fruit rich in vitamin C, to support psychological health and wellbeing in adults with mild to moderate mood disturbance through increased vitamin C intake.

In Study 1, a rapid review of the literature was undertaken to identify intervention trials that used a green or gold kiwifruit intervention and assessed mood outcomes. The rapid review sought to identify any supporting evidence within sub-clinical mental health populations, and to explore the potential clinical implications of kiwifruit as a dietary intervention in mood-disturbed populations. The review identified nascent research that reported gold kiwifruit was associated with improved mood and wellbeing in otherwise healthy adults with sub-optimal vitamin C status.

Study 2 was a multiple N-of-1 feasibility trial that assessed the practicality of recruiting adults aged 18 to 60 years with mild to moderate mood disturbance and sub-optimal vitamin C status. The feasibility trial demonstrated difficulties with participant recruitment, which likely reflected the strict exclusion criteria. Results suggested that a larger trial was feasible but required careful consideration of criteria due to the impact on recruitment and compliance with data collection.

Study 3 was a two-period, non-blinded crossover trial in which participants (n = 26) with mild to moderate mood disturbance were randomised to a counter-balanced sequence. During each 4-week period, participants consumed either two SunGold kiwifruit daily or

their usual diet, with the periods separated by a two-week washout. Mean change in total mood disturbance ($p < 0.001$) and wellbeing ($p < 0.01$) were greater in the kiwifruit condition relative to diet as usual. Vitamin C ($p = 0.002$) and vitality ($p = 0.001$) also improved in the kiwifruit condition. These results highlight the potential for gold kiwifruit to improve mood in adults with mild to moderate mood disturbance.

This dissertation presents three studies that contribute to the emerging work focussed on diet and nutrient intake as adjuvant treatments for mental health. The studies demonstrate that gold kiwifruit is well-positioned to serve as a nutritious whole food that confers positive benefits to psychological health. Further research to identify the mechanisms of action of the panoply of nutrients in gold kiwifruit across diverse populations is required.

Chapter 1: Introduction

1.1 Overview

This dissertation considers the potential benefits of kiwifruit as a whole food dietary intervention as one element of lifestyle-based mental health care, in supporting the psychological health of adults with mental health concerns. Kiwifruit are a nutrient-dense fruit exceptionally high in vitamin C relative to other fruits, that have been shown to deliver health benefits. The present chapter leads with an overview of mental health and depression, explores the influence of diet and nutrition on psychological health and closes with a review of the potential pathways through which kiwifruit might deliver benefits to psychological health. Chapter 2 is an exegesis that offers insight into the rationale and overview of the thesis. Chapter 3 (Study 1) presents a review of the literature relating to kiwifruit and psychological health that provides the context for the development of the feasibility trial (Study 2) described in Chapter 4. Chapter 5 details a randomised crossover trial (Study 3) that examined the efficacy of gold kiwifruit on the psychological health of adults with mild to moderate mood disturbance through increased vitamin C intake. A summary of results and discussion regarding the implications, strengths, limitations and future research directions is presented in Chapter 6. Chapters 3, 4 and 5 are prepared in accordance with specific guidelines of each Journal. There are minor differences in terminology and spelling used throughout the different studies as requested by reviewers. The American Psychological Association (Seventh Edition) formatting has been used throughout this thesis. The three studies are presented in manuscript format, with the same typeset as the main body of the thesis and with placement of tables and figures adjusted to suit thesis presentation. With regard to nomenclature, *psychological health, psychological wellbeing* and *mental health* are used interchangeably throughout the thesis. Unless otherwise stated, the term *depression* refers to clinical or diagnosed depression (i.e., Major Depressive Disorder, MDD) and the term *depressive symptomatology* refers to symptoms of depression (e.g., depressed mood, loss of energy/fatigue, psychomotor agitation). The term *mood disturbance* refers to feelings of distress (e.g., worried, angry or fearful) or sadness, or symptoms of depression.

1.2 Mental Health

Mental health disorders are widespread and contribute significantly to the global burden of disease. A recent World Health Organisation (WHO) Mental Health Report (WHO, 2022) indicated that 13% of the global population (970 million) were living with a mental health disorder in 2019. Between 1990 and 2019, the global number of disability adjusted life years (DALYs) due to mental health disorders increased from 80.8 million to 125.3 million with the proportion of global DALYs climbing from 3% to 5% (GBD, 2022). The global economic consequences of mental health disorders continue to rise in line with prevalence and burden. Forward estimates have suggested that the aggregated global impact of mental health disorders in terms of lost economic output could amount to US$16 trillion between 2010 and 2035 (Whiteford et al., 2013). The direct economic cost to each individual impacted by a mental health disorder was estimated at US$5,703 in 2018 (Christensen et al., 2020). Similarly, the economic burden of mental health care in Australia continues to grow. Between 2018 and 2022 government expenditure on mental health-related services increased from AUD$10.9 billion to AUD$12.2 billion, equating to 7% of total government expenditure (Australian Institute of Health & Welfare, AIHW, 2023).

In 2019, depressive disorders were the sixth leading cause of DALYs, accounting for 29% (280 million people) of global DALYs and 6% of global years of healthy life lost due to disability (YLD; Vos et al., 2020; WHO, 2022). Alarmingly, post-COVID-19 pandemic estimates suggested a 28% increase in prevalence rates (Nochaiwong et al., 2021). MDD is the most common mood disorder and is characterised by mood and affective disturbances including persistent depressed mood, loss of interest or pleasure in activities previously enjoyed, feelings of worthlessness or inappropriate guilt, energy loss and fatigue, reduced concentration, disturbances in appetite, weight or sleep, and recurrent thoughts of death, spanning a period not less than two weeks (Marx et al., 2023b). The quality of life of individuals with MDD is substantially reduced and is associated with increased health care costs, inter-personal relationship difficulties, occupational instability, medical comorbidities and increased mortality risk (Bulloch et al., 2009; Charlson et al., 2015; Culpepper et al., 2022; Desmond et al., 2022).

Despite considerable heterogeneity of definition, mild to moderate mood disturbance, variously referred to as mild or moderate depression, prodromal depression, sub-clinical depression or sub-syndromal depression, has been characterised by the presence of between two and five depressive symptoms, including at least one of depressed mood or loss of pleasure or interest persisting for two weeks or more (Kroenke, 2017). Prevalence rates for mild to moderate depression have been estimated at between 3% to 10% in primary care settings and between 1% to 17% in community-based settings (Rodríguez et al., 2012). Not unlike MDD, mild to moderate mood disturbance is associated with reduced quality of life, greater health care service use, occupational impairment, physical and psychiatric comorbidities, poor health perception and increased number of days lived with a disability (Rodríguez et al., 2012). Between 10% to 20% of individuals with mild to moderate mood disturbance will go on to develop MDD and they are three times more likely than non-depressed individuals to develop the disorder (Kroenke, 2017; Zhang et al., 2023).

Current evidence-based treatments for depression include pharmacotherapy (e.g., anti-depressants), psychological therapies (e.g., Cognitive behavior therapy (CBT)), electro-convulsive therapy (ECT) and lifestyle-based mental health care (e.g., exercise, diet) (Malhi et al., 2021). With regard to efficacy, a recent meta-analysis reported that although CBT was no more effective than pharmacotherapy in the short-term, CBT and pharmacotherapy in combination was more effective than pharmacotherapy alone (Cuijpers et al., 2023). Lifestyle-based mental health care interventions are generally considered a safe, low-cost option able to be delivered as stand-alone interventions (depending on symptom severity) or as an adjunctive treatment alongside established therapies (Marx et al., 2023a). Lifestyle-based mental health care involves the assessment and modification of lifestyle elements such as diet and nutrition, exercise/physical activity, sleep and social support networks (Sarris et al., 2014). Evidence for the efficacy of lifestyle-based interventions to reduce symptoms of depression in clinical (e.g., MDD) and sub-clinical populations continues to build (Firth et al., 2020).

Despite the growing prevalence and burden of clinical and mild to moderate depression, treatment rates, when determined by engagement in psychotherapy and/or pharmacotherapy, remain suboptimal (Thornicroft et al., 2017). Globally, around one in three people with depression receive treatment and only 40% of these receive treatment that satisfies minimally adequate standards (Mekonen et al., 2021). Initiatives designed to close the treatment gap have not realised any significant improvements in many developed nations (Moitra et al., 2022). Thus, new treatment avenues such as lifestyle-based approaches that can serve as stand-alone or adjuvant treatments to traditional therapies in the prevention and treatment of mental health conditions are crucial to reduce the individual, societal and global burden of depression.

1.3 Diet and Physiological Health

Over the last several decades, the growing prevalence of chronic disease states and mental health disorders has coincided with increased availability and consumption of energy-rich, ultra-processed foods. Consumption of such foods is a hallmark of the *Western diet,* which typically comprises foods such as processed meats, take-away foods, sugar, white bread and sweetened flavoured drinks (González Olmo et al., 2021; Jacka et al., 2010). The western diet is now implicated in dysbiosis of the microbiota and pathogenic effects on the immune system and neuroinflammation, the latter contributing to neurogenerative disorders and depression (González Olmo et al., 2021). Diet-related chronic disease states are now the leading cause of mortality and morbidity and effect between 50% to 65% of individuals in Western countries (Cordain et al., 2005).

It is readily acknowledged, and indeed, actively promoted, that a healthy diet comprising primarily wholefoods meets not only basic nutritional needs but has health-promoting and disease preventive effects (Wallace et al., 2020). For example, food groups such as fruits and vegetables are the cornerstone of a healthy whole diet and adequate intake is associated with reduced all-cause mortality and reduced mortality from chronic diseases such as cancer and cardiovascular disease (Joffe & Robertson, 2001). Benefits to human health from fruit and vegetable consumption comes, in part, from the diverse nutrient, dietary fibre and phytochemical content which act synergistically to deliver numerous physiological health benefits (Dreher, 2018). Positive associations between fruit and vegetable consumption and psychological health are now emerging from observational and intervention trials (Adenuga-Ajayi et al., 2024).

1.4 Diet and Psychological Health

The human diet is purported to be a crucial element in the pathogenesis and prevalence of mental health disorders with peak nutrition bodies advocating for diet and nutrition to be recognised as central determinants of mental health (Sarris et al., 2015). Elements within lifestyle-based mental health care such as diet and nutrition interventions enjoy both clinical and public favour (Morgan & Jorm, 2009) and are recommended as foundational actions, or 'non-negotiables' within an individualised treatment plan for depression (Malhi et al., 2021).

To date, the bulk of the evidence examining the role of diet in psychological health has emerged from cross-sectional and longitudinal studies that have examined intake of whole dietary patterns, individual foods/food groups or single nutrients. Meta-analyses of prospective studies have suggested that consuming a healthy diet may decrease the risk of depression (Y. Li et al., 2017). Adequate raw fruit and vegetable intake has been associated with higher positive mood, greater life satisfaction and a sense of flourishing (Brookie et al., 2018), and dietary intake of vitamins C and E are inversely associated with risk of depression (Ding & Zhang, 2022). Results may reflect reverse causation given the bi-directional associations between mental health and dietary intake (Eliby et al., 2023). Although drawn from a smaller pool of studies, reviews of clinical trials have reported that adherence to a healthy dietary pattern (e.g., the Mediterranean dietary pattern (MDP)) reduced depressive symptoms (Firth et al., 2019), that individual food groups (e.g., fruits and vegetables) are associated with improved psychological wellbeing (Adenuga-Ajayi et al., 2024), and that whole food-delivered nutrients (e.g., folate) have potential benefits as mono- or adjuvant therapies for depression (Lai et al., 2012).

The remainder of this section will provide a summary of the evidence to date for each of whole diet, food groups and nutrients to support psychological health, and close with an overall summary of findings and considerations for future research from all three dietary elements (Section *1.4.4*).

1.4.1 The Effect of Whole Dietary Interventions on Psychological Health

A diet consisting of higher intake of wholefoods including fruits, vegetables, nuts, legumes, seafood, lean meats and whole grains is likely to supply the necessary nutrients to confer greater protection against the development of mental health disorders (Sarris et al., 2015). Greater adherence to this dietary pattern has also been associated with emotional regulation, resilience and positive affect (Flor-Alemany et al., 2022). While a determination of the optimum dietary approach remains unclear, there is broad consensus that an unhealthy diet is associated with increased risk of depressive symptoms in otherwise healthy individuals

(Ceolin et al., 2022; Lai et al., 2014) and increased severity of symptoms in individuals with clinical depression and mild to moderate mood disturbance (Firth et al., 2019; Matison et al., 2021).

The benefits of whole-of-diet interventions on psychological health have been examined in cross-sectional, prospective and randomised controlled trials (RCTs). To date, the bulk of the research has focussed on the MDP, or dietary patterns thematically similar to the MDP that are often generically termed a ‘healthy dietary pattern’. The MDP is a diet high in fruits, vegetables, wholegrains, legumes, seafood, nuts, seeds and olive oil, while being low in sugar, red meat, and processed and refined foods (Bayes et al., 2022). Other dietary patterns that have been or are becoming the subject of scientific scrutiny include the dietary approaches to stop hypertension (DASH) diet, the ketogenic diet (KD), the Nordic diet (ND) and the Japanese diet (JD). The DASH diet (Appel et al., 1997) was designed to support reduction of blood pressure (BP) in hypertensive subjects and is a diet rich in fruits, vegetables, low-fat dairy products and with reduced intake of saturated fats and cholesterol. The KD is described as a high-fat, low protein, low carbohydrate diet with restricted caloric and fluid intake and is hypothesised to possess mood-stabilising properties through altering the excitatory/inhibitory signalling of neurotransmitters such as dopamine (Ceolin et al., 2022). The ND is characterised by intake of fruits and berries, vegetables, legumes, oats/barley, low-fat dairy products, fatty fish (e.g., salmon, herring and mackerel) and nuts (Adamsson et al., 2011). The JD is rich in vegetables, mushrooms, seaweeds, soybean products, potatoes, green tea, fruits, fish and low in rice (Miki et al., 2018).

A recent meta-analysis of prospective studies reported that a ‘healthy dietary pattern’ was associated with a significantly reduced risk of depression (k = 17, N = 127,973, OR = 0.77; Molendijk et al., 2018). Considering specific dietary patterns, a meta-analysis found that high adherence to a MDP was associated with a reduced risk of depression (k = 5, N =

36,556, *OR* = 0.67; Lassale et al., 2019). In a harmonised meta-analysis of observational and prospective studies, following a MDP or DASH diet was associated with fewer depressive symptoms and reduced risk of developing depressive symptoms after controlling for baseline depression severity (Nicolaou et al., 2020). Prospective analyses on the JD have returned mixed results with high adherence to the diet associated with reduced risk of depression at 3-years in working Japanese adults (n = 903, p = 0.024; Miki et al., 2018), whereas no such associations were found in a cohort of elderly Japanese adults (n = 1,112, p = 0.52) at 20-year follow-up (Okubo et al., 2019). The observational research examining the ND is limited to a single study involving young females aged 18 - 25 years (n = 181), which found no associations between adherence to a ND and depression or quality of life (Abbaszadeh et al., 2020).

RCTs offer a higher level of evidence than observational studies and maximise causal claims regarding the intervention and population of interest (Cartwright, 2007). A small but promising body of RCTs have returned positive preliminary findings for the efficacy of dietary interventions on depression symptoms. A recent meta-analysis of 16 RCTs (N = 45,826) reported that dietary interventions had a small positive effect on symptoms of depression (Firth et al., 2019). The MDP has shown the most promise as a dietary intervention for the treatment of depression. A 12-week RCT (SMILES trial; Jacka et al., 2017) reported that adults with diagnosed depression (n = 31) who consumed a modified Mediterranean diet with dietitian-delivered dietary support recorded significant reduction in depression scores ($p < 0.001$) and higher rates of depression remission compared to controls (n = 25; 32% versus 8%, respectively). Delivering a fish oil-supplemented Mediterranean diet with fortnightly cooking classes to adults with depression for 12-weeks, Parletta *et al.* (2019) reported that compared to controls, Mediterranean diet consumers had significant reductions in depressive symptoms (p = 0.027). The MDP has demonstrated efficacy in reducing depressive symptoms in young adults ($n = 101$) when compared to diet as usual over brief (21-day) time periods (Francis et al., 2019); when delivered across 12-weeks with reduced clinician/dietician intervention (three appointments at 6-weekly intervals) compared to controls in young males with moderate to severe depression ($n = 72$; Bayes et al., 2022); and in elderly Type II diabetics when the MDP was supplemented with nuts in a 3-year follow-up randomised trial (PREDIMED trial; Sánchez-Villegas et al., 2013).

A recent systematic review of RCTs ($n = 6$) examining the DASH diet concluded that the diet may have positive effects on psychological health, but the results were inconsistent across the studies due to high heterogeneity in cohorts and outcome measures (Tan et al., 2023). For example, healthy post-menopausal women ($n = 95$) randomised to receive a DASH-type diet or a healthy diet (controls) for 14-weeks found that both groups experienced significant improvements in mood ($p < 0.01$), with a significant reduction in anger being the only observed difference between the groups favouring the DASH-type diet (Torres & Nowson, 2012). A 14-week RCT comparing a DASH diet plus exercise to a lifestyle intervention (e.g., exercise, yoga, stress management, rice diet) reported no improvements on a quality of life measure for participants consuming the DASH diet (Ziv et al., 2013).

With regard to RCTs examining other dietary patterns, the ND was examined in a small pilot study in adults ($n = 16$) with MDD and although underpowered for statistical analysis and of short duration (8-days), the authors observed a greater mean reduction in depressive symptoms in participants with mild to moderate depression who consumed the ND compared to non-depressed controls (Sabet et al., 2021). The KD is currently the subject of incomplete research in depressed populations (Bambokian, 2022) and to the author's knowledge, there have been no RCTs examining the effect of the JD on depression.

1.4.2 The Effect of Individual Food Group Interventions on Psychological Health

The association between intake of certain food groups such as fruits and vegetables and psychological health are well-documented. A review of observational studies (k = 61) reported that greater fruit and vegetable intake and intake of some specific subgroups (e.g., citrus and green leafy vegetables) was associated with reduced risk of depression. Of interest to the present thesis, Glabska *et al.* (2020), noted that among a limited number of raw fruits, gold and green kiwifruit were identified as being uniquely related to better mental health. Longitudinally, fruit and vegetable consumption was associated with lower prevalence of symptoms of depression and anxiety in older adults (Nguyen et al., 2017); was predictive of increased wellbeing, life satisfaction and happiness (Mujcic & Oswald, 2016); conferred lower odds of depression (McMartin et al., 2013); and was associated in a dose-response fashion to subjective life satisfaction and happiness (Blanchflower et al., 2013; Ocean et al., 2019).

A meta-analysis of intervention trials investigating the efficacy of fruit and vegetable consumption on psychological health as distinct interventions concluded that the evidence was limited and drawn from a small, heterogenous pool of studies (Adenuga-Ajayi et al., 2024). Young, otherwise healthy adults (n = 174) aged 18 - 25 years provided with a two-week supply of fruits and vegetables showed improvements in psychological wellbeing, but not mood or depressive symptoms, compared to a diet as usual control condition (Conner et al., 2017); and adults (n = 110) who increased daily serves of vegetables to meet dietary guidelines recorded significantly greater levels of happiness after eight-weeks compared to controls (De Leon et al., 2021). In a between-subjects snacking intervention trial, young adults (n = 100) who consumed a healthy snack (i.e., apple, orange or banana) for 10 consecutive days experienced small, non-significant reductions in depression scores compared to a significant increase in depressive symptoms for participants who consumed an unhealthy snack (e.g., chocolate, chips; Smith & Rogers, 2014).

Whilst there exists some evidence for beneficial influences of fruit and vegetable consumption, evidence for other broad food groups such as meat, dairy, nuts and fish is mixed. For example, a meta-analysis found there was no significant association between meat consumption and depression prevalence ($k = 8$, $OR = 0.89$, $p = 0.47$), although there was evidence of a moderately higher risk of depression ($k = 3$, $RR = 1.13$, $p = 0.013$; Zhang et al., 2017). However, others (Dobersek et al., 2023) have reported that, compared to non-meat eaters, meat consumers had reduced depressive symptomatology ($k = 20$, $N = 171{,}802$). A systematic review of observational studies ($k = 13$) that examined the association between dairy-food intake and depressive symptoms reported conflicting and inconsistent findings across studies with considerable heterogeneity of dairy type, gender and cohort (Hockey et al., 2020). A recent randomised crossover trial reported that, compared to a low-fat control diet, a Mediterranean diet with 3 - 4 daily serves of dairy food was found to be associated with improved mood disturbance and reduced depression symptomatology in healthy older adults ($n = 41$, $M = 60.2$ years, $SD = 6.9$ years; Wade et al., 2020). A meta-analysis of observational ($n = 6$) and controlled trials ($n = 4$) examining the associations between nut consumption and mood reported that, despite mixed results across the studies, there was sufficient evidence to suggest that higher nut consumption could be associated with reduced risk of depression, fewer depressive symptoms and better mood states (Fernández-Rodríguez et al., 2022). In a meta-analysis of observational studies ($k = 31$, $N = 255{,}076$), Grosso *et al.* (2016) noted that fish consumption was associated with a reduced risk of depression, however, there is insufficient evidence from RCTs to draw causal inferences (Appleton et al., 2007). When considered as part of an overall healthy diet that included other food groups (i.e., fruit, legumes, vegetables and whole grain), fish consumption was associated with a reduced risk of depression (k = 18, N = 147, OR = 0.89; Molendijk et al., 2018).

1.4.3 The Effect of Individual Nutrients on Psychological Health

The therapeutic use of dietary supplements, nutrient-based nutraceuticals and plant-based phytoceuticals is common. In the most recent clinical guidelines for the treatment of psychiatric disorders with nutraceuticals and phytoceuticals (Sarris et al., 2022), a number of nutraceuticals and phytoceuticals have received either supportive or provisional recommendation for use across a range of mental health conditions, however due to limited evidence, many have received weak endorsement while others demonstrated no therapeutic benefit. Current clinical guidelines for lifestyle-based interventions for the treatment of depression suggests the clinical use of dietary interventions should be prioritised over supplement use due to the multiple benefits to physical and metabolic health received from dietary interventions (Marx et al., 2023a).

There is increasing evidence for the role of oxidative stress and inflammation in the pathophysiology of depression as well as the multiple neurobiological pathways promoted as potential conduits (Manosso et al., 2020). These include pathways such as inflammation, oxidative stress, tryptophan-kynurenine metabolism, gut microbiome (gut-brain axis) and the hypothalamic-pituitary-adrenal axis (Marx et al., 2021; Marx et al., 2017). To date, studies examining the associations between nutrient intake and psychological health have reported mixed findings. The bulk of the evidence is drawn primarily from cross-sectional and prospective studies plus a small body of intervention trials (i.e., RCTs). The primary focus of this thesis is dietary interventions for psychological health and the following section provides an overview of the specific micronutrients implicated in the aetiology of depression, the existing evidence to support associations with depression and recommendations for future research opportunities.

Vitamin E is a fat-soluble antioxidant that donates electrons and reduces harmful free radicals (Ding & Zhang, 2022). It is implicated in the modulation of adult neurogenesis, a key process for mood regulation (Manosso et al., 2020). Highlighting the synergistic cooperativity between micronutrients, vitamin E is regenerated back to its active form (e.g., α-tocopherol) by vitamin C (Shahidi et al., 2021). Dietary sources of vitamin E include edible oils, nuts, cereals, legumes and non-citrus fruits (Agudo et al., 2004). A meta-analysis of observational studies (k = 25, N = 91,966) reported that dietary vitamin E intake was negatively associated with depression (RR = 0.84, p = 0.02) and that depressed subjects had lower dietary vitamin E intake compared to non-depressed controls (Ding & Zhang, 2022). Although there were mixed results across studies, a narrative review (Manosso et al., 2020) of clinical trials concluded that vitamin E had potential use as an adjuvant treatment for depression.

Zinc is an essential trace element with anti-inflammatory and antioxidant properties that is involved in neurotransmitter regulation and neurogenesis pathways (Wang et al., 2018). As the efficiency of zinc absorption from the diet is low, it is vulnerable to rapid depletion, such that zinc deficiency may depress levels of neurogenesis and neuroplasticity, thereby increasing vulnerability to psychological stress (Solomons, 2001). Evidence suggests that zinc has demonstrated protective effects against lipid peroxidation, that it decreases C-reactive protein levels, and can elevate brain-derived neurotrophic factor (BDNF), all of which may confer an antidepressant action (Manosso et al., 2020). Dietary sources of zinc include crustaceans, leafy and root vegetables, whole grains, dairy products and nuts (Solomons, 2001). A meta-analysis of observational studies (k = 17) reported that depressed subjects (n = 1,643) had significantly lower levels of serum zinc compared to non-depressed controls (n = 804; Swardfager et al., 2013). A review of a small body of intervention studies (n = 4) concluded there were potential benefits to zinc supplementation as a stand-alone treatment for depression or as an adjuvant to antidepressant treatment in depressed populations and the general female population, however there was insufficient evidence to assert a determination with respect to males (Lai et al., 2012).

It has been suggested that dietary fibre has the potential to influence psychological health through the gut-brain axis by modulating the gut environment and supporting a healthy gut microbiome (Aslam et al., 2023). Dietary sources of fibre include cereals, nuts, fruits and vegetables (Dhingra et al., 2012). Pooled analysis from case-controls studies (n = 4) revealed that consumption of dietary fibre in depressed adults was significantly lower than matched healthy controls (Fatahi et al., 2021). A meta-analysis of cross-sectional and longitudinal studies (k = 23, N = 181,405) reported inverse associations between dietary fibre intake and depressive symptoms and depressive outcomes in the observational work, however there was no difference between dietary fibre supplementation and placebo in intervention trials (k = 10, N = 740; Aslam et al., 2023). There have been limited studies in clinically depressed populations and current evidence does not support the use of dietary fibre supplementation for improving psychological health.

Folate is an essential, water-soluble B-vitamin considered necessary for the synthesis of dopamine, adrenaline and serotonin (Zheng et al., 2020). Folate is involved in neuronal methylation and the homeostasis of neuronal lipids, processes that are reflected in mood, irritability and sleep (Tardy et al., 2020). Dietary sources of folate include dark leafy green vegetables, whole grains, dairy products and fruit (Looman et al., 2018). A recent meta-analysis (k = 43, N = 35,801) reported that depressed individuals had significantly lower folate levels and lower dietary intake of folate compared to non-depressed individuals (Bender et al., 2017). Current evidence for the use of folate is mixed, however based on meta-analyses (Taylor et al., 2004; Zheng et al., 2020), clinical guidelines for the treatment of depression state that methyl-folate, the active form of folate, may be beneficial as an adjunct treatment for depression and may be more efficacious in individuals with folate deficiency (Malhi et al., 2021; Sarris et al., 2016).

Tryptophan is an endogenous, essential amino acid that must be supplied through the diet and is a precursor for nicotinamide (vitamin B_3), melatonin and tryptamine, and the sole precursor of serotonin (Friedman, 2018; Jenkins et al., 2016). Dietary sources of tryptophan include legumes, wheat flour, rice, cheese and meats (Kałużna-Czaplińska et al., 2019). Tryptophan depletion studies have demonstrated that in otherwise healthy individuals, tryptophan depletion had little to no effect on mood, however those at high familial risk of depression demonstrated disturbances in processing of affective stimuli, suggesting a possible premorbid vulnerability in serotonin regulation (Feder et al., 2011). Furthermore, a RCT found that healthy young adults (n = 25) who consumed a high tryptophan diet recorded significantly greater positive mood compared to a low tryptophan diet at the end of the two-week intervention (Lindseth et al., 2015). A systematic review of RCTs (k = 4, N = 181) concluded that daily tryptophan supplementation improved mood outcomes in healthy adults (Kikuchi et al., 2021).

Magnesium is a micronutrient involved in numerous neurobiological functions including nerve transmission, neuromuscular coordination, blood pressure and insulin metabolism (Kirkland et al., 2018). Its relationship to mental health is thought to exist through its role as a potentiating factor in glutaminergic excitatory signalling, thus protecting against oxidative stress and neuronal cell death (Kirkland et al., 2018). Dietary sources of magnesium include green leafy vegetables, nuts, legumes, whole grains, milk and meats (Bae et al., 2010). Evidence for the role of magnesium in mental health is conflicting. Cross-sectional evidence has reported inverse relationships between magnesium levels and magnesium intake and depressive symptoms (Wang et al., 2018). Prospective studies have found no associations between magnesium intake and depression risk in adults with no history of depression (*n* = 15,863) at 10-year follow-up (Martínez-González & Sánchez-Villegas, 2016), or in a 6-year study in a cohort of Spanish University students (*n* = 12,939; Derom et al., 2012). To date, magnesium supplementation trials have produced mixed results. For example, depressed adults (*n* = 60) with hypomagnesemia supplemented with 500 mg magnesium daily for 8-weeks recorded significant improvements in depressive symptoms ($p = 0.02$; Rajizadeh et al., 2017), as did adults with sub-clinical depression (*n* = 126, $p < 0.001$) following 6-weeks supplementation at 250 mg/d (Tarleton et al., 2017). Others have reported no such associations between geriatric depressive scores and magnesium supplementation in elderly people with diabetes (*n* = 23; Barragán-Rodríguez et al., 2008) or in women with post-partum depression (Fard et al., 2017).

Selenium is an essential micronutrient involved in anti-inflammatory and antioxidant processes that exerts modulatory effects on dopamine, serotonin and adrenaline (Pasco et al., 2012). Dietary sources of selenium include meats, fish, nuts, fruits and vegetables (Peters et al., 2016). Evidence for associations between selenium and depression are inconclusive, although there is support for bi-modal associations in some populations (Wang et al., 2018). For example, a cross-sectional study of healthy university students aged 17 - 25 years (*n* = 978) found that both low and high serum selenium concentrations were associated with increased depressive symptoms, although depressive symptoms were greater at lower serum concentrations compared to high concentration (Conner et al., 2015). A nested case-control study of non-depressed females aged 20 - 89 years (*n* = 1,494) found that lower dietary selenium intake was associated with an increased risk of subsequent depression (*OR* = 2.95; Pasco et al., 2012), whereas others have found no such associations in rural-living, elderly Chinese adults (Gao et al., 2012), or in haemodialysis patients (Ekramzadeh et al., 2015). Pregnant women supplemented with selenium (100 µg/d) for approximately 6 months recorded significantly reduced depressive symptoms compared to placebo (Mokhber et al., 2011), however there were no differences in mood outcomes following supplementation at either 100 µg, 200 µg or 300 µg/d compared to placebo in elderly adults in a separate 6-month trial (Rayman et al., 2006).

Associations between iron deficiency and risk for depression have been reported (Z. Li et al., 2017) but quantifying the relationship between iron deficiency and psychological health remains difficult (Berthou et al., 2022). Neuro-bioavailability of blood iron is necessary for the synthesis of serotonin, tryptophan, dopamine and adrenaline, such that decreased circulating iron is associated with tryptophan degradation and serotonin and dopamine pathway dysregulation (Berthou et al., 2022). Cross-sectional studies reported that higher dietary iron intake was inversely associated with prevalence of depressive symptoms in American (n = 14,834; Li et al., 2018) and Japanese adults (n = 2,006; Miki et al., 2015). Compared to non-depressed controls, depressed adults (n = 416) had significantly greater prevalence of iron deficiency ($p < 0.001$, 12% *vs*. 27%, respectively; Berthou et al., 2022).

Omega-3 polyunsaturated fatty acid (n-3 PUFAs) benefit neurotransmission by increasing cell membrane fluidity and enhancing neurogenesis (Sarris, 2017) and are considered critical for the development and function of the central nervous system (CNS) (Deacon et al., 2017). Dietary sources of PUFAs include green leafy vegetables, fish, fish oil, beef, seeds and nuts (Saini & Keum, 2018). N-3 PUFA deficiency leads to the development of mood disorders and high n-3 PUFA intake is associated with low prevalence rates of depression (Deacon et al., 2017). The available evidence suggests that omega-3 fatty acid supplements have demonstrated therapeutic effects on depression at certain doses, however it is recommended as an adjuvant to psychopharmacology rather than a monotherapy (Liao et al., 2019; Malhi et al., 2021).

Vitamin C is a water-soluble vitamin that humans do not synthesise naturally, despite having an absolute requirement for vitamin C for a range of important biological functions including regulating the epigenome, generating metabolic energy and protecting against oxidative damage (Harrison et al., 2014). Vitamin C acts as an antioxidant and free radical scavenger and is an essential cofactor in enzymatic reactions including that of dopamine *β*-hydroxylase, an enzyme that is central to the synthesis of adrenaline from dopamine. Vitamin C serves as an essential cofactor in the metabolism of tryptophan, a necessary requirement for the synthesis of serotonin (Evans-Olders et al., 2010; Pullar et al., 2018a; Schlueter & Johnston, 2011). Altered dopamine *β*-hydroxylase activity has been described in a range of mood and anxiety disorders (Gonzalez-Lopez & Vrana, 2020) and acute tryptophan depletion has been associated with reduced serotonin levels and lowered mood states (Jenkins et al., 2016). Vitamin C is required for the synthesis of neurotransmitters including dopamine, adrenaline and serotonin, all of which are implicated in mood regulation and depression (Pullar et al., 2018a). Vitamin C must be obtained via dietary intake, with fruits and vegetables considered the primary source (Pearson et al., 2017). Despite extensive cross-sectional and mechanistic research involving diverse populations, evidence for the association between vitamin C and psychological health remain mixed. In cross-sectional research, vitamin C status was found to be inversely related to total mood disturbance ($r = -0.18$, $p < 0.05$; Pullar et al., 2018a) and depression scores in healthy adult males aged 18 - 35 years with adequate vitamin C status (Appel et al., 2008). Conversely, no such associations were found in mixed-gender samples of similar age and vitamin C status (Fletcher et al., 2021; Sim et al., 2022) or in a community sample of adults aged 49 - 51 years (Pearson et al., 2017). In an RCT involving non-depressed adults with sub-optimal vitamin C status ($n = 48$), supplementation with 1000 mg/d vitamin C for four weeks improved attentional focus and work motivation but not mood compared to placebo (Sim et al., 2022).

When used as an adjuvant for treating depression in adults with diagnosed depression, daily administration of vitamin C (up to 1000 mg) with *de novo* citalopram (up to 60 mg/d) did not increase efficacy of citalopram compared to citalopram plus placebo (Sahraian et al., 2015). A meta-analysis of RCTs (k = 10, N = 836) that examined the effect of vitamin C supplementation on mood in adults with clinical or mild to moderate depression reported no significant improvements in mood in the overall analysis (p = 0.47; Yosaee et al., 2021). However, a sub-group analysis revealed a significant improvement in mood favouring vitamin C over placebo in participants with mild to moderate depression who were not taking antidepressants (k = 5, n = 540, p = 0.041). Importantly, there was no evidence of between-study heterogeneity in the sub-analysis (p = 0.5).

1.4.4 Diet and Psychological Health – Summary

Evidence continues to build to support the role of nutrition as a critical factor in the pathophysiology of psychological health (Sarris et al., 2015). Meta-analyses of cross-sectional, prospective studies and RCTs confirm the associations between consuming a healthy, nutrient-rich diet and reduced risk of depression across multiple populations and age groups (Marx et al., 2023a) and has provided preliminary evidence of a positive effect on depression (O'Neill et al., 2022). Overall, pooled effect sizes from RCTs demonstrate small, significant effects of whole dietary interventions on depressive symptoms (Firth et al., 2019). Compared to meat, dairy, fish and nuts, the evidence for the benefits of fruit and vegetable consumption on psychological health is more substantial but limited to a small, heterogenous pool of studies (Adenuga-Ajayi et al., 2024). Fruit and vegetable consumption has been associated with improved psychological health, greater levels of happiness and reduced risk of depression in certain populations (Conner et al., 2017; McMartin et al., 2013; Mujcic & Oswald, 2016). The strength of the evidence for the relationships between specific nutrients and psychological health is mixed and relatively contemporary (Marx et al., 2023a). For example, zinc and the active form of folate, methyl-folate, have received provisional recommendation for use as adjuvants in the treatment of MDD (Malhi et al., 2015), whereas other nutrients (e.g., dietary fibre and vitamin E) require more research to determine their potential efficacy, while some (e.g., vitamin C) have received tentative support for use in sub-clinical populations (Manosso et al., 2020; Sarris et al., 2022; Yosaee et al., 2021).

Arriving at any definitive causal conclusions is difficult given the considerable between-study heterogeneity with regard to inclusion criteria (e.g. mild to moderate mood disturbance *vs.* clinical depression), sub-group analyses, method of intervention delivery (e.g., dietician/nutritionist *vs.* research support staff) and diverse control conditions (e.g., social-group protocols *vs.* healthy diet). These factors limit generalisability of findings to clinical, sub-clinical and general populations (Firth et al., 2019; Marx et al., 2017). The challenge of accurately determining participant compliance with dietary protocols is endemic to nutrition studies and the use of self-report measures continues to introduce biases (Jacka, 2017). Another issue that plagues nutrition studies, and in particular whole of diet or wholefood interventions, is the difficulty in blinding participants and researchers to condition, which can introduce expectation biases and threats to participant retention (Weaver & Miller, 2017).

The present research identified three aspects of the extant literature that warranted further investigation. First, a critical issue in dietary RCTs is the lack of objective assessment of nutrient biomarkers. Assessing nutrient biomarkers is vital to strengthen the quality of future research findings (O'Neill et al., 2022). A number of individual nutrients have plausible pathways through which they might affect psychological health (see Section *1.4.3*) and accurate assessment of the individual nutrients (e.g., vitamin C) with known associations with psychological health within foods would support determining the mechanisms of action.

A second issue identified was that the majority of dietary intervention trials have recruited adults with mild to moderate mood disturbance, a critical imbalance to address moving forward, but one that does not diminish the need for continued research within this population. The burden of depressive disorders continues to escalate and there is a pressing need to deliver efficacious and accessible preventative treatments for at-risk populations to avoid the personal and societal costs of clinical depression (Firth et al., 2019). Elucidating the mechanisms of action of preventative treatments for mild to moderate depression and determining what works and for whom was a key consideration of the present research.

The third matter observed in the literature pertains to the shift in focus from individual nutrients and single foods to whole-of-diet interventions (Jacka, 2017). Given that micronutrients are not consumed in isolation, it is more consequential to examine the effect of whole foods on psychological health (O'Neill et al., 2022), however, the redirection of research energy should not negate the value of continuing to examine the individual parts of the whole. Examining a nutrient-dense food has the dual benefit of informing whole-of-diet approaches of foods that possess mood-enhancing properties, and identifying stand-alone dietary interventions that could function as an efficacious lifestyle-based dietary intervention when the pragmatic and individual barriers to implementing a wholesale change of diet cannot be overcome (Barre et al., 2011; Scannell et al., 2020).

Considering the triune of mechanistic assessment of nutrients, preventative approaches for mental health in sub-clinical populations and the import of establishing the relative contribution of a single whole food within a whole-of-diet intervention, the present research made a determination to examine the role of vitamin C in supporting psychological health. This decision was taken based on a number of considerations. First, there are numerous plausible pathways through which vitamin C is implicated in mood and psychological health (Pullar et al., 2018a). Second, there is a dearth of RCTs that had examined the efficacy of vitamin C in the prevention and treatment of depression (Sahraian et al., 2015). Third, findings from a meta-analysis had offered tentative support for the mood-enhancing properties of vitamin C in adults with sub-clinical depression (Yosaee et al., 2021). Fourth, there was preliminary evidence that consuming a vitamin C-rich fruit was associated with greater adherence to a healthy dietary pattern and indirectly associated with reduced depression symptomatology (Pham et al., 2021). Lastly, that vitamin C intake and sub-optimal vitamin C status are associated with mood disturbance (Appel et al., 2008; Ding & Zhang, 2022).

1.5 Dietary Sources of Vitamin C

Humans have an absolute requirement for vitamin C, despite having lost the ability to endogenously synthesise it, therefore, vitamin C must be obtained directly from the diet (Pearson et al., 2017). The highest concentrations of vitamin C in food are found in vegetables and fruit. Vegetables considered excellent sources of vitamin C include green chilli peppers, kale, cauliflower, broccoli, brussels sprouts, spinach and potatoes (Mieszczakowska-Frąc et al., 2021). Vitamin C is subject to oxidation and subsequent degradation from heating and cooking processes. For example, boiling, steaming and microwaving vegetables (e.g., cauliflower) resulted in total vitamin C losses of 50 - 60%, 40% and 10%, respectively (Buratti et al., 2020). When vegetables are cooked for short periods of time (e.g., blanching broccoli for 30 seconds), vitamin C losses are as high as 19% (Mieszczakowska-Frąc et al., 2021). Even briefly rinsing vegetables in water has been shown to reduce vitamin C content by as much as 35% (Vandekinderen et al., 2009). Thus, unless vegetables are consumed raw, fruit can provide more than 50% of dietary vitamin C intake (Agudo et al., 2004).

Fruit sources considered to have high vitamin C content include blackcurrant, kiwifruit, papaya, orange, pineapple, lemons, strawberry, mango and raspberry (Mieszczakowska-Frąc et al., 2021). The vitamin C content of commonly consumed fruits is displayed in Table 1. The vitamin C content of SunGold kiwifruit sets it apart from other commonly consumed fruits. A single SunGold kiwifruit (*Actinidia chinensis* var. *chinensis* ‘Zesy002’) delivers almost double the amount of vitamin C than the green kiwifruit and more than three times the vitamin C of oranges, a fruit that, from a consumer perspective, is synonymous with vitamin C (Kurzer et al., 2019). Other fruits such as strawberry, raspberry and pineapple are good sources of vitamin C but contain considerably less than SunGold kiwifruit. Compared to other fruits, SunGold kiwifruit is exceptionally high in vitamin C and one gold kiwifruit daily has been shown to raise plasma vitamin C to healthy levels (> 50 µmol/L) within 7-days in adults with sub-optimal concentrations (< 50 µmol/L; Carr et al., 2012). Similarly, young adult males with sub-optimal vitamin C concentration supplemented with two SunGold kiwifruit per day recorded plasma vitamin C concentration at saturation levels (~ 70 µmol/L) within one week (Bozonet et al., 2015).

Table 1

Vitamin C Content (mg per 100g) of Commonly Consumed Fruits. Fresh, Uncooked. (Source: New Zealand Food Composition Database)

Fruit	Vitamin C content (mg per 100g)	Percentage of RDI*
Apple (Red delicious)	5	11
Apricot	4	9
Banana	6	14
Green kiwifruit	88	220
Orange	52	130
Pineapple	25	62
Strawberry	46	114
SunGold kiwifruit	152	380
Raspberry	14	34

*Percentage of recommended dietary intake (RDI) based on average adult diet of 8700kJ as per Australian Dietary Guidelines.

The degradation of vitamin C through heating processes and the necessary requirement for trial participants to consume equivalent amounts of vitamin C from a whole food dietary intervention made fruit the most appropriate choice for the present studies. Additionally, given the high vitamin C content and the proven capacity to restore sub-optimal vitamin C status to adequate levels, it was determined that the SunGold kiwifruit would be the most appropriate fruit vector through which to deliver vitamin C to trial participants.

1.6 Kiwifruit – A Short History

The kiwi plant is of the genus Actinidia and is a deciduous, woody vine that produces an edible fruit (Singletary, 2012). Actinidia are native to the mountainous regions of south-west China and more than 70 cultivars have been identified to date. Only a relatively small number have been domesticated and of these, *Actinidia deliciosa* ‘Hayward’ (green kiwifruit) and *Actinidia chinensis* (gold kiwifruit) are the most widely recognised cultivars in commercial production (Ma, Lan, Geng, et al., 2019).

Kiwifruit were introduced to New Zealand as a botanical curio in 1904 by schoolteacher Isabel Fraser upon her return from China with seeds from *A. deliciosa* (Ward & Courtney, 2013). In the 1920s, nurseryman Hayward Wright catalogued kiwi plants and sold them as a “fruiting climber” that produced a winter-ripening fruit. Large scale plantings of *A. deliciosa* were established during the 1930s with the first commercial exports of New Zealand kiwifruit beginning in the 1960s (Nishiyama, 2007).

China is the world’s largest producer of kiwifruit, and together with New Zealand, Italy, Iran, Chile and Greece produce more than 90% of the world’s kiwifruit (Hazarika et al., 2022). New Zealand is the largest producer of kiwifruit outside of China and is responsible for around 30% of global trade volume (Ward & Courtney, 2013). The two cultivars of current commercial significance in New Zealand are the *Actinidia deliciosa* “Hayward” and the SunGold kiwifruit. The SunGold kiwifruit is the most commonly produced and traded gold-fleshed kiwifruit and came to prominence when a previous gold-fleshed cultivar, *A. chinensis* "Hort16A" proved susceptible to a bacterial canker (*Pseudomonas syringae* pv. *Actinidiae*) during the first decade of the twenty-first century (McCann et al., 2017). Other cultivars such as the smooth, hairless, grape-sized *Actinidia arguta* (the kiwiberry) and the red-fleshed *Actinidia chinensis* Planch. (Hongyang) continue to be the subject of commercialisation and research (Latocha, 2017; Li et al., 2015).

The 'Hayward' cultivar produces a small oval-shaped fruit, roughly the size of a large hen egg, covered by a dull-brown hairy skin. The flesh is bright green and contains rows of edible, black seeds encircling the white core of the fruit (Figure 1a; Stonehouse et al., 2013). The SunGold cultivar produces a fruit slightly larger than its green cousin and is a bright, yellow-fleshed fruit with reduced seed proliferation surrounded by a smooth, hairless, bronze-coloured skin (Figure 1b; Richardson et al., 2018). The green kiwifruit delivers a unique tangy, sweet and sour taste experience, while the gold kiwifruit has a sweet and tropical taste (NZIPFRL, 2021).

Figure 1

*Zespri™ Green Kiwifruit (*Actinidia deliciosa *"Hayward") (1a.), and Zespri™ SunGold™ Kiwifruit (*Actinidia chinensis var. chinensis *'Zesy002') (1b.)*

(1a) (1b)

1.6.1 Nutritional Profile of Kiwifruit

Kiwifruit are a nutrient-dense fruit that contain numerous bioactive compounds including vitamins, minerals, polyphenols, phytonutrients, lipids, amino acids and secondary metabolites such as flavonoids (Drummond, 2013; Ma, Lan, Ju, et al., 2019). Kiwifruit are exceptionally high in vitamin C and contain nutritionally relevant levels of dietary fibre, potassium, folate and vitamin E (Richardson et al., 2018).

To date, over 500 metabolites have been identified in kiwifruit extracts, however the extant literature is limited to the 40 - 50 compounds associated with health enhancing properties such as vitamins, minerals, folate, dietary fibre and polyphenols (McGhie, 2013). Green and gold kiwifruit share a similar composition profile for water, energy, protein, sodium, magnesium, potassium and vitamin E per 100g of edible flesh (Table 2). The green cultivar possesses more than twice the amount of total dietary fibre and vitamin K, and 33% more vitamin A than the gold kiwifruit. In comparison, the gold kiwifruit contains twice the amount of selenium and more sugar and folate than the green.

The individual nutrients that separate the two cultivars are vitamin C and dietary fibre. SunGold kiwifruit contains approximately 70% more vitamin C than the green kiwifruit, whereas the green kiwifruit has more than double the amount of total dietary fibre than the SunGold. A single SunGold kiwifruit can provide almost four times the RDI of vitamin C (NHMRC, 2013). The vitamin C content of SunGold kiwifruit is such that it is eligible for authorised health claims in the European Union (EU) for vitamin C functions such as protection of cells from oxidative stress, the reduction of tiredness and fatigue, increasing iron absorption and contributing to normal psychological function (Richardson et al., 2018). When compared to other commercially available fruits, the vitamin C content of SunGold kiwifruit (152 mg per 100 g flesh) easily surpasses the levels found in oranges (52 mg), strawberries (46 mg), mango (30 mg), papaya (62 mg), mandarins (21 mg), blueberries (4 mg) and pineapple (21 mg; NZIPFRL, 2021).

Table 2

Nutritional Composition of Kiwifruit. SunGold Kiwifruit, Flesh and Seeds, Raw; Green Kiwifruit, Flesh and Seeds, Raw. Single Serve 100g. (Source: New Zealand Food Composition Database)

Nutrient	**Units**	**SunGold Kiwifruit**	**Green Kiwifruit**	**%RDI* per 100g**	
Scientific name		*Actinidia chinensis var. chinensis* 'Zesy002'	*Actinidia chinensis var. deliciosa* 'Hayward'	Gold	Green
Energy	kJ	224	220	3	3
Protein	g	0.9	0.8	2	2
Fibre, total dietary	g	1.1	2.3	4	8
Folate, total	µg	82	73	41	36
Magnesium	mg	12	14	4	4
Potassium	mg	298	300	8	8
Selenium	µg	0.6	0.3	1	0
Sodium	mg	1	1	0	0
Sugars, total	g	11	9.7	12	11
Vitamin A, retinol equivalents	µg	3	4	0	0
Vitamin C	mg	152	88	380	220
Vitamin E, alpha-tocopherol equivalent	mg	1.1	1.2	11	12
Vitamin K	µg	6.5	15.0	8	19
Water	g	81.5	82.2		

*Percentage of RDI based on average adult diet of 8700kJ as per Australian dietary guidelines

Kiwifruit are considered an excellent source of soluble and insoluble dietary fibre with the total dietary fibre content approximately 2 - 3% and 1% of fresh weight for the green and SunGold cultivars respectively (Sims & Monro, 2013). Although the relative ratio of soluble to insoluble fibre is similar between the two cultivars the green kiwifruit contains around twice the amount of total dietary fibre than the gold kiwifruit (Sims & Monro, 2013).

SunGold and green kiwifruit are relatively high in vitamin E (1.1 mg and 1.2 mg/100 g, respectively) and a single fruit can supply more than 10% of the RDI of vitamin E (NHMRC, 2006). These levels are sufficient for kiwifruit to receive endorsement for nutrient function claims in the EU (Richardson et al., 2018). Likewise, the folate content of SunGold and green kiwifruit (82 μg and 73 μg/100 g, respectively) meets EU standards to make a source claim with a single fruit able to deliver more than one-third of the RDI of folate (NHMRC, 2006; Richardson et al., 2018). SunGold and green kiwifruit are considered good sources of potassium (298 mg and 300 mg/100g, respectively) that can provide more than 10% and 8% of the adequate intake values for potassium for adult females and males, respectively (NHMRC, 2006).

1.6.2 Kiwifruit and Physiological Health

The physiological health benefits of kiwifruit consumption are well-documented. Research has generally focussed on either the individual constituents of kiwifruit that possess known efficacy on human physiology (e.g., folate & dietary fibre) or that are found in higher-than-average concentrations compared to other fruits (e.g., vitamin C). Of the many micro- and macronutrients identified within kiwifruit to date, vitamin C, vitamin D, dietary fibre, folate and potassium have been the subject of the greater body of work. The benefits to physiological health from kiwifruit consumption are evident across multiple health domains including cardiovascular health, gastrointestinal functioning, sleep, metabolic health, immune responses and anti-inflammatory processes (Singletary, 2012). A brief overview of the work to date follows.

With regard to cardiovascular health, consuming 2 - 3 kiwifruit per day has been associated with significant reductions in systolic and diastolic BP in elderly male smokers, pre-diabetic adults and hypertensive adults (Karlsen et al., 2013; Svendsen et al., 2015; Wilson et al., 2018). For example, an eight-week, randomised parallel groups design trial involving moderately hypertensive otherwise healthy subjects (aged 55 ± 9 years, $n = 118$) who consumed three green kiwifruit daily for eight weeks had significantly lower systolic and diastolic BP compared to controls consuming one apple per day in addition to their usual diet ($p = 0.04$; Svendsen et al., 2015). SunGold kiwifruit has also demonstrated cardio-protective reductions in systolic and diastolic BP in a 12-week trial involving elderly pre-diabetic adults ($n = 26$) who consumed two kiwifruit daily for 12-weeks. Other cardio-protective properties from kiwifruit consumption were observed in healthy adults aged 21 - 50 years ($n = 30$) who recorded significant reductions in platelet aggregation (18%, $p < 0.05$) and blood triglyceride levels (15%, $p < 0.05$) after consuming 2 - 3 green kiwifruit daily for 28-days compared to controls (Duttaroy & Jørgensen, 2004).

With regard to immune health, kiwifruit consumption has been associated with reduced duration and severity of symptoms of upper respiratory tract infections in elderly adults and children. A randomised crossover trial involving elderly otherwise healthy adults ($n = 32$) reported that participants who consumed four gold kiwifruit (two fresh kiwifruit and two freeze-dried kiwifruit) daily for four weeks experienced a significant reduction in the duration of a sore throat ($p = 0.024$) and the severity and duration of head congestion ($p = 0.015$ and $p = 0.029$, respectively) compared to when they consumed two bananas daily (Hunter et al., 2012). Similar reductions in severity symptoms of sore throat and head congestion were observed in 66 pre-school aged children provided two gold kiwifruit daily for 28-days (Adaim, 2010).

Daily consumption of kiwifruit has also been associated with improved sleep quality, total sleep time and sleep efficiency in sleep-compromised and sleep healthy populations. In a free-living, self-controlled diet design, 24 Chinese participants with self-reported poor sleep quality consumed two green kiwifruit one hour before their usual bedtime for four weeks. There were significant differences ($p < 0.05$) in total sleep time and sleep efficiency as measured by actigraphy following the kiwifruit intervention (Lin et al., 2011). In a randomised, single-blind crossover trial, males ($n = 24$) consuming two green kiwifruit as dried powder mixed with water with the evening meal reported increased morning alertness and reduced morning sleepiness irrespective of sleep quality compared to controls (water only; $p < 0.05$; Kanon et al., 2023). Poor sleepers ($n = 12$) reported a 24% improvement in ease of awakening ratings ($p = 0.005$) following dried kiwifruit consumption while those who consumed fresh kiwifruit had a trend toward improved awakenings ($p = 0.052$) compared to controls. Both kiwifruit groups recorded increased urinary output of serotonin metabolites ($p = 0.004$).

Kiwifruit are internationally recognised for their dietary fibre content and established positive effects on gastrointestinal functioning in gut-compromised and healthy populations (Bayer et al., 2022a). Daily consumption of ~ 2.4 green kiwifruit for three weeks was associated with increased laxation frequency and softer stools in healthy older adults (> 60 years) in a free-living crossover design (Rush et al., 2002); and increased stool frequency, stool form and colonic volume in healthy adults aged 18 - 65 years ($n = 14$) in a controlled crossover trial (Wilkinson-Smith et al., 2019). In adults with irritable bowel syndrome (IBS), consuming two green kiwifruit daily for four weeks was associated with increased bowel movements and reductions in stool transit time, abdominal pain and indigestion compared to healthy controls (Chang et al., 2010; Gearry et al., 2022). Green and gold kiwifruit consumption has also increased frequency of bowel movements, decreased need for laxatives, improved stool consistency, improved gut comfort and reduced straining (Chan et al., 2007; Cunillera et al., 2015; Gearry et al., 2022). Green and gold kiwifruit consumption significantly improved gastrointestinal functioning but with fewer side effects in adults with chronic constipation compared to an over-the-counter fibre-matched laxative (psyllium) and a known natural remedy (prunes; Bayer et al., 2022b; Chey et al., 2021).

Overall, the evidence for the nutritional properties and health benefits of green and gold kiwifruit is substantial. Growing consumer awareness and acceptability of kiwifruit as a nutritious, appetising whole food (Pinto & Vilela, 2018) and the recognition within the health and dietetics professions of the benefits of kiwifruit consumption to human health, have kiwifruit well-placed as a whole-food dietary strategy to support health and wellness (Richardson et al., 2018).

1.6.3 Kiwifruit and Psychological Health

Kiwifruit have the potential to affect not only physiological health, but psychological health through a number of pathways. Kiwifruit contain nutritionally relevant levels of vitamins C and E, folate and dietary fibre, all of which have been implicated in the pathophysiology of depression (Bender et al., 2017; Ding & Zhang, 2022; Lydiard, 2001). Furthermore, kiwifruit contain numerous amino acids (e.g., serotonin and tryptophan) that are implicated in mood regulation within the CNS and gastrointestinal motility in the gut (Briguglio et al., 2018). The putative pathways are reviewed below.

SunGold and green kiwifruit are considered a good source of dietary folate (82 µg and 73 µg/100 g, respectively) and compare favourably alongside other commonly consumed fruits (apple 3 µg, orange 39 µg and strawberry 20 µg per 100 g; NZIPFRL, 2021). Current evidence for the use of folate in depression is mixed, however there is sufficient evidence for the active form of folate, methyl-folate, to be promoted as an adjuvant therapy to psychopharmacological treatment of depression (Malhi et al., 2015; Sarris et al., 2016).

SunGold and green kiwifruit contain nutritionally relevant levels of vitamin E (NZIPFRL, 2021), a micronutrient with antioxidant and anti-inflammatory properties, processes linked to the attenuation of depressive symptoms (Manosso et al., 2020). Depression has been associated with low serum vitamin E concentration, suggestive of reduced antioxidant defences (Maes et al., 2000).

Dietary fibre has the potential to influence psychological health by modulation of the microbiota-gut-brain-axis (Aslam et al., 2023). The gut-brain axis is a bi-directional communication network linked by the autonomic nervous system, hypothalamic-pituitary-adrenal axis and nerves within the gastrointestinal tract (Appleton, 2018). Changes in the microbiota can directly and indirectly effect the emotional and cognitive activity of the brain (Appleton, 2018). For example, in the context of kiwifruit, an *in vitro* study demonstrated that the non-digestible carbohydrates in SunGold kiwifruit effected favourable changes to the composition of human colonic microbiota (Blatchford et al., 2015). A comprehensive review of earlier work noted that consumption of kiwifruit positively modulated colonic microbiota, and that the polyphenolics, non-digestible carbohydrates and vitamins in kiwifruit support the health of the large intestine and overall wellbeing (Ansell et al., 2013).

The acknowledged associations between gastrointestinal health and depression (Farhadi et al., 2018) and symptom relief from adequate dietary fibre intake (Barber et al., 2020) suggest that the dietary fibre within kiwifruit may indirectly support psychological health by improving gastrointestinal functioning. Functional gastrointestinal disorders such as IBS and Functional Constipation (FC) are characterised by chronic abdominal pain, bloating, constipation, diarrhoea and other debilitating symptoms (Lovell & Ford, 2012). Individuals with these disorders exhibit greater levels of psychological and biological reactivity to stressors which subsequently informs gut discomfort and pain perception (Markert et al., 2014). FC-compromised populations exhibit high comorbidity with depression (30%) and suicidal ideation is present in 15% to 38% of individuals with IBS (Van Oudenhove et al., 2016). Kiwifruit stand to support psychological health outcomes from improved gastrointestinal functioning through enhanced dietary fibre intake.

Kiwifruit contain high levels of serotonin (between 6.0 to 9.52 µg/g; Herraiz & Galisteo, 2003; Islam et al., 2016), a monoamine neurotransmitter involved in a number of pathophysiological pathways in the CNS such as glucose metabolism, mood regulation, sleep, appetite and gastrointestinal motility (Briguglio et al., 2018). Gold kiwifruit also contain tryptophan (7 µg/g) and high levels of a tryptophan metabolite, tryptamine (9 µg/g; Drummond, 2013). The role of tryptophan in serotonin synthesis is considered an important factor in mood regulation (Richard et al., 2009). Serotonin synthesis occurs in the neurons of the gut and tryptophan is a substrate for the amino acid transporter system which successfully crosses the blood-brain barrier to allow serotonin innervation throughout diffuse networks within the brain and CNS (Jenkins et al., 2016). Diets high in tryptophan have been associated with greater positive mood states compared to a low tryptophan diet (Lindseth et al., 2015).

The mood-enhancing properties of vitamin C from kiwifruit may be enhanced by its interaction with vitamin E, whereby vitamin C supports vitamin E bioavailability by recycling it back to its original form (Shahidi et al., 2021). Furthermore, dietary vitamin C intake is recognised for its ability to enhance iron absorption when consumed with meals (Beck et al., 2011), and low dietary iron intake and iron deficiency has been associated with depression in observational and intervention studies (Li et al., 2018; Lomagno et al., 2014).

1.6.4 Kiwifruit and Psychological Health – Trial Outcomes

To date, there have been two dedicated trials conducted that examined the effects of increased vitamin C intake through kiwifruit consumption and psychological health. These are examined in greater detail in Chapter 3, but a brief overview is provided hereunder.

In the first trial, young adults aged 18 - 35 years (n = 167) with sub-optimal vitamin C status (< 50 µmol/L) were randomised to receive either 2 SunGold kiwifruit/d, an equivalent dose of synthetic vitamin C in tablet form (250 mg/d) or placebo (1 tablet/d - a sham intervention described to participants as having the same nutritional profile as kiwifruit and similar in appearance to the vitamin C tablet) for 28 days (Conner et al., 2020). Consumption of SunGold kiwifruit significantly improved mood and wellbeing, with improvements in wellbeing sustained across a two-week washout compared to the supplement condition. SunGold kiwifruit consumption improved mood and vitality within four days and peaked around 14 - 16 days, whereas the supplement marginally improved mood up to day 12 before reducing thereafter (Conner et al., 2023). Although plasma vitamin C concentration had increased significantly after 14 days of the 28-day trial in the gold kiwifruit and supplement conditions, gold kiwifruit consumption was associated with a greater mean increase and higher total plasma vitamin C concentration compared to the supplement (Conner et al., 2023). Increased wellbeing was observed in the supplement condition, but only for participants who had persistently low vitamin C status during the two-week lead-in (Conner et al., 2020). There were no effects on psychological health for the placebo condition.

In another trial, otherwise healthy adult males aged 18 - 35 years (n = 35) with sub-optimal vitamin C status (< 40 µmol/L) were supplemented with either half a kiwifruit or two gold kiwifruit daily for six weeks (Carr et al., 2013a). Compared to the half kiwifruit condition, consuming two gold kiwifruit was associated with a 35% reduction in mood disturbance (p = 0.06) and a 32% decrease in depression scores (p = 0.024). A sub-group analysis of participants with higher-than-average baseline mood disturbance scores (n = 8) who consumed two kiwifruit daily highlighted significant reductions in fatigue (38%, p = 0.048) and mood disturbance (38%, p = 0.029) and a trend toward increased feelings of vigour (34%, p = 0.075).

1.6.5 Kiwifruit – Summary

Kiwifruit have been pronounced as unequalled in their nutrient density, health benefits and consumer appeal compared to other commercially available fruit (Stonehouse et al., 2013). The exceptionally high vitamin C content of kiwifruit, along with other nutrients associated with psychological health make it ripe for continued research to identify the individual and synergistic contribution to psychological outcomes from the panoply of nutrients therein. To date, a small body of work has emerged exploring the potential benefits of SunGold kiwifruit to psychological health from what is considered the flagship nutrient of gold kiwifruit, vitamin C. Further research involving larger, randomised trials across diverse populations is warranted.

1.7 Conclusions

Depression continues to contribute to the significant individual, societal and global burden of disease (Vos et al., 2020). Despite a large body literature concerning the aetiology, prevention and treatment of depression, prevalence rates continue to climb, treatment seeking rates remain low and a sizeable proportion of evidence-based treatments do not result in remission (Thornicroft et al., 2017). The availability of accessible, affordable, minimally adequate psychological services is currently insufficient to meet the treatment needs of clinical and mild to moderately depressed populations (Andrade et al., 2014; Thornicroft et al., 2017). Thus, it is not surprising that lifestyle-based mental health care interventions are the focus of considerable current scientific research. Indeed, this growth of research mirrors the growing public awareness, use of, and demand for healthy, affordable adjunctive treatments for depression (Xue et al., 2007).

Whole-of-diet interventions such as the MDP have demonstrated efficacy in reducing depression in clinical and sub-clinical populations when delivered by accredited dietitians/nutritionists (Owens et al., 2020). It is likely that the intensive, multi-disciplinary paradigms applied in some of the RCTs (e.g., SMILES trial; Jacka et al., 2017) are beyond the financial and pragmatic reach of many individuals, particularly those experiencing depressive symptomatology. Thus, it is incumbent on the nutrition research community to continue to identify additional avenues, such as single-food or targeted single-nutrient dietary applications with evidence-based impacts on psychological health to inform both clinicians and the public of preventative and adjuvant dietary treatment approaches to mental health.

While there have been consistent associations between psychological health and dietary intake of individual food groups (i.e., fruits) in prospective studies (Głąbska et al., 2020), the evidence base for single foods is limited. Research has typically examined individual micronutrients (e.g., vitamin C, polyphenols) associated with depression and psychological health, and to date, results are promising (Kontogianni et al., 2020; Zhang et al., 2011). The aim of the present research was to augment this work and provide critical new information regarding the potential for a particular wholefood, namely, kiwifruit to support the psychological health of adults with mild to moderate mood disturbance through increased vitamin C intake.

Chapter 2: Exegesis

The direction and development of this thesis was generated from a number of personal, pragmatic and professional factors. The broad subject matter was pre-determined as part of a joint industry PhD (iPhD) initiative. Overall, the research aimed to explore *the role of kiwifruit in supporting psychological health and wellbeing*.

My career as a Clinical Psychologist has taught me that mental health is not just about thoughts and feelings. It is not just about thinking differently about our interactions with the world around us in the hope that our feelings will change. It is also about the body. Mental health, and depression in particular, is characterised by mood, cognitive and affective disturbances and reduced quality of life (Marx et al., 2023b). The negative symptoms of depression such as fatigue, loss of motivation and negative self-view, make engaging in any form of behavioural change particularly problematic. The application of lifestyle-based interventions in mental health care holds intuitive appeal and offers low-risk, low-cost strategies to augment the first-line treatments (psychology and psychopharmacology) in the prevention and management of depression (Sarris et al., 2014).

Behavioural and health determinants are considered major risk and protective factors for depression. Maintaining good physical health by engaging in regular physical activity, adopting a healthy day-night structure and consuming a nutrient-dense diet are considered important protective factors against depression and sit opposite their counterpoint risk factors of physical inactivity, substance use and poor diet (Marx et al., 2023b). Thus, the potential for a whole food dietary intervention such as kiwifruit to support psychological health and form part of a broader lifestyle-based treatment intervention plan is a promising proposition.

The overarching framework of the thesis was first, to develop a solid understanding of the literature regarding diet and nutrition and the associations with psychological health, and to identify gaps in the literature that warranted further investigation (Study 1); second, to undertake a feasibility trial to determine the practicability of conducting a larger intervention trial with the chosen population of interest (Study 2); and finally, to conduct a randomised controlled trial to examine the benefits of kiwifruit consumption on psychological health (Study 3).

2.1 Study 1

The purpose of Study 1 was to conduct a review of the literature to collect and synthesise the existing research from randomised controlled trials examining the effects of kiwifruit consumption on psychological health in adult populations. It was identified *a priori* that research involving kiwifruit and psychological health was in its infancy and this was borne out in the limited volume of work retrieved. There was, however, a considerable body of evidence from observational, epidemiological and intervention studies that had established the influence of diet and nutrient intake on mental health and in particular, the associations between vitamin C and mood outcomes. The decision was taken to conduct a rapid review based on, a) the volume of existing literature, and b) that this method of literature review is particularly suited to answering a defined research question, as was the case in the present research (Watt et al., 2008b).

From the existing literature on kiwifruit, it was evident that the two commercially dominant cultivars, *Actinidia deliciosa* “Hayward” (Green kiwifruit) and the *Actinidia chinensis* var. *chinensis* ‘Zesy002’ (SunGold kiwifruit), were regarded as nutrient-dense fruits with established health benefits. Consumption of green and gold kiwifruit was linked to improvements in nutritional status, digestive health, immune support and metabolic health (Richardson et al., 2018). Where the foci of the research on each cultivar differed however, had been primarily driven by the predominant constituent of each, in terms of the quantity compared to other commercially available fruits. Those being, the high dietary fibre content of the green kiwifruit and the exceptionally high vitamin C content of the gold kiwifruit. The search terms for the literature review included both cultivars however, as the green kiwifruit is also recognised for its substantial vitamin C content. Additionally, it was identified *a priori* that there was likely to be only a small set of studies devoted to kiwifruit and psychological health.

The literature search identified two randomised trials that had delivered gold kiwifruit interventions and measured psychological outcomes such as mood, vitality and wellbeing (Carr et al., 2013a; Conner et al., 2020). Participants in the two trials were otherwise healthy adults aged 18 - 35 years with sub-optimal vitamin C concentrations (< 50 µmol/L). In both cases, subjects were not recruited based on mental health status. This was considered an important distinction and something that warranted further investigation. Additionally, the previous trials had recruited adults aged 18 - 35 years, further limiting the generalisability of findings. Considered a strength of the two foundational studies, the present research maintained a focus on positive affective states of psychological health such as feelings of wellbeing and vitality rather than a singular focus on negative affective states such as depression and anxiety. Thus, the decision was made to examine the effect of a SunGold kiwifruit intervention on psychological health in adults aged 35 - 60 years with mild to moderate mood disturbance. This study and its results are the subject of Chapter 4.

In summary, the purpose of Study 1 was to conduct a search of the literature to collect any available evidence from research that had undertaken human intervention trials involving either kiwifruit cultivar with constructs of psychological health as the primary outcome of interest; and to identify any gaps in the literature that warranted further investigation.

2.2 Study 2

Given the generally positive findings uncovered in Study 1, the purpose of Study 2 was to design and implement a randomised feasibility trial to assess the practicability of conducting a larger trial recruiting adults aged 35 - 60 years with mild to moderate mood disturbance and sub-optimal vitamin C status. This cohort was chosen for a number of reasons. First, the findings of Carr *et al.* (2013a) highlighted that participants with higher baseline mood disturbance experienced greater mood improvement compared to those with low baseline mood disturbance. Second, it was necessary to recruit a cohort with sub-optimal vitamin C status in order to maximise the possibility of observing an effect from increased vitamin C intake (Lykkesfeldt & Poulsen, 2010). Finally, Carr *et al.* (2013a) and Conner *et al.* (2020) recruited 18 - 35 year olds and the present research saw value in examining a different age cohort (35 - 60 years), and in particular, one that is associated with a higher prevalence of mood disturbance and MDD (Arias de la Torre et al., 2021). This was later expanded to 18 - 60 years to combat under-recruitment. A multiple N-of-1 baseline design was chosen as it is well-suited to an early-stage trial where there is not substantial evidence for the efficacy of the intervention and when the intervention is expected to confer effects in the short-term, as was the case in the feasibility trial. Participants were randomised in a staggered-start fashion to either a two- or four-week baseline prior to completing a 28-day intervention (2 SunGold kiwifruit/day) followed by a two-week post-observation period. The staggered start was established to counter any potential challenges in recruitment and to ensure research staff and clinic resources were not over-burdened.

We attempted to use similar methodology to the two previous studies (Carr et al., 2013a; Conner et al., 2020) where appropriate to our research question and study aims. This decision was based on the understanding that a degree of homogeneity between all studies would support any future systematic review or meta-analysis. Thus, the choice of intervention, dose rate and duration of the intervention period were similar to the previous trials. We used a number of the same psychological assessment instruments as the preceding trials with the addition of a subjective measure of vitality. The latter measure was included as there were observed improvements in psychological concepts aligned with vitality, conceptualised as feelings of less fatigue, improved mood, decreased levels of depression and anxiety and having a zest for life, in one of the trials (Conner et al., 2020) and neither trial had assessed vitality as a distinct construct. The current project extended the research further by incorporating a measure of gastrointestinal functioning. Study 1 identified that kiwifruit had demonstrated efficacy in reducing gastrointestinal symptoms such as constipation and abdominal pain in adults with functional gastrointestinal disorders (Gearry et al., 2022), conditions with established positive associations with depression (Mukhtar et al., 2019). Assessing gastrointestinal functioning had the dual purpose of adding to the nascent research examining the efficacy of SunGold kiwifruit in supporting gut health and controlling for any indirect effects on psychological health from improved gut functioning.

The decision to recruit from the narrow bandwidth of adults with mild to moderate mood disturbance and sub-optimal vitamin C contributed to under-recruitment. Additionally, using a non-validated measure of subjective dietary vitamin C intake as a screening tool contributed to a substantial number of applicants being ineligible. A number of protocol amendments were initiated to aid recruitment including expanding the eligible age range from 35 - 60 years to 18 - 60 years of age, securing additional media advertising and conducting a bulk mail-out to an existing Commonwealth Scientific and Industrial Research Organisation (CSIRO) volunteer database. Despite these amendments, the study failed to achieve the target sample size ($N = 30$). The trial was undertaken between September to November 2021, during the COVID-19 pandemic when pandemic travel restrictions and temporary lockdowns in Adelaide were at their most severe. The degree to which this may have affected interest, recruitment or participation in the study is unquantifiable. Additionally, a brief psychological assessment instrument delivered weekly by smartphone application suffered from poor compliance. Despite the many challenges, trial results suggested that a larger, randomised trial was feasible, but would require careful consideration of eligibility criteria and other issues identified during the feasibility trial.

In summary, the purpose of Study 2 was to design and implement a feasibility trial to determine the practicability of conducting a larger, randomised trial in adults with mild to moderate mood disturbance and sub-optimal vitamin C concentration.

2.3 Study 3

Findings from the aforementioned feasibility study were used to guide the development of Study 3: A randomised crossover trial examining the effect of daily consumption of gold kiwifruit on psychological health in adults with mild to moderate mood disturbance.

Forewarned with the lessons learnt from Study 2, certain eligibility criteria, screening instruments and assessment protocols were not incorporated into the design of Study 3. It was decided to remove the plasma vitamin C concentration as an eligibility criterion. Although this introduced a potential confound in that participants might enter the trial vitamin C-replete, the trial aimed to recruit a sufficient number of participants to allow for a sub-group analysis to be carried out on participants with sub-optimal vitamin C concentrations. However, it was subsequently determined that this sub-analysis could not be performed due to insufficient participant numbers. The self-report vitamin C dietary intake screening tool was also removed, as data analysis from Study 2 revealed that it was poorly correlated with objective blood screen results. Other changes included establishing the age eligibility criterion as 18 - 60 years from the outset and removing a smartphone-delivered, weekly psychological assessment instrument that had suffered from poor compliance in Study 2.

Study 3 was a two-period, non-blinded crossover trial with participants randomised to a counter-balanced sequence. During each 4-week period, participants consumed either two SunGold kiwifruit daily or their usual diet, with the periods separated by a two-week washout. This design was chosen as it served to reduce the sample size required and had each participant serving as their own control (Harris & Raynor, 2017). A common disadvantage of crossover designs is the potential for increased dropouts due to participant burden from extended trial duration (Lim & In, 2021). However, dropout rates from the previous trials (Study 2; Carr et al., 2013a; Conner et al., 2020) were low and the removal of the weekly smartphone assessment of mood reduced participant burden. Ideally, the inclusion of a placebo condition and/or a supplement intervention delivering the same quantity of vitamin C as the kiwifruit would have at the very least, introduced a single-blind within the experiment. However, achieving a double-blind in the present dietary intervention would be challenging and it was also not possible within the pragmatic constraints of a PhD project. Other than the smartphone assessment, all other measures were retained for Study 3. Thankfully, a repeat of the recruitment difficulties from Study 2 was not replicated and the final sample size (N = 26) was just short of target (N = 30). The COVID-19 pandemic continued across the trial period and some data points were lost due to participant illness or contact restrictions. On these occasions when blood sampling could not be undertaken, participants were asked to complete the psychological assessments in their home via an online survey platform.

In summary, the purpose of Study 3 was to examine the effect of a SunGold kiwifruit intervention on the psychological health of adults with mild to moderate mood disturbance through increased vitamin C intake.

Chapter 3: Study 1

The Role of Kiwifruit in Supporting Psychological Well-Being: A Rapid Review of the Literature

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NOTE: The following chapter is identical to the published article except for modifications to section numbering, table numbering and figure numbering to maintain consistency throughout this dissertation

3.1 Statement of Authorship

Principal Author

Name of Principal Author (Candidate)	Michael Billows		
Contribution to the Paper	Collaboratively developed the research objectives; performed literature searching; wrote initial draft; collaborated on editing of final drafts.		
Overall Percentage (%)	80		
Certification	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual arrangements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	07 March 2024

[1] Billows, M., Kakoschke, N., & Zajac, I. T. (2022). The Role of Kiwifruit in Supporting Psychological Well-Being: A Rapid Review of the Literature. *Nutrients*, 14, 4657. https://doi.org/10.3390/nu14214657

Co-author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate to include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution

Name of Co-Author	Ian T. Zajac		
Contribution to the Paper	Collaboratively developed the research objectives; discussed results; edited drafts; advised on responses to reviewers; acted as corresponding author		
Signature		Date	07/03/2024

Name of Co-Author	Naomi Kakoschke		
Contribution to the Paper	Collaboratively developed the research objectives; discussed results; edited drafts; advised on responses to reviewers		
Signature		Date	26/02/2024

3.2 Abstract

Consumption of vitamin-rich fruits and vegetables is emerging as a recommendation for the prevention and treatment of depression and anxiety. This review sought to examine literature investigating the role of kiwifruit in supporting psychological well-being in adult populations through increased vitamin C intake. The literature search using CINAHL, Embase and PubMed databases was restricted to English-language articles published from 2005 through July 2022. Inclusion criteria were randomised trials that delivered kiwifruit interventions to adult populations assessing psychological well-being. Studies were assessed for bias using the Joanna Briggs Institute (JBI) critical appraisal tool for randomized controlled trials. The literature search identified two eligible trials involving 202 participants that delivered gold kiwifruit interventions and evaluated aspects of psychological well-being

(e.g., mood disturbance, vitality, vigor, depression). Daily consumption of two gold kiwifruit was associated with significant reductions in mood disturbance and fatigue, and significant increases in well-being and vigor. Larger effects were observed in participants with higher baseline mood disturbance. Additional research involving a broader range of cohorts and isolating the effects of other micronutrients within gold kiwifruit implicated in the pathophysiology of depression is warranted. Overall, preliminary evidence suggests that daily consumption of two gold kiwifruit might improve psychological well-being in adult populations.

3.3 Introduction

3.3.1 Mental Health and Psychological Well-being

The global burden attributable to depressive and anxiety disorders in adults is considerable with depressive and anxiety disorders ranked as the sixth and fifteenth leading cause of disability-adjusted-life-years (21.6 & 28.7 million respectively) in adults aged 25-49 years in 2019 (Vos et al., 2020; Xiong et al., 2022). Recognising the lifespan prevalence and the growing burden of depressive disorders, between 1990 and 2019 depressive disorders rose from the nineteenth to the thirteenth leading cause of disability-adjusted-life-years across all ages (GBD, 2022). The World Health Organization (WHO) estimated that in 2015, 4% of the global population (322 million) were living with depression (WHO, 2017). Twelve-month and lifetime prevalence rates of depression in adults have been calculated at 7% and 11%, respectively (Lim et al., 2018). The psychosocial burden on individuals living with depression is substantial including negative effects on quality of life, activities of daily living, cognition and mood, employment status, mortality and interpersonal relationships (Kennedy, 2008; Proudman et al., 2021). The financial cost associated with depression for individuals and society are not inconsequential. In developed nations, health care costs for individuals with depression can be 30% greater than those in the general population (Culpepper et al.,

2022) and societal costs in the USA were estimated at USD$326.2 billion in 2018 (Proudman et al., 2021).

Despite the high prevalence rates and level of disease burden wrought by depression, and seemingly at odds with our knowledge of the condition and efficacious treatments (e.g., pharmacotherapy and psychological interventions), the frequency of help-seeking rates remains concerningly low. Global estimates of the treatment gap for depression, representing the difference between the prevalence of the disorder and the proportion of individuals treated for depression, suggest more than half (56%) of all individuals with depression do not receive any treatment (Kohn et al., 2004). A review paper examining the WHO's World Mental Health Surveys reported that 57% of individuals with Major Depressive Disorder identified the need for treatment (Thornicroft et al., 2017). Of these, 71% had attended at least one visit to a service provider, however only 41% received treatment that satisfied minimal standards.

Although depression is diagnosed and treated in health care settings, barriers exist to professional treatment delivery. Access to treatment providers, costs of treatment, and demand for services that outstrip supply contribute to low levels of treatment and high prevalence rates (Thornicroft et al., 2017). Fortunately, treatment for depression is not restricted to pharmacotherapy and psychological interventions. Lifestyle factors such as regular exercise, positive social supports, stress management, adaptive sleep hygiene behaviors and healthy dietary patterns have been associated with reduced risk of depression and higher psychological well-being (Marx et al., 2021; Piotrowski et al., 2021; Sapranaviciute-Zabazlajeva et al., 2022). Moreover, many of these factors are accessible outside of formal treatment pathways and allow the individual to exercise influence over their psychological well-being. Supporting the positive consumer perception of the value of lifestyle factors in moderating mental health outcomes, a recent national survey identified that almost 61% of respondents took some form of self-initiated action to improve their psychological well-being (ABS, 2020). These actions included increasing their level of physical activity (37%), accessing social supports (24%) and practicing relaxation techniques (23%). Recognising growing public interest in the effect of diet and nutrition on mental health outcomes, more than 20% of respondents reported changing their diet and 15% initiated vitamin and supplement intake to maximise their psychological well-being.

3.3.2 Diet and Psychological Well-being

A recent randomized controlled trial (HELFIMED trial) examined the influence of a Mediterranean-style diet, characterised by high intake of legumes, nuts, seeds, wholegrains, fruit, vegetables and olive oil, supplemented with fish oil in adults with self-reported depression (Parletta et al., 2019). Results at three months showed that adherence to the Mediterranean diet was associated with increased consumption of fruit, nuts and vegetables and was associated with reductions in symptoms of depression. A Mediterranean diet intervention was also associated with improved self-reported quality of life and decreased depression symptomatology in young males (Bayes et al., 2022). Offering another pathway to improved psychological well-being, provision of nutrition education counselling (i.e., emphasising the benefits from fruit and vegetable consumption and biological effects of active constituents such as vitamin C) was associated with increased fruit and vegetable consumption, increases in plasma vitamin C concentrations and improvements in quality of life in a community setting (Steptoe et al., 2004).

The consequences of inadequate fruit and vegetable intake on adult psychological well-being are substantial. Population-based surveys have reported that higher fruit and vegetable consumption was associated with reduced odds of experiencing an anxiety or mood disorder, positive mental health, and greater psychological well-being (Emerson & Carbert, 2019; Sapranaviciute-Zabazlajeva et al., 2017). Elsewhere, it has been reported that five serves of fruit and vegetables per day conferred reduced risks of anxiety and cognitive impairment

(Péneau et al., 2011; Wu et al., 2018). Longitudinal studies have reported that increased fruit and vegetable consumption was associated with reduced psychological distress and risk of depression, and increased well-being, life satisfaction and happiness (McMartin et al., 2013; Mihrshahi et al., 2015; Mujcic & Oswald, 2016; Nguyen et al., 2017). Thus, evidence to date suggests that dietary interventions, both those that adopt specific food group or generalised approaches to improved dietary intake, might offer useful adjunctive avenues for the prevention and treatment of common mental health disorders and improve psychological well-being.

3.3.3 Vitamin C and Psychological Well-being

In addition to considering the impacts of whole of diet and food-group approaches on well-being and mental health, research has also considered the role of specific vitamins and minerals. Vitamin C is one such micronutrient that has garnered significant attention in the diet and well-being landscape. Vitamin C is a water-soluble micronutrient that humans, along with only several other species, are unable to synthesize themselves despite having an absolute requirement for vitamin C for a range of important biological functions (Harrison et al., 2014). The dialectical opposition between an absolute requirement for vitamin C and our species' loss of ability to synthesise it, has been explained by the concept that our early ancestors relied on diets rich in vitamin C which led to the eventual pruning of genes involved in endogenous vitamin C synthesis (Amin, 2016). Therefore, vitamin C must be obtained exclusively from diet, principally through the consumption of fruits and vegetables (Pearson et al., 2017). Vitamin C acts as an antioxidant and free radical scavenger and is an essential cofactor in numerous enzymatic reactions including that of dopamine β-hydroxylase, an enzyme that is central to the synthesis of adrenaline from dopamine. Vitamin C also acts as an essential cofactor in the metabolism of tryptophan, a necessary requirement for the synthesis of serotonin (Evans-Olders et al., 2010; Pullar et al., 2018a; Schlueter &

Johnston, 2011). Altered dopamine *β*-hydroxylase activity has been described in a range of psychiatric conditions including mood and anxiety disorders and disorders of the digestive tract (Gonzalez-Lopez & Vrana, 2020) and acute tryptophan depletion has been associated with reduced serotonin levels and lowered mood states (Jenkins et al., 2016). Emerging work in the field of epigenetics indicates that vitamin C contributes to epigenetic modifications in early development which in turn may influence key psychological and physiological outcomes across the lifespan (Stover et al., 2018; Young et al., 2015). Reinforcing its role in neurocognitive functioning, the highest concentrations of vitamin C in humans are found in the brain and cerebrospinal fluid and vitamin C is preferentially retained in these areas even when plasma and other organs in the body are depleted of vitamin C (Hansen et al., 2014).

The relationship between vitamin C and psychological well-being in adult populations has been examined through cross-sectional studies, albeit with mixed results. Depression symptoms along with overall mood disturbance, anger and confusion were inversely related to plasma vitamin C concentrations in a cross-sectional study of male tertiary students (Pullar et al., 2018a). In contrast, others have reported no significant associations between fatigue and mood in a similar-aged cohort (Sim et al., 2022) nor in a cohort of healthy adults aged 50-years old (Pearson et al., 2017). Heterogeneity of ethnicity may have contributed to the mixed results between these studies (Fletcher et al., 2021). Intervention studies delivering vitamin C in supplement form have also returned mixed results. Acutely hospitalised elderly patients supplemented with 500 mg vitamin C twice-daily for 7-14 days experienced reductions in mood disturbance scores and psychological distress (Evans-Olders et al., 2010; Wang et al., 2013; Zhang et al., 2011). Healthy young adults supplemented with 1000 mg/day vitamin C (3x/day) for 14 days exhibited a reduced subjective stress response (Brody, 2002), and 500 mg/day supplementation of vitamin C was associated with mood improvements and increased vigor in healthy adult males (Kennedy et al., 2010). Conversely, no associations were found between vitamin C supplementation and levels of fatigue or mood in healthy adults supplemented with 1000 mg/day in a recent placebo-controlled trial (Sim et al., 2022). Against the backdrop of the established associations between adequate fruit intake, plasma vitamin C concentrations and psychological well-being, the equivocal results from supplement studies compels researchers to investigate whether mental health outcomes might be supported by daily consumption of fruits that are recognised for their high vitamin C concentrations.

3.3.4 Kiwifruit

Kiwifruit, the commercial designation of plants from the genus Actinidia are a nutrient-dense fruit that contain high levels of micronutrients including vitamins, minerals, proteins as well as compounds such as phytonutrients, enzymes and other antioxidants (Fletcher et al., 2021). Importantly, kiwifruit are recognised for their exceptionally high vitamin C content. The two most commercially popular and studied varieties are Actinidia chinensis var. chinensis ‘Zesy002’ Zespri^{TM} SunGold and Actinidia deliciosa ‘Hayward’ kiwifruit (hereinafter referred to as gold kiwifruit and green kiwifruit, respectively).

A growing body of research has demonstrated the putative health benefits associated with gold and green kiwifruit consumption. Specifically, both varieties have positive associations with digestive and metabolic health outcomes (Richardson et al., 2018). More recently, research has begun to link potential benefits of gold kiwifruit consumption to improved psychological well-being. A single serve (90 g) of gold kiwifruit delivers more than three times the recommended daily intake of vitamin C for adults (45 mg/d) and contains almost 70% more vitamin C than the green kiwifruit (137 mg & 79 mg respectively; NHMRC, 2006; NZIPFRL, 2021). When judged against other commercially popular fruits, the vitamin C content of gold kiwifruit easily surpasses the levels typically found in oranges (46.9 mg), strawberries (41 mg), bananas (5 mg), blueberries (3.5 mg) and pineapple (22.5

mg) per single serve (NZIPFRL, 2021). The high vitamin C content of gold kiwifruit has it well-placed to serve as an important whole food vector for the delivery of vitamin C, a micronutrient with established associations with psychological well-being.

3.4 Aim of Review

The aim of this rapid review is to summarise the available literature from randomized controlled trials that have examined the impact of kiwifruit interventions on psychological well-being in adult populations

3.5 Method

3.5.1 Research Question

Does kiwifruit consumption support psychological well-being in adult populations through increased vitamin C intake?

3.5.2 Design

This review was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA 2020 statement) and PRISMA for abstracts (Beller et al., 2013; Page et al., 2021) with consideration given to applicability of PRISMA 2020 statement items to a rapid review. The rapid review method was selected as the authors identified a priori that a paucity of literature existed pertaining to the research question. Furthermore, it was recognised that this style of review was well suited to introducing primary research articles, informing clinical practice of the development of new treatments, and responding to specific research questions, as was the case in the present article (Abrami et al., 2010; Watt et al., 2008b). Rapid reviews have been shown to produce similar results compared to systematic reviews, are rooted in the scientific method, and can offer adequate advice for clinical decision-makers (Ganann et al., 2010; Moher et al., 2015; Visram et al., 2016).

3.5.3 Inclusion and Exclusion Criteria

Eligibility criteria were determined using the PICO (population, intervention, comparisons and outcome) framework (Page et al., 2021) and was arrived at through author consensus. Studies were included if they were randomized controlled trials or observational trials of adult (≥18 years of age) populations. Studies were selected if the active intervention was identified as any form (i.e., whole fruit or kiwifruit-derived nutritional ingredients) of gold or green kiwifruit, or if, in the case of observational studies, kiwifruit was identified as an explanatory variable. Intervention studies that utilised a methodologically justifiable comparator (i.e., placebo or another dietary condition) were included. Studies were excluded if they did not quantify the amount of kiwifruit consumed, delivered kiwifruit as part of a larger intervention (i.e., MDP), did not contain original data or if results of the outcome(s) of interest were not measured or reported.

The primary outcome measure of interest was psychological well-being. Psychological well-being was considered a catch-all term to encompass a range of constructs including mood, psychological distress, depression, anxiety, stress, vitality, vigor and mood disturbance. Only studies that assessed psychological well-being with validated and reliable psychometric assessment instruments were considered for inclusion. A secondary outcome measure was improvements in vitamin C concentrations determined by validated assessment tools (e.g., blood plasma pathology protocols). Studies that reported on vitamin C concentrations but did not assess psychological well-being were excluded. Eligibility criteria for inclusion was restricted to articles written in the English language and published between 2005 to the date of the database search. Restricting the search to English-language articles located in major bibliographic databases (Table 3) can produce results comparable to reviews using more comprehensive searches sans language restrictions and is considered a viable methodological protocol for rapid reviews (Garritty et al., 2021; Watt et al., 2008a).

3.5.4 Databases

Multiple databases (interface/platform) were utilised in the literature search to maximise integrity of the review (Abrami et al., 2010). CINAHL with full text (EBSCOhost), Embase (Ovid) and PubMed (NCBI) were searched on 05/07/2022.

Table 3

Search Terms (Search Conducted 5 July 2022)

Key Concept→ ↓Database (Platform)	Kiwifruit	Mental Health	Vitamin C
CINAHL with full text (EBSCOhost)	MH Kiwi + OR TI "Kiwi fruit" OR AB "Kiwi fruit" OR TI Kiwifruit OR AB Kiwifruit OR TI "Actinidia Deliciosa" OR AB "Actinidia Deliciosa" OR TI "Actinidia Chinensis" OR AB "Actinidia Chinensis" OR TI "Gold kiwifruit" OR AB "Gold kiwifruit" OR TI "Green kiwifruit" OR AB "Green kiwifruit" OR TI Zesy002 OR AB Zesy002 OR TI Sungold OR AB Sungold AND	MH "Mental health" OR MH Affect OR MH Depression OR AB Vitality OR TI Vitality OR MH "Psychological well-being" OR TI "Psychological well-being" OR AB "Psychological well-being" OR TI "Psychological well-being" OR AB "Psychological well-being" OR TI "Psychological distress" OR AB "Psychological distress" OR TI "Mood disturbance" OR AB "Mood disturbance" OR TI "Mood improvement" OR AB "Mood improvement" AND	MH "Ascorbic acid" + OR TI "Vitamin C" OR AB "Vitamin C"
Embase (Ovid)	exp Kiwifruit OR Kiwi fruit.ti,ab OR Kiwifruit.ti,ab OR exp Actinidia OR exp Actinidia chinensis OR Actinidia chinensis.ti,ab OR exp Actinidia deliciosa OR Actinidia deliciosa.ti,ab OR Gold kiwifruit.ti,ab OR Green kiwifruit.ti,ab OR Zesy002.ti,ab OR Sungold.ti,ab AND	exp Mental health OR Mental health.ti,ab OR exp Affect OR Affect.ti,ab OR exp Mood OR Mood.ti,ab OR exp Depression OR Depression.ti,ab OR Vitality.ti,ab OR exp Psychological well-being OR exp Psychological well-being OR Psychological well-being.ti,ab OR Psychological well-being.ti,ab OR Psychological distress.ti,ab OR Mood disturbance.ti,ab OR Mood improvement.ti,ab AND	exp Ascorbic acid OR Vitamin C.ti,ab
PubMed (NCBI)	Kiwi fruit[tiab] OR Kiwifruit[tiab] OR "Actinidia" [mh] OR Actinidia deliciosa[tiab] OR Actinidia Chinensis [tiab] OR Gold kiwifruit[tiab] OR Green kiwifruit[tiab] OR Zesy002[tiab] OR Sungold[tiab] AND	"Mental health" [mh] OR Mental health[tiab] OR "Affect" [mh] OR Affect[tiab] OR Mood[mh] OR Mood[tiab] OR "Depression"[mh] OR Depression[tiab] OR Vitality[tiab] OR Psychological well-being[tiab] OR Psychological well-being[tiab] OR Psychological distress[tiab] OR Mood disturbance[tiab] OR Mood improvement[tiab] AND	"Ascorbic acid" [mh] OR Vitamin C[tiab]

3.5.5 Search Terms

The key concepts identified in the research question (Kiwifruit, mental health, and vitamin C) were used to generate search terms developed by the first author. Final search terms were arrived at via consensus following review and discussion between MB and co-authors, NK and IZ. Two studies (Carr et al., 2013a; Conner et al., 2020) previously identified as pertinent to the research question were reviewed for key words to support formulation of search terms. An experienced and qualified librarian was engaged to help develop the search strategy and identify suitable databases and a basic logic grid was created and applied to the individual databases. Search terms (Table 3) remained consistent across databases with adjustments made to reflect differences in subject headings, field codes and truncations used within each database. The three key concepts were combined with AND in the search (i.e., Kiwifruit AND Mental health AND Vitamin C) to ensure that results mentioned all key concepts in the same article. The first author was responsible for undertaking the database search.

3.5.6 Screening

Title, abstract and full text screening of articles were completed by the first author.

3.5.7 Critical Appraisal

The first author was responsible for critical appraisal of the selected studies. Studies were appraised using the JBI critical appraisal checklist for randomized controlled trials (JBI, 2020).

3.6 Results

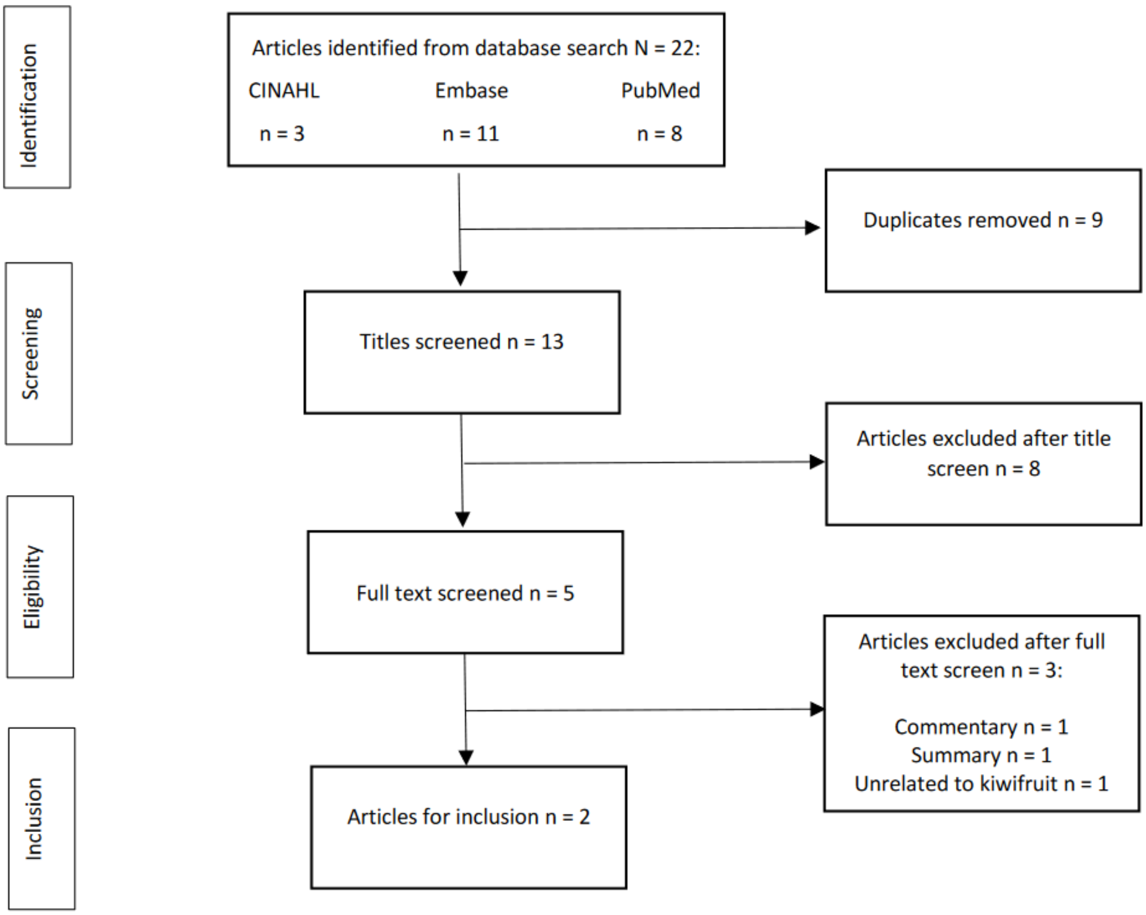
3.6.1 Search Outcomes

Twenty-two articles were captured in the initial search of the databases (CINAHL (n = 3), Embase (n = 11) and PubMed (n = 8). The study selection process is summarised in the

PRISMA flowchart (Figure 2). The citations were exported and combined into a single library using Endnote 20 software (EndNote, 2013). Full-text documents were retrieved for all articles.

Figure 2

PRISMA Flow Diagram of Rapid Review



After the removal of duplicates (*n* = 9), thirteen articles remained for title screening. Of these, eight were assessed as irrelevant to the research question and excluded. Five assessed kiwifruit micronutrient profiles or kiwifruit harvesting outcomes (Li et al., 2010; Ma et al., 2017; Oz, 2010; Qiu et al., 2020; Shan et al., 2021), one addressed chemotaxis and oxidant generation in humans (Bozonet et al., 2015), another examined the impact of functional foods on bone health (Kruger et al., 2015), and one article was identified as a study methodology that considered the relationship between kiwifruit and sleep (Kanon et al., 2019). Three of the remaining five articles were removed following full-text screening. These included an article identified as a commentary on one of the other articles (Belvoir, 2021), an article providing a summary of studies that examined nutritional intake and neurocognitive health (Bhatti, 2008), and a cross-sectional study that examined the relationship between blood plasma vitamin C status and psychological well-being without kiwifruit specificity (Fletcher et al., 2021). The remaining two articles (Carr et al., 2013a; Conner et al., 2020) were assessed as eligible for inclusion and critical appraisal.

3.6.2 Critical Appraisal

The included articles by Carr *et al.* (2013a) and Conner *et al*. (2020) satisfied more than half (9 and 8 items, respectively out of 13 items) of the criteria on the JBI appraisal tool and were deemed suitable for inclusion in the review. Both studies failed to satisfy checklist criterion related to the blinding of participants and researchers, an issue regularly encountered in clinical trials delivering whole-food interventions (Weaver & Miller, 2017).

3.6.3 Description of Included Studies

A summary of the studies included is provided at Table 4. Carr *et al.* (2013a) investigated the potential mood-enhancing properties of gold kiwifruit in young adult males ($N = 35$) with sub-optimal vitamin C concentrations at screening using a parallel-arms design. Participants were randomized to receive either one half of a gold kiwifruit per day or two gold kiwifruit per day across a 6-week intervention period following a 5-week lead-in. Psychological health as indicated via mood (65-item POMS) and plasma vitamin C assessment was completed at baseline and at the end of the intervention period. Following the intervention, participants ($n = 17$) supplemented with two gold kiwifruit per day displayed a trend towards a 35% decrease in total mood disturbance ($p = 0.061$) and depression ($p =$

0.063) on the POMS. A sub-group analysis of participants (*n* = 8) in the two kiwifruit/d condition with higher-than-average baseline total mood disturbance revealed a 38% decrease in mood disturbance (*p* = 0.029), a 38% decrease in fatigue scores (*p* = 0.048), a 31% increase in vigour (*p* = 0.023) and a 34% decrease in depression trending toward significance (*p* = 0.075). No effect on mood scores was observed in participants (*n* = 9) in the two kiwifruit/d condition with lower-than-average baseline total mood disturbance scores. Analysis of participants (*n* = 18) in the ½ kiwifruit per day condition revealed no effect of the intervention on mood outcomes. Plasma vitamin C concentrations increased significantly in both the low-dose and high-dose conditions following the intervention; however, a 15-fold increase in urinary vitamin C excretion was observed in the high-dose condition suggesting plasma ascorbate saturation for the high-dose group only.

Conner *et al.* (2020) employed a randomized, placebo-controlled trial examining the effects of gold kiwifruit on psychological well-being and subjective vitality. Young adults (*N* = 167, 61% female) aged 18-35 years with sub-optimal plasma vitamin C (<40 µmol/L) were randomized to receive either two gold kiwifruit per day, a daily 250 mg vitamin C supplement or a placebo tablet (1 tablet/day) across the 28-day intervention period, book-ended by two-week lead-in and two-week washout periods. Participants completed psychological well-being (POMS-SF, MFSI & WEMWBS) and fasting plasma vitamin C assessments at fortnightly intervals throughout the 8-week trial. Participants who consumed gold kiwifruit reported significant (*p* = 0.03) improvements in mood and well-being during the intervention period; and well-being improvements (*p* = 0.02) persisted during washout. Participants in the supplement condition exhibited non-significant improvements in well-being and decreased fatigue across the intervention period. Participants in the kiwifruit and supplement conditions returned significant improvements in plasma vitamin C. No effects on any outcomes were observed in the placebo condition.

Table 4

Summary of Included Studies

Citation	Participants	Study Design	Intervention	Study Timeline	Primary Outcome Measures	Main Findings
Carr et al. (2013a)	Males (*n* = 35), Mean age = 21 ± 3 years	Experimental with randomized parallel-arms, no control group	½ kiwifruit/d (*n* = 18), 2 kiwifruit/d (*n* = 17)	5-wk lead-in, 6-wk intervention	POMS–TMD; plasma vitamin C	Trend toward decrease in TMD ($p = 0.06$) and depression ($p = 0.06$) in 2 kiwifruit condition. No effect in ½ kiwifruit condition. Participants in 2 kiwifruit condition with higher baseline TMD experienced decrease in TMD ($p = 0.03$), decrease in fatigue ($p = 0.05$), increase in vigour ($p = 0.02$) and trend ($p = 0.07$) toward decrease in depression. Significant increase ($p < 0.0001$) in venous vitamin C in both conditions.
Conner et al. (2020)	Males and females (*n* = 167, 61% female), Mean age = 21 ± 3 years	Randomized placebo-controlled experimental design with comparator	2 Gold kiwifruit/d (*n* = 57), 1 Vitamin C supplement/d (*n* = 56), 1 Placebo tablet/d (*n* = 54)	2-wk lead-in, 4-wk intervention, 2-wk washout	POMS-SF TMD; MFSI; WEMWBS; plasma vitamin C	Decrease in TMD ($p = 0.03$) in kiwifruit condition. Increase in well-being in kiwifruit ($p = 0.02$) and supplement condition ($p = 0.09$). Decrease in fatigue ($p = 0.052$) at week 2 of intervention in kiwifruit condition. Increase in venous vitamin C ($p < 0.0001$) in kiwifruit and supplement condition(s). No effects observed in placebo condition.

POMS-SF = profile of mood states-short form (35-item), TMD = total mood disturbance, MFSI = multi-dimensional fatigue symptom inventory, WEMWBS = Warwick Edinburgh mental well-being scale, POMS = profile of mood states (65-item)

3.7 Discussion

The purpose of this review was to identify and describe studies that have examined the potential role of kiwifruit in supporting psychological health and well-being in adult populations. The review identified a very small but promising body of work that provided preliminary evidence of benefits to psychological well-being from consumption of gold kiwifruit. The search did not reveal any studies that had examined the effect of green kiwifruit on psychological well-being. This is not surprising given the substantial difference in vitamin C concentrations between the green and SunGold cultivars (79 mg and 137 mg per 90 g, respectively) and the recognised links between vitamin C intake and mental health (NHMRC, 2006; Sim et al., 2022). The primary findings reported in the studies identified in the review were that consumption of gold kiwifruit tended to improve overall mood in young adult males with sub-optimal vitamin C concentrations and moderate mood disturbance (Carr et al., 2013a); and that vitamin C intake via gold kiwifruit improved subjective vitality, and conferred additional benefits compared to a vitamin C supplement in adults with suboptimal vitamin C status (Conner et al., 2020).

Strengths of the two studies (Carr et al., 2013a; Conner et al., 2020) in the current review included the use of validated and reliable measures of psychological well-being and plasma vitamin C concentrations, recruiting participants with sub-optimal vitamin C levels, comprehensive screening protocols, lead-in periods to stabilise dietary intake, and intervention periods of sufficient length to assess reliable indices of change from the intervention. The findings in Conner *et al.* (2020) are strengthened by the inclusion of a placebo and comparator group, as well as multiple assessment timepoints across the trial. Nevertheless, the generalisability of results from the two studies is limited by several factors. These include the small sample size ($N = 35$) of young adult males and the small sample size ($n = 8$) included in sub-analyses (Carr et al., 2013a), restricting recruitment to otherwise healthy adults aged 18-35 years old (Carr et al., 2013a; Conner et al., 2020) and lack of a washout period (Carr et al., 2013a). Furthermore, micronutrients (i.e., folate, zinc, selenium, magnesium and serotonin) found in gold kiwifruit that have been implicated in the pathophysiology of depression (Adan et al., 2019; Dalvi-Garcia et al., 2021; Parker & Brotchie, 2011; Wang et al., 2018) were not isolated or measured by either study, leaving the potential relative contribution to mood outcomes from these nutrients undetermined.

As with most whole food nutrition trials, blinding of participants and researchers to condition allocation is virtually impossible (Weaver & Miller, 2017) and both studies were not immune to this challenge. One study (Conner et al., 2020) did incorporate double blinding, but only between the placebo and comparator conditions and not in the active intervention. Non-blinding issues notwithstanding, and although not directly addressed by Carr *et al*. (2013a), the authors may have nullified any placebo effect with the inclusion of the low-dose intervention condition. Delivering an intervention at non-therapeutic levels is an established methodology to isolate the curative agent as the only difference between the groups receiving the intervention (Sucuoğlu & Soydaş, 2021; Wirz-Justice et al., 2011). Carr *et al.* (2013a) recruited participants with sub-optimal vitamin C levels (≤50 µmol/l) and delivered 53 mg of vitamin C to participants in the low-dose condition, well below the estimated intake (83.4 mg) required to achieve optimal plasma concentrations (> 50 µmol/l; Brubacher et al., 2000). Results support the authors' choice to deliver 53 mg as the non-therapeutic dose with results demonstrating that although vitamin C concentrations increased significantly between baseline and post-intervention in the low-dose condition, participants remained vitamin C-deplete (46 µmol/l) at the end of the trial. Similar, non-therapeutic effects have been reported in other studies delivering 50 mg as a low-dose vitamin C intervention (Harats et al., 1998). Others (Vorland et al., 2021) have taken issue with the randomisation protocols used by Conner *et al.* (2020) and proposed that a mix of randomisation methods were employed (i.e., stratification and block randomisation), and that some participants were not randomly allocated to groups thereby reducing the strength of causal inferences that might be drawn from results.

Generalisability of results to other populations (e.g., adults 35+ years, non-students, adults with moderate mood disturbance or different ethnicities) remains problematic. Applicability of results to both sexes remain limited as only one of the studies (Conner et al.,

2020) included female participants. Taken together, results from Carr et al. (2013a) and Conner *et al.* (2020) highlight the potential mood and vitality-enhancing properties of gold kiwifruit and offer a tantalising taste of its utility as a whole-food vector for vitamin C delivery in some adult populations. The differences in effects observed between whole-food and supplement-delivered vitamin C suggest that there are quantifiable, additional benefits from whole fruit over-and-above those conferred by supplements in otherwise healthy adults (Conner et al., 2020). Likewise, the enhanced mood and vitality outcomes observed in individuals with greater psychological distress demand further attention and greater individuation of the therapeutic benefits of the panoply of nutrients found in gold kiwifruit.

The scarcity of research exploring the relationships between kiwifruit and psychological well-being offers a range of possibilities for future research. First, given the significant burden of mental illness, it is necessary to replicate the current findings in larger randomized controlled trials involving participants with elevated psychological distress and sub-optimal vitamin C status. Second, opportunity exists to extend research to include child, adolescent, middle-aged and elderly cohorts. Third, given the burden of mental health disorders globally, preliminary evidence of benefits of kiwifruit consumption on psychological health should be extended to populations with clinical or at least sub-clinical symptoms of psychopathology to examine potential benefits of increased kiwifruit consumption, and therefore vitamin C intake, on mental health symptoms and psychological well-being. This is particularly important because the overall influence of kiwifruit on mood outcomes may depend on severity of underlying mental health conditions. Fourth, emerging concepts at the nexus of epigenetics and nutrition such as the influence of diet and nutrient intake in epigenetic regulation and individual differences in response to hypo-nutrition warrant ongoing investigation of the role of essential micronutrients, such as vitamin C, on physiological and psychological outcomes. This would support the development of dietary patterns that could inform individual-specific dietary management strategies to promote life-long psychological well-being.

Whilst Vitamin C has been defined as a putative pathway for the observed benefits of kiwifruit intake, this hypothesis does not preclude other nutritional aspects that may contribute to observed effects. Future studies would benefit from investigating the individual or synergistic contribution to psychological well-being from other micronutrients found at dietary relevant levels in gold kiwifruit with established links to depression pathogenesis (Adan et al., 2019; Dalvi-Garcia et al., 2021; Parker & Brotchie, 2011; Wang et al., 2018). For example, gold kiwifruit contain nutritionally relevant levels of vitamin E, a micronutrient linked to mood regulation (Manosso et al., 2020) and thought to act synergistically with vitamin C in an antioxidant capacity (Schneider, 2005). Furthermore, examination of other minerals and micronutrients endogenous or exogenous to kiwifruit that possess a synergistic relationship with vitamin C is warranted. For example, the bioavailability of iron, a trace element essential for serotonin and dopamine synthesis (Beard, 2003) and implicated in alterations in mood and behavior (Młyniec et al., 2014), is enhanced by vitamin C intake. Indeed, preliminary research has already reported that consumption of gold kiwifruit with an iron-fortified meal improved iron status in women with low iron stores (Beck et al., 2011). Although not measured in the studies included in this review, gold kiwifruit may confer indirect benefits to psychological well-being through other vectors. The dietary fibre in kiwifruit is recognised as a natural, palatable remedy for improving gastrointestinal function and laxation markers in some populations (Rush et al., 2002). Recent research has identified that gold kiwifruit intake increased bowel frequency and reduced markers of gastrointestinal discomfort (e.g., bloating, indigestion) in constipation-compromised adults (Eady et al., 2019; Eady et al., 2020). Given the association between dietary fibre intake and the risk for development of depression (Barber et al., 2020), the examination of indirect pathways to improving psychological well-being offered by gold kiwifruit may prove fruitful.

The strength of this review is reinforced by utilising multiple databases in the initial search, an extensive and rigorous suite of selection criteria, use of a librarian in the formulation of the search strategy, and three-author consensus of selection criteria and search terms. In line with recommendations of the Cochrane Rapid Reviews Methods Group, restricting articles to English-language only was considered a practical and viable methodology and one which would not necessarily affect overall conclusions (Garritty et al., 2021). To support review rigor, manual screening of the reference list of the two studies included in the review was also undertaken to detect any missed studies omitted from electronic searching.

Although author consensus determined final search terms, the ensuant articles were screened for title, abstract and full text, and were submitted for critical appraisal by a single reviewer (MB). Conclusions offered by the review or suggestions for future research are naturally limited by the small sample size and heterogeneity between the studies. Future reviews in this field will be assisted by an increased volume of research. Imposing a restriction to publication date (2005 to July 2022) may have led to some articles being missed (Garritty et al., 2021). The decision to establish a publication date restriction was taken however, given *a priori* knowledge that research in this area is in its chronological infancy.

3.8 Conclusions

The aim of this review was to examine the available literature from randomized controlled trials and intervention studies that have investigated the associations between kiwifruit and psychological well-being in adult populations. This review is the first to examine the discrete relationship between kiwifruit, recognised for its exceptionally high vitamin C concentration, and psychological well-being. Results from the two studies concord with previous research that has equivocally established the relationships between vitamin C intake and mental health. Despite the small number of studies included in the review, results warrant further investigations across an expanded range of cohorts and settings to further determine the impact of gold kiwifruit on psychological well-being. Recognising the impact of diet, and in particular whole fruit, on not only physiological, but psychological health, gold kiwifruit may yet take its place within a clinical framework as an appetising option within the dietary intervention space in the prevention and treatment of depression.

Chapter 4: Study 2

The Role of SunGold Kiwifruit in Supporting Psychological Health and Wellbeing: A Randomised Feasibility Trial

Submitted for publication to *Pilot and Feasibility Studies,* November 2023[2]

NOTE: The following chapter is identical to the article submitted for publication except for modifications to section numbering, table numbering and figure numbering to maintain consistency throughout this dissertation

4.1 Statement of Authorship

Principal Author

Name of Principal Author (Candidate)	Michael Billows		
Contribution to the Paper	Collaboratively developed the research objectives; methodology and materials; managed data collection; performed analyses; wrote initial draft; collaborated on editing of final drafts; acted as corresponding author		
Overall Percentage (%)	80		
Certification	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual arrangements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	07 March 2024

[2] Billows, M., Kakoschke, N., & Zajac, I. T. The role of SunGold kiwifruit in supporting psychological health and wellbeing: a randomised feasibility trial. *Pilot and Feasibility Studies.* Submitted for publication November, 2023.

Co-author Contributions
By signing the Statement of Authorship, each author certifies that:
i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate to include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution

Name of Co-Author	Ian T. Zajac		
Contribution to the Paper	Collaboratively developed the research objectives; discussed results; edited drafts; advised on responses to reviewers		
Signature		Date	07/03/2024

Name of Co-Author	Naomi Kakoschke		
Contribution to the Paper	Collaboratively developed the research objectives; discussed results; edited drafts; advised on responses to reviewers		
Signature		Date	26/02/2024

4.2 Abstract

Background Consumption of SunGold^{TM} kiwifruit, a fruit rich in Vitamin C, has been associated with improved mood, vitality, and wellbeing in healthy individuals. However, studies have not assessed this relationship exclusively in persons with elevated mood disturbance. Therefore, we conducted a feasibility trial to determine the practicability of conducting a larger, randomised trial in mood disturbed participants.

Methods Participants (N=4) were randomised to either a two- (n=3) or four-week (n=1) baseline period with staggered start times prior to completing a 28-day nutrition intervention (2 SunGold kiwifruit per day), followed by a two-week post-intervention observation period. The primary feasibility outcomes were the recruitment rate (target rate = 10 participants/month), response rate on an ecological momentary assessment (EMA) measure

(minimum 80%), percentage of participants available for follow-up (minimum 83%), and degree of compliance with the intervention (minimum 80%). Secondary outcomes included plasma vitamin C, mood disturbance, wellbeing, vitality and gastrointestinal functioning.

Results The rate of recruitment across the 68-day recruitment window was 1.7 participants per month and two of the four participants failed to achieve the minimum EMA response rate. All participants were available for follow-up and exceeded the intervention compliance target.

Conclusion Results suggest that randomised clinical trials examining the impact of SunGold Kiwifruit consumption on psychological wellbeing in mood-disturbed adults are feasible but require careful consideration of inclusion/exclusion criteria given their impact on recruitment rates, and frequency of study data collection in relation to participant burden.

4.3 Key Messages Regarding Feasibility

- We were uncertain whether it was possible to recruit and retain sufficient participants based on the primary eligibility criteria of mild to moderate mood-disturbance and sub-optimal vitamin C levels. The capacity for mood-disturbed adults to demonstrate satisfactory levels of compliance with assessment and intervention protocols in a novel nutrition intervention study was unknown.
- The blood plasma vitamin C eligibility criterion contributed to under-recruitment. There was sub-standard compliance with an Ecological Momentary Assessment measure, however there was high compliance with intervention protocols and all enrolled participants were available for follow-up.
- Based on the results of this feasibility trial, it was apparent that a larger randomised study, although feasible, would require modifications to study protocols to avoid issues with poor recruitment and compliance with assessment measures, to maximise recruitment and reduce participant burden.

4.4 Background

Depression is one of several recognised mood disorders and is the most common mental health condition in the general population (Lim et al., 2018). Despite high prevalence rates, access and availability to adequate treatment remains limited and demands continued research to identify safe, effective and accessible interventions (Thornicroft et al., 2017). The current evidence for the relationships between lifestyle interventions such as diet and psychological wellbeing is encouraging. A significant body of work has examined the interplay between micro- and macro-nutrients, whole foods, or whole-of-diet approaches and how these positively influence mood and psychological wellbeing (Brookie et al., 2018; Marx et al., 2021; Parletta et al., 2019). More frequent fresh fruit consumption has been associated with a host of positive outcomes including higher odds of experiencing improved psychological wellbeing and reduced risk of developing mood disorders (Emerson & Carbert, 2019; Nguyen et al., 2017; Sapranaviciute-Zabazlajeva et al., 2022).

Vitamin C, a micro-nutrient found in abundance in certain fruits (e.g., kiwifruit), is thought to influence psychological wellbeing through its role as a co-factor in the synthesis of dopamine to adrenaline, and as an essential cofactor in the metabolism of tryptophan, a necessary requirement for the synthesis of serotonin (Carr & Maggini, 2017; Tveden-Nyborg, 2021). To date, cross-sectional and clinical trials exploring the relationships between vitamin C supplementation and psychological wellbeing have produced conflicting results (Pearson et al., 2017; Pullar et al., 2018a; Sim et al., 2022). On the contrary, two studies examining vitamin C delivered by gold kiwifruit, recognised internationally for its high vitamin C content (Richardson et al., 2018), and psychological wellbeing have produced preliminary evidence of benefit.

In the first of those studies (Carr et al., 2013a), 35 young adult males with sub-optimal vitamin C levels (< 50 μmol/L) were randomised to consume half of a gold kiwifruit or two gold kiwifruit per day for six weeks. Participants who consumed two gold kiwifruit per day displayed a trend towards decreased mood disturbance. A sub-group analysis of participants (n = 8) with higher-than-average mood disturbance revealed a significant 38% decrease in mood disturbance and fatigue and a 31% increase in vigor. In the second study, Conner *et al*. (2020) randomised adults aged 18 - 35 years (N = 167) with sub-optimal vitamin C levels (<40 µmol/L) to receive either two SunGold kiwifruit, an equivalent dose (250 mg) of vitamin C via a supplement or a placebo tablet daily for 28-days. Participants who consumed kiwifruit reported significant improvements in mood and wellbeing during the intervention period, with improvements in wellbeing maintained across the 2-week post intervention observation period.

These two studies possessed several methodological strengths; however, the results are limited in their generalisability to certain populations. Specifically, neither study recruited a mood-disturbed population, a cohort that, based on a sub-analysis (Carr et al., 2013a) and as reported in a recent review (Yosaee et al., 2021), stand to receive greater psychological benefit from vitamin C intake. The purpose of this article is to describe a feasibility trial undertaken to inform the development of the SunGold Kiwifruit and Psychological Health (GoKiPH) study. The GoKiPH study aimed to examine the effects of increased vitamin C intake through daily consumption of SunGold kiwifruit on mood disturbance in adults with sub-optimal vitamin C levels.

4.4.1 The Current Trial

Somewhat of a 'try before you buy' model, or as Thabane et al. (2010) borrowed from an African proverb in their tutorial on pilot (feasibility) studies, "*You never test the depth of a river with both feet",* feasibility trials are an essential pre-requisite to support the design and success of larger, clinical studies. Specifically, feasibility trials offer the opportunity to assess processes such as recruitment and retention, eligibility criteria, non-compliance and participant burden. This is particularly important when considering a clinical trial endeavouring to deliver a novel nutrition intervention to a population (i.e., mood-disturbed adults) already associated with atypical recruitment and retention challenges (Hughes-Morley et al., 2015).

The objectives of the current feasibility trial were to 1) determine the feasibility of recruiting, assessing and following-up a cohort of mood-disturbed adults with sub-optimal vitamin C levels and 2) establish the potential for SunGold kiwifruit to support psychological wellbeing and increased vitamin C intake. Specifically, the primary objective of the feasibility trial was to determine the recruitment rate, the degree of compliance with an EMA measure, the number of participants available for follow-up and compliance with the intervention. The secondary objectives of the trial were to assess the degree of change in mood disturbance, vitamin C levels, vitality, wellbeing, and gastrointestinal symptoms between pre- and post-intervention. In this article, we discuss the outcomes of the feasibility trial with respect to primary and secondary objectives and our assessment of the feasibility of conducting the GoKiPH study.

4.5 Methods

4.5.1 Feasibility Trial Design

The feasibility trial was a randomised, multiple-baseline design with a 1:1 allocation ratio to a two- or four-week baseline period. There was no control group and participants were enrolled in a staggered-start fashion across the enrolment period. Upon completion of their assigned baseline period, each participant commenced the 4-week intervention immediately followed by a two-week post-intervention observation period (an ABA design).

4.5.2 Participants

Eligibility criteria are detailed in Table 5. Participants aged between 18 - 60 years old with mild to moderate mood disturbance and sub-optimal vitamin C levels were recruited through the Commonwealth Scientific and Industrial Research Organisation (CSIRO) Research Clinic in Adelaide, Australia, from September to November 2021. Participants were recruited via advertisements on the CSIRO Facebook page, an existing research clinic volunteer database and University noticeboards.

Table 5

Feasibility Trial Eligibility Criteria

Inclusion criteria	Exclusion criteria
Males and females aged 18 - 60 years	Allergy/intolerance to kiwifruit and/or latex
Plasma vitamin C levels >10 & <50 µmol/L	Recent smoker or NRT (within 6 months)
Non-smoker (within last 6 months of baseline)	Taking vitamin C supplements (within 3 months of baseline)
DASS-21 scores in the mild and moderate ranges on minimum of one of the subscales	Diabetes Mellitus, Bleeding Disorders
Willing to provide written informed consent	Needle phobia or fainting due to fear of needles
Access to smartphone and willing to download free application from app store	Score in high range (≥ 7) on HDIvC
Able to access own email address/service	Taking prescription medication for gastrointestinal conditions (within 3 months of baseline)
Fluent in English	Initiation of, or alteration to, a course of anti-depressant, anxiolytic or antipsychotic (within 6 months of baseline)
	Received an investigational drug (within 3 months of baseline)

DASS-21: Depression Anxiety Stress Scale – 21-item; NRT: Nicotine Replacement Therapy; HDIvC: Habitual Dietary Intake of vitamin C questionnaire

4.5.3 Recruitment and Screening

After responding to trial advertisements, applicants were directed through a sequential, three-stage screening process that incorporated: (1) a medical screening questionnaire; (2) a telephone-delivered assessment of mood and habitual dietary intake of vitamin C; and (3) a fasting blood plasma vitamin C assessment. The lead researcher (MB) was responsible for reviewing the medical screening questionnaire and participants deemed eligible were invited to complete a telephone-delivered assessment of mood and vitamin C intake. Verbal consent was obtained prior to conducting the assessment. Participants assessed as eligible following the telephone assessment were invited to attend the research clinic to provide a fasting blood sample to assess vitamin C concentration. Participants were remunerated AUD$40 per visit on a pro rata basis (maximum remuneration $AUD 200) for their participation. Written, informed consent was obtained prior to sampling. Eligible participants were subsequently invited to enrol in the trial.

4.5.4 Procedure

Participants were asked to maintain their habitual dietary intake for their assigned baseline period but refrain from consuming supplements containing vitamin C or kiwifruit. No other dietary restrictions were placed on participants. Participants were assessed at five timepoints and required to attend the research clinic on four occasions (Baseline, pre-intervention, mid-intervention and post-intervention visits) at which they provided a fasting blood sample for vitamin C analysis, completed the psychometric assessment measures and basic anthropometric measures were collected. At the pre- and mid-intervention visits, participants were provided a fortnight's supply of gold kiwifruit, received instructions on storage, consumption and disposal of unused kiwifruit, and provided with a daily compliance log to record consumption and adverse events. Participants were asked to provide a photographic record of any unused study product at the completion of the intervention period. During the two-week post-observation period, participants returned to their habitual dietary intake. For the fifth assessment timepoint (Post-observation visit), participants received an email with a link to the assessment battery which they completed remotely. A fasting blood sample was not taken at this timepoint due to logistical challenges with phlebotomy services. Participants also completed an 11-item EMA measure of mood (Bostic et al., 2000) delivered at weekly intervals at a pre-arranged time (ACST 7:00 p.m.) via an automated smartphone application.

4.5.5 Intervention

Participants consumed two SunGold kiwifruit ('Zesy002^{TM} , *Actinidia chinensis* var. *chinensis)* daily for 28 days. Participants consumed the kiwifruit at a time of their choosing, and either both in a single sitting or separately throughout the day (i.e., one at a time). Participants were instructed to store the kiwifruit in domestic refrigeration to maximise ripeness, and to remove the skin prior to eating (consume the flesh only).

4.5.6 Protocol Amendments

Protocol amendments initiated to counter under-recruitment were an extension to the age eligibility criteria (from initial 35-60 years to 18-60 years), undertaking a bulk mail-out utilising an existing volunteer data base and securing additional screen media advertising. Participants provided written, informed consent when study protocols were amended.

4.5.7 Outcome Measures

4.5.7.1 Feasibility Trial Primary Outcomes. The pre-determined outcome measures for the feasibility trial were the recruitment rate, compliance with an EMA assessment of mood, percentage of participants available for follow-up and degree of compliance with the intervention. Specifically, these were expressed as a recruitment rate of 10 participants per month; a response rate of 80% or greater on an EMA measure; a minimum of 83% of the recruitment target available for follow-up (25 of 30 participants); and a minimum consumption compliance rate of 80%.

4.5.7.2 Feasibility Trial Secondary Outcomes. The principal secondary outcome of the feasibility trial was the degree of change between pre- and post-intervention in total mood disturbance scores derived from the Profile of Mood States - Short Form (McNair & Heuchert, 2005). Additional trial outcomes were vitamin C levels (via fasting blood sample);

wellbeing (Warwick Edinburgh Mental Wellbeing Scale; Tennant et al., 2007); vitality (Subjective Vitality Scale; Bostic et al., 2000), gastrointestinal functioning (Gastrointestinal Symptom Rating Scale; Revicki et al., 1998), and an EMA of mood (Profile of Mood States – Brief; Cella et al., 1987). A measure of dietary intake (CSIRO Short Food Survey) was completed at baseline and post-intervention to assess diet quality and degree of compliance with Australian dietary guidelines (Hendrie et al., 2017). The screening measures used in the present trial were the Depression Anxiety Stress Scale - Short Version (DASS-21; Lovibond & Lovibond, 1995) and the Habitual Dietary Intake of Vitamin C questionnaire (HDIvC). The HDIvC provides an estimate of habitual vitamin C intake based on self-reported fruit and vegetable consumption and vitamin C supplement use in a typical week. The HDIvC is yet to be validated, however, descriptive and scoring ranges have been calculated as a function of vitamin C concentrations in plasma identified in existing empirical literature (Brubacher et al., 2000).

4.5.8 Sample Size

It was determined that a target sample size of N = 30 participants would be required to sufficiently power the study and allow for attrition. This was supported by a previous clinical trial that used an identical intervention as well as primary mood outcome measures and vitamin C analysis that reported an attrition rate of 7%, albeit in a non-mood-disturbed sample (Conner et al., 2020). A further 10% attrition (3/30) was apportioned to allow for dropouts given the recruitment and retention difficulties often cited in studies involving mood compromised individuals (Hughes-Morley et al., 2015). Additionally, it was determined that if the trial achieved the target recruitment rate of 10 participants per month (i.e., N = 30), the viability and quality of the kiwifruit could not be guaranteed beyond the date the 30^{th} enrolled participant would be expected to exit the trial.

4.5.9 Randomisation Allocation and Blinding

Participants were block randomised to baseline condition according to the calendar week of enrolment with baseline condition assigned to alternate calendar weeks. The lead researcher (MB) was responsible for generating the allocation sequence and enrolling participants to their assigned baseline period. Researchers and participants were unblinded to baseline condition and intervention.

4.5.10 Data Analysis and Statistical Methods

The final sample size was too small to permit traditional statistical analysis or determine indices of change on primary and secondary outcomes. Data analysis was restricted to visual inspection of results for all outcome measures.

4.5.11 Statement of Ethics

The trial was prospectively registered with the Australian and New Zealand Clinical Trial Registry (Trial ID: ACTRN12621001321831) and approved (Ethics ID: 2021_047_HREC) by the Executive of the CSIRO Health and Medical Research Ethics Committee (CHMHREC). The CHMHREC is a National Health and Medical Research Council Registered Human Research Ethics Committee (Registration: EC00187). All participants provided written informed consent.

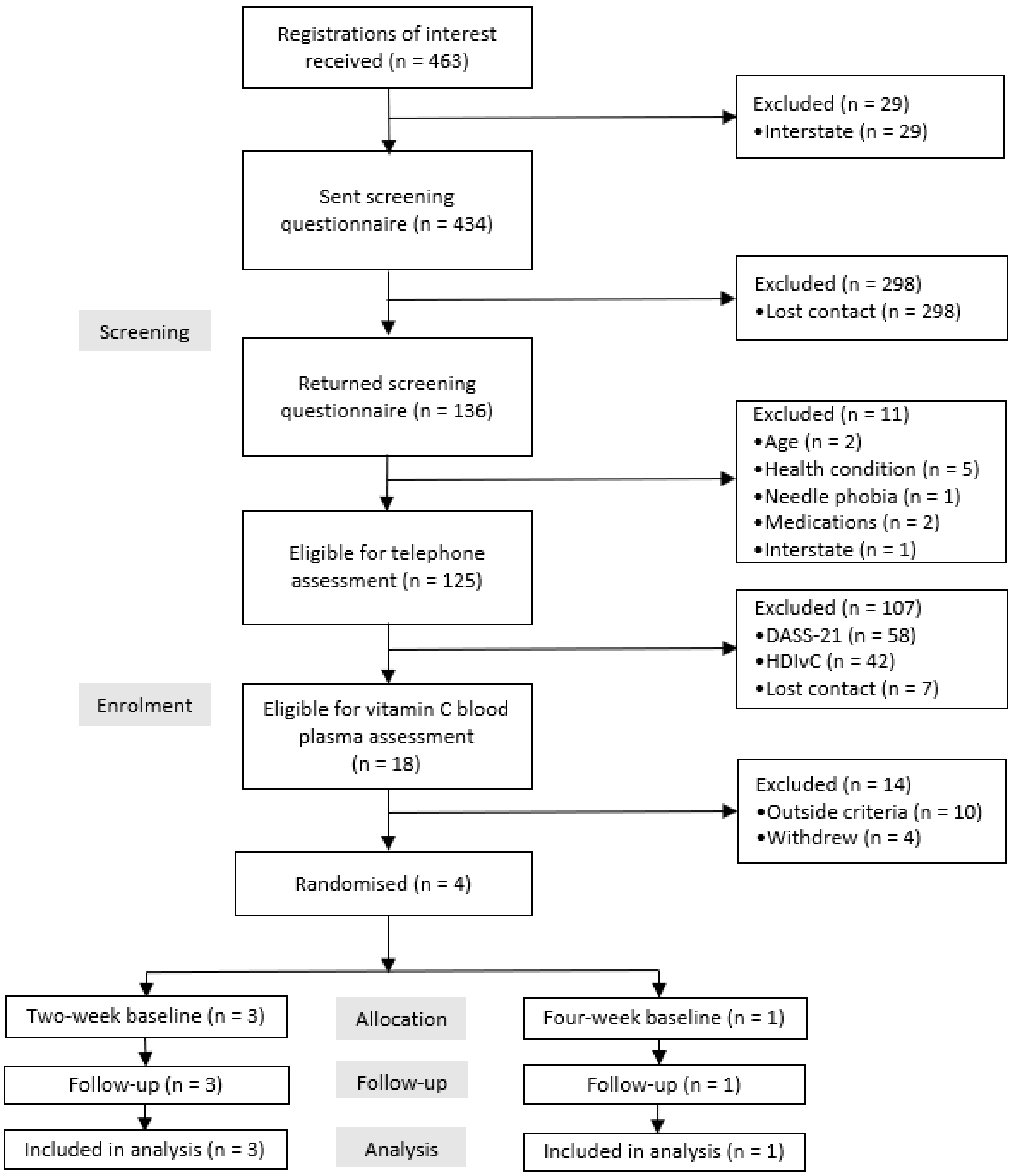
4.6 Results

4.6.1 Recruitment

The movement of participants through the recruitment process is presented in Figure 3. The study received a considerable amount of interest with just under a third (31%, 136 of 463) of applicants returning the medical screening questionnaire.

Figure 3

CONSORT Flowchart of Movement of Participants Through Screening, Enrolment, Allocation and Follow-up



Only 8% of applicants were excluded based on existing medical conditions or domicile location, however over 49% of applicants screened for mood disturbance (n = 58) and 63% (n = 42) of those screened for habitual dietary intake of vitamin C were excluded from participation. Of the participants who progressed to the vitamin C blood screen, more than 70% (n = 10) did not satisfy eligibility criteria.

4.6.2 Participant Characteristics

Four participants were sequentially enrolled in the trial with only one allocated to the four-week baseline condition. The enrolled participants were female and total mood disturbance at baseline was relatively high, with higher scores indicating greater mood disturbance (Table 6). Although at screening plasma vitamin C levels were confirmed to meet entry criteria, these levels at baseline for two participants were now above screening criteria (>50 µmol/L). Wellbeing and vitality scores for the sample were moderate with higher scores indicating greater wellbeing and vitality (minimum score 14 to maximum score 70; and six to 42, respectively). Scores on the five sub-scales of the GSRS were in the low range with minimum and maximum possible scores on the diarrhea, constipation and abdominal discomfort subscales of three to 21, indigestion subscale four to 28, and reflux subscale two to 14. Results from the CSIRO Short Food Survey indicated that the sample had many areas of the diet inconsistent with Australian Dietary Guidelines with higher scores (maximum score 100) reflecting greater adherence to guidelines.

4.6.3 Feasibility Trial Primary Outcomes

The results for the feasibility trial primary outcomes are presented at Table 7. The trial recruitment rate was well below target at 1.7 participants per month, and two of the four participants failed to meet the minimum EMA compliance rate. All participants (4 of 4) were available for follow-up and exceeded the target intervention compliance rate.

Table 6

Baseline Characteristics for Individual Participants

	Participant ID			
Variable	**KIF001**	**KIF002**	**KIF003**	**KIF004**
Age (years)	44	57	53	60
Gender	Female	Female	Female	Female
Baseline condition	4-week	2-week	2-week	2-week
BMI	29.7	25.7	23.7	28.4
POMS-SF TMD	56	33	44	37
POMS-SF Vigour	7	7	7	8
Vit C Screen (µmol/L)	46	13	35	33
Vit C Base (µmol/L)	58	12	42	68
WEMWBS	41	51	38	42
SVS	26	24	19	24
GSRS subscales				
Diarrhea	6	3	4	8
Indigestion	12	5	12	7
Constipation	6	3	8	7
Abdominal discomfort	9	4	6	7
Reflux	3	2	2	2
CSIRO SFS	45.7	42.3	58.1	55.3

BMI = Body Mass Index; POMS-SF TMD = Profile of Mood States – Short Form Total Mood Disturbance; WEMWBS = Warwick-Edinburgh Mental Wellbeing Scale; SVS = Subjective Vitality Scale; GSRS = Gastrointestinal Symptom Rating Scale; CSIRO SFS = Short Food Survey

Table 7

Primary Feasibility Outcome Results Against Target

Primary feasibility outcome	Target	Actual	Achieved/Not achieved
Recruitment rate	10 ppts per month	1.7 ppts per month	Not achieved
EMA Compliance	80% minimum	2 of 4 ppts	Not achieved
Follow-up	83% minimum	4 of 4 ppts	Achieved
Intervention compliance	80% minimum	4 of 4 ppts	Achieved

4.6.4 Feasibility Trial Secondary Outcomes

All four participants recorded decreased total mood disturbance and increased blood plasma vitamin C concentrations between pre- and post-intervention (Figure 4). Results for the wellbeing, vitality and gastrointestinal functioning showed some trends indicating improvement within and across individual participants (Table 8).

4.6.5 Adverse Events

There were no serious adverse events reported across the trial. One participant experienced mild dizziness on two occasions at blood sampling and one participant reported loose stools at the commencement of the intervention that persisted for 48 hours before spontaneous remission.

Figure 4

Plasma Vitamin C Concentrations (A) and Total Mood Disturbance Scores (B) Across the Study Period for Individual Participants. (B):Higher Scores Reflect Greater Mood Disturbance

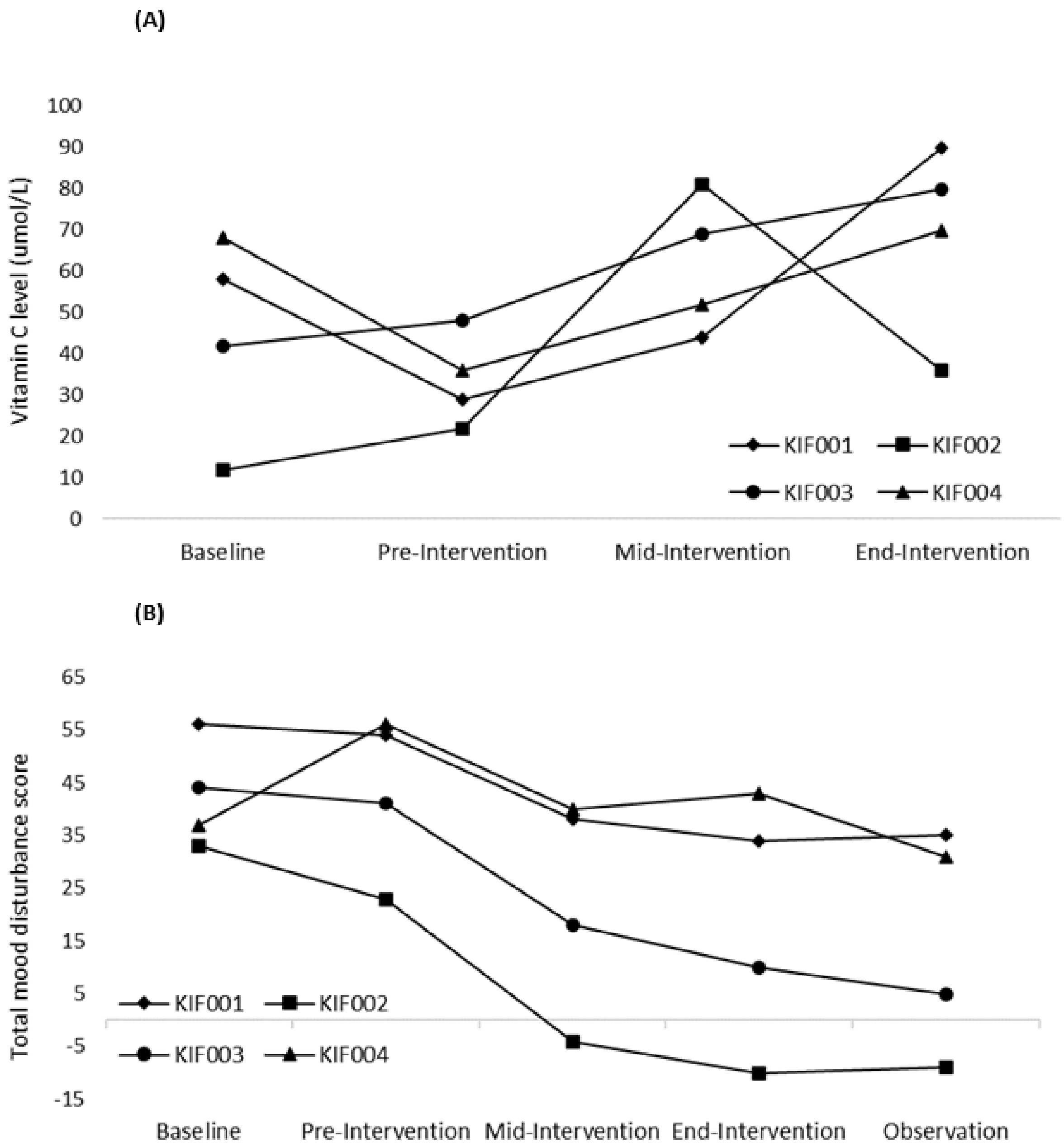


Table 8

Observed Outcomes and Percentage Change in Secondary Variables of Interest Between Pre- and Post-intervention for Individual Participants

Participant	WEMWBS		% Δ	SVS		% Δ	GSRS		% Δ
	Pre-int	Post-Int		Pre-int	Post-Int		Pre-int	Post-Int	
KIF001	38	39	3	20	24	20	20	32	60
KIF002	52	55	6	22	33	50	18	16	-11
KIF003	37	43	16	19	24	26	40	21	-48
KIF004	40	43	8	21	23	10	22	22	0

WEMWBS, Warwick-Edinburgh Mental Wellbeing Scale – higher scores indicate greater wellbeing; SVS, Subjective Vitality Scale – higher scores reflect greater vitality; GSRS, Gastrointestinal Symptom Rating Scale – higher scores indicate greater symptom severity; Pre-int, Pre-intervention; Post-Int, post-intervention

4.7 Discussion

The primary objective of the present trial was to examine the feasibility of conducting the GoKiPH study with respect to recruitment rate, degree of compliance with the intervention and with an EMA measure, and percentage of participants available for follow-up. The trial did not achieve the recruitment and EMA compliance target rates. However, the number of participants available for follow-up and intervention compliance targets were achieved. Regarding secondary objectives, results demonstrated that all participants recorded increased vitamin C levels, reductions in mood disturbance, and increased wellbeing and vitality. There were mixed results across participants for gastrointestinal functioning.

The expectation that recruitment and selection would prove challenging was substantiated and these difficulties were reflected in attrition rates across recruitment and the final sample size. Gathering a sample large enough to provide statistical power to support findings was challenged by the decision to recruit from a narrow bandwidth of a mood-disturbed, vitamin C-deplete population, albeit one most likely to benefit from the intervention. Adapting swiftly to low recruitment numbers, amendments to study protocol such as expanding the age range eligibility criteria from 35 - 60 years to 18 - 60 years, utilising an existing volunteer database and broadening the advertising reach of the study through local media proved insufficient to boost enrolment. The recruitment time window was governed by the kiwifruit growing season (March to May) and the viability of the study product in storage. It was necessary to cease enrolment at a pre-determined end-date (i.e., 68 days after trial commencement) to ensure that the kiwifruit remained suitable for human consumption for the duration of the trial. We acknowledge also that recruitment for the trial occurred during the COVID pandemic and the degree to which localised short-term lockdowns and travel restrictions might have affected interest and enrolment in the study remained undetermined. Similarly, the degree to which participants were affected by these restrictions or the negative health effects of COVID symptoms from infection during the trial remain undetermined and are a potential confound to trial results.

Recruitment difficulties for studies involving mood-compromised individuals are well-documented (Hughes-Morley et al., 2015). Striking a balance between recruiting a population considered at risk of poor or labile mood states and designing a study that does not over-burden these individuals with taxing interventions or data collection processes calls for nuanced judgement on behalf of researchers, and the capacity of the participant to make a sound decision to enter a trial, in addition to their ability to maintain a positive attitude toward the research after selection and recruitment (Hughes-Morley et al., 2015).

The vitamin C criteria (<50 µmol/L) for the trial was informed by the two previous trials exploring mood outcomes following gold kiwifruit consumption (Carr et al., 2013a; Conner et al., 2020). To the authors' knowledge, there are few studies on vitamin C deficiency within Australian populations and those in existence are limited to surgical patients (Ravindran et al., 2018). Additionally, demographic and socioeconomic factors such as gender, age, race, education and income status are known to affect vitamin C concentrations. For example, older age groups, females and Caucasians are reported to have higher vitamin C status compared to their counterpoints (Carr & Rowe, 2020). The high attrition rate seen in the vitamin C blood screening in the present trial may reflect a combination of any number of these factors, particularly given that the trial initially targeted individuals aged 35 - 60 years old and that 85% (12 of 14) of applicants who underwent vitamin C blood screen were female. Another consideration and potential confound to results is that the inherent variability in an individual's vitamin C concentrations saw two participants increase vitamin C levels to above trial criteria between baseline and pre-intervention.

The present trial was designed in such a manner to minimise participant burden. For example, rather than completing the full suite of psychometric measures on alternate weeks to their clinic visit, participants were required to complete an EMA measure that took approximately two minutes to complete. Despite its brevity, there was substandard compliance with this procedure. Mood-disturbed populations can exhibit poor compliance with measures delivered in this manner due to factors such as severity of acute mood disturbance and the potential for de-motivation arising from the requirement to complete repetitive questionnaires (Wenze & Miller, 2010). Greater non-compliance in the latter half of the trial was consistent with previous findings in similar populations (De Angel et al., 2023). Although compliance with the EMA measure observed in the present trial was below the target rate of 80%, it was consistent with response rates found in the EMA literature (Kivelä et al., 2022).

Recruitment and EMA compliance issues aside, the SunGold kiwifruit intervention was well-tolerated by participants as indicated by the high compliance rate and the single adverse event related to the study product that did not affect compliance. Qualitative feedback from participants reflected that incorporating the intervention into their daily dietary regime was not difficult, and that the study product was appealing and enjoyable to consume. Some participants stated they would continue to consume the kiwifruit once the study was completed. Importantly, all enrolled participants were available for follow-up. This supports the retention of the feasibility trial intervention protocols for the GoKiPH study.

4.7.1 Strengths and Limitations

The use of validated assessment measures for mood, blood plasma vitamin C, wellbeing, vitality and gastrointestinal functioning strengthen study results and provides justification for their inclusion in future clinical trials. Likewise, the difficulties experienced with completing an EMA measure of mood in a mood-compromised population offers valuable insight into the challenges of compliance and participant burden that may be encountered when studying mood-disturbed adult populations in the future. To that end, the present trial was considered a success and highlighted the value of feasibility trials in avoiding methodological pitfalls and supporting cost conservation in full-blown clinical trials (Morgan et al., 2018). Results from the trial are limited due to the small sample size, the all-female cohort, as well as lack of ethnic diversity and restricted age range. Randomisation was impacted by sample size and remained of limited utility given the one to three ratio between baseline conditions. The randomisation method utilised in the trial, at best a combination of block and manual non-randomisation, would have compromised validity of results had the trial achieved its target recruitment number.

4.7.2 Future Directions

This trial assessed the feasibility of delivering a novel nutrition intervention to a mood-disturbed population. The overall aim was to inform and refine aspects of recruitment, enrolment, compliance and eligibility criteria as necessary for a larger randomised study.

Although a considerable proportion (49%) of applicants were excluded from participation based on the mood disturbance criterion, the trial had exceeded its target recruitment number at that stage of the screening process, prior to proceeding to the dietary vitamin C and blood plasma screening. This demonstrates the feasibility of recruiting a mood-disturbed sample for the GoKiPH study. Regarding factors that negatively impacted recruitment, as reflected in the CONSORT diagram (Figure 3), plasma vitamin C entry criteria were particularly problematic. Seventy percent of participants were excluded on this criterion in the present trial and there was considerable variability in plasma vitamin C between screening and baseline, thus questioning its utility as a study criterion. Furthermore, the age inclusion criterion should be established as 18 - 60 years from study outset. This would provide access to a larger pool of participants and sub-group analyses of different age cohorts could be undertaken if sample size permits. Whilst the Habitual Dietary Intake of Vitamin C questionnaire was designed to increase the number of participants who would meet plasma vitamin C criteria as a result of low dietary vitamin C intake, this measure did not appear to be particularly accurate such that 71% of people who satisfied low intake criteria failed the blood screen.

With respect to the use of an EMA measure, results of the current feasibility trial indicate that compliance targets might not be met in the GoKiPH study. Therefore, removing this outcome would circumvent poor adherence to this as well as serve to reduce participant burden, albeit with some reduction in data capture. The proposed crossover design of the GoKiPH study would increase statistical power and in concert with an additional visit over and above the present trial, may counter any data loss. Conversely however, retaining the EMA may help to identify if compliance was something peculiar to the present sample or if rates of return are replicated in future cohorts.

The number of participants available for follow-up and compliance with the intervention in this trial advocate preserving feasibility trial intervention protocols for the GoKiPH study. The intervention was well-tolerated, consumption compliance was very high, and we received positive qualitative feedback regarding the study product. Additionally, results highlighted participants achieved near-saturation levels of vitamin C (M = 61.5 μmol/L) within two-weeks of commencing the intervention. Other general considerations for the GoKiPH study include recruiting from more diverse socio-cultural demographics, inclusion of a control or placebo condition and adopting other measures as practicable to achieve full- or partial-blinding of participants and researchers. Adopting computer-generated randomisation would maximise the allocation ratio and strengthen conclusions.

4.8 Conclusions

Based on the results of this feasibility trial, it was apparent that a future randomized trial of gold kiwifruit consumption in mood-disturbed participants is feasible but requires modifications to selection criteria to avoid the recruitment and data collection challenges identified herein. The principal challenges to the feasibility trial were low recruitment rates and compliance with an EMA measure. Once participants entered the trial however, compliance and tolerability for the gold kiwifruit intervention was excellent. The outcomes of this feasibility study demonstrate the importance of such trials in order to refine selection criteria and methodology for larger clinical studies so that a more nuanced balance between the risks associated with recruitment and the rewards of data collection might be achieved.

Chapter 5: Study 3

SunGold Kiwifruit and Psychological Health (GoKiPH): A Randomised Controlled Crossover Trial

Submitted for publication to *British Journal of Nutrition*, March 2024[3]

NOTE: The following chapter is identical to the article submitted for publication except for modifications to section numbering, table numbering and figure numbering to maintain consistency throughout this dissertation

5.1 Statement of Authorship

Principal Author

Name of Principal Author (Candidate)	Michael Billows		
Contribution to the Paper	Collaboratively developed the research objectives; methodology and materials; managed data collection; performed analyses; wrote initial draft; collaborated on editing of final drafts; acted as corresponding author		
Overall Percentage (%)	80		
Certification	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual arrangements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	07 March 2024

[3] Billows, M., Kakoschke, N., & Zajac, I. T. (2022). SunGold Kiwifruit and Psychological Health (GoKiPH): a randomised controlled crossover trial. *British Journal of Nutrition,* Submitted for publication March, 2024.

Co-author Contributions
By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate to include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution

Name of Co-Author	Ian T. Zajac		
Contribution to the Paper	Collaboratively developed the research objectives and methods; performed analyses; provided feedback on interpretation of results; edited drafts		
Signature		Date	07/03/2024

Name of Co-Author	Naomi Kakoschke		
Contribution to the Paper	Collaboratively developed the research objectives and methods; edited drafts		
Signature		Date	26/02/2024

5.2 Abstract

Background: Consumption of SunGold kiwifruit, a fruit rich in vitamin C, has been associated with improved mood in healthy individuals with low vitamin C levels. However, no previous studies have examined this relationship in individuals with elevated mood disturbance. This study examined the potential for SunGold kiwifruit to improve psychological wellbeing in mood-disturbed adults.

Methods: This study was a two-period, non-blinded crossover trial. Adults (n = 26) aged 18 - 60 years with mild to moderate mood disturbance were randomised with a two-week washout between periods. During each 4-week period, participants consumed either two SunGold kiwifruit daily or their usual diet. The primary outcome was mean change in total mood disturbance scores from the kiwifruit period compared to the diet as usual period. Secondary outcomes were blood plasma vitamin C concentration, wellbeing, vitality and gastrointestinal symptoms. Participants and researchers were unblinded to condition and intervention.

Results: Scores for total mood disturbance ($p < 0.001$), wellbeing ($p < 0.01$) and vitality ($p = 0.001$) significantly improved in the kiwifruit condition compared to usual diet. Vitamin C ($p = 0.002$) concentrations also improved and gastrointestinal symptom reduction was evident during kiwifruit consumption ($p = 0.003$). There were no serious adverse events.

Conclusions: SunGold kiwifruit consumption resulted in significant reductions in total mood disturbance scores and improvements in wellbeing and vitality. Vitamin C concentration also increased significantly, and gastrointestinal symptom severity significantly reduced. These results provide preliminary evidence of the potential benefits of kiwifruit for reducing mood disturbance in adult populations. Further studies in diverse groups, including clinical populations, are warranted.

5.3 Introduction

Mental health disorders were amongst the top ten leading causes of disease burden worldwide in 2019. The Global Burden of Disease Study 2019 (GBD) estimated that major depressive disorder and dysthymia jointly contributed to 46.9 million disability-adjusted life years (Vos et al., 2020). Depression is one of the most common mental health disorders in the general population (Lim et al., 2018). Recent global estimates have reported a 28% increase in depression post-COVID-19 such that global prevalence is now 3% (Santomauro et al., 2021). Despite the high prevalence rates, approximately 30% of individuals with depression receive treatment and of those, at least 60% do not receive adequate treatment (Mekonen et al., 2021). Hence, there is a pressing need to deliver efficacious, accessible treatments for depression to reduce the individual and global burden. Beyond the treatment offered by specialised mental health services (e.g., psychological or pharmacological treatments), there are a growing number of adjunctive treatments gaining consumer and empirical support (Jorm & Griffiths, 2006).

Associations between mental health and diet quality are well-established, particularly in relation to fruit and vegetable consumption (Głąbska et al., 2020). Results from cross-sectional studies and clinical trials highlight that diets comprising higher daily servings of fruits and vegetables were positively associated with psychological wellbeing, vitality, flourishing, mood and reduced depressive symptoms (Brookie et al., 2018; Conner et al., 2017; Ocean et al., 2019). Raw fruits and vegetables such as dark leafy greens, bananas, apples and kiwifruit, are associated with better mental health outcomes, most likely because they deliver greater amounts of nutrients than when cooked or canned (Brookie et al., 2018). Clinical trials that have examined the psychological wellbeing-diet dyad at the micro-nutrient level (e.g., vitamin C) also report positive associations between mood and wellbeing (Kennedy et al., 2010; Kontogianni et al., 2020; Watson et al., 2018).

Vitamin C is one micro-nutrient that has received considerable attention in the diet and wellbeing literature. Vitamin C is a water-soluble vitamin that is not endogenously produced in humans despite having an absolute requirement for a range of important biochemical functions (Harrison et al., 2014). Therefore, vitamin C must be derived from exogenous sources, principally through the consumption of fruits and vegetables (Pearson et al., 2017). Vitamin C is more highly concentrated in the brain compared to plasma and is thought to play an important biochemical role in psychological wellbeing by acting directly and indirectly in the synthesis of neurotransmitters such as serotonin, dopamine, and oxytocin (Carr & Vissers, 2012). Vitamin C supplementation has been associated with reduced mood disturbance, psychological distress and fatigue, as well as improved mood and vigour in heterogenous samples (Sim et al., 2022; Wang et al., 2013; Zhang et al., 2011). Conversely, sub-optimal vitamin C status (< 50 µmol/L) and clinical deficiency (< 10 µmol/L) are associated with fatigue, irritability and low mood (Carr & Rowe, 2020; Rowe & Carr, 2020). As vitamin C is inherently unstable and easily destroyed through processes such as cooking and prolonged storage, the inclusion of vitamin C-rich foods (e.g., certain fruits and vegetables) in habitual diets is recommended to maintain adequate concentrations and maximise vitamin C bioavailability (Schlueter & Johnston, 2011).

Kiwifruit is widely acknowledged as a vitamin C-rich fruit, in addition to containing nutritionally relevant levels of vitamin E, dietary fibre, potassium and folate (Richardson et al., 2018). The two cultivars of greatest current commercial significance are the *Actinidia deliciosa* "Hayward" (Green kiwifruit) and the *Actinidia chinensis* var. *chinensis 'Zesy002'* (SunGold kiwifruit). The green kiwifruit contains ~88 mg of vitamin C, whilst the SunGold kiwifruit contains ~152 mg of vitamin C per 100 g flesh weight, more than three times the Australian recommended daily vitamin C intake (45 mg; NHMRC, 2013). Compared to other commercially available fruits, the vitamin C content of SunGold kiwifruit eclipses levels found in oranges (52 mg), strawberries (46 mg), pineapple (21 mg), bananas (5 mg) and blueberries (4 mg) per 100 g (NZIPFRL, 2021). In recognition of the substantial vitamin C content of gold kiwifruit, an emerging subset of studies have examined the potential for vitamin C-rich gold kiwifruit to increase vitamin C concentrations and improve psychological health.

Intervention trials have demonstrated that gold kiwifruit consumption increased blood plasma vitamin C concentrations at different dose rates and in samples with adequate (> 50 µmol/L) and sub-optimal vitamin C levels (23 - 50 µmol/L). For example, consuming as little as half a gold kiwifruit (equivalent to ~ 50 mg vitamin C) daily for six weeks significantly increased blood plasma vitamin C from 23 µmol/L to 46 µmol/L ($p < 0.001$) in young adult males with sub-optimal vitamin C status ($n = 36$; Carr et al., 2013b). Comparable increases in vitamin C concentration (38 µmol/L to 62 µmol/L, $p < 0.05$) were observed when young adult males (n = 15) with sub-optimal vitamin C status consumed two gold kiwifruit daily for six weeks (Carr et al., 2012). Healthy adults aged 44 - 85 years (n = 26) with adequate vitamin C status recorded significantly higher plasma vitamin C concentration after consuming two SunGold kiwifruit daily for twelve weeks (Wilson et al., 2018). Findings of these studies are supported by extended lead-in periods to stabilise dietary intake and weekly vitamin C analysis (Carr et al., 2013b; Carr et al., 2012). Generalisability to other populations (e.g., over 35-year-olds, non-students, adults with mood disturbance) is limited and only one study included a mixed-gender sample (Wilson et al., 2018).

Nascent research has begun to examine the potential benefits of kiwifruit-delivered vitamin C on psychological health and returned promising results. Carr *et al.* (2013a) randomised young adult males with sub-optimal vitamin C status (< 50 µmol/L; n = 35) to receive either half a gold kiwifruit or two gold kiwifruit daily for six weeks. Participants who consumed two gold kiwifruit significantly increased vitamin C levels ($p < 0.001$) and displayed a trend towards decreased mood disturbance and reduced symptoms of depression. A sub-group analysis of participants (n = 8) with higher-than-average mood disturbance showed significant 38% decreases in mood disturbance and fatigue ($p = 0.029$ and $p = 0.048$, respectively), a 31% increase in vigor ($p = 0.024$) and a 34% trend towards decreased depression, whilst no such effects were observed in those with lower-than-average mood disturbance (n = 9) following supplementation with two gold kiwifruit. More recently, Conner *et al*. (2020) conducted a randomised, three-arm clinical trial involving adults aged 18 - 35 years (n = 167) with sub-optimal vitamin C status (< 40 µmol/L). Participants consumed either two SunGold kiwifruit, an equivalent dose vitamin C supplement (250 mg) or a chewable placebo matched for appearance and flavour to the supplement daily for 28-days. Participants who consumed two SunGold kiwifruit had significantly increased vitamin C concentration ($p < 0.001$) and reported reduced mood disturbance ($p = 0.026$) and improved wellbeing (p = 0.052), with wellbeing improvements preserved across the two-week washout relative to both of the other groups.

5.3.1 The Current Trial

Previous studies (Carr et al., 2013a; Conner et al., 2020) examining the effect of gold kiwifruit consumption provide preliminary evidence of benefits for vitamin C status and mood disturbance. Findings of the two studies are strengthened by the inclusion of validated psychometric instruments, mechanistic vitamin C assessment and intervention periods of sufficient length to assess indices of change. However, generalisability of results is limited by the small sample size of young adult males and under-powered sub-analysis (Carr et al., 2013a), restricting the samples to 18 - 35-year-olds and lack of blinding. Therefore, generalisability of those results to other populations, such as individuals with elevated mood-disturbance is unclear. The current trial sought to expand on previous findings by examining the influence of gold kiwifruit consumption on vitamin C status and mood in participants with mild to moderate mood disturbance, a cohort who might arguably derive greater benefit than other populations. The principal aim was to examine whether consumption of SunGold kiwifruit twice daily for 28-days improved psychological wellbeing in mood-disturbed adults. Secondary outcomes included blood plasma vitamin C concentration, wellbeing, vitality, and gastrointestinal symptoms.

5.4 Method

5.4.1 Trial Design

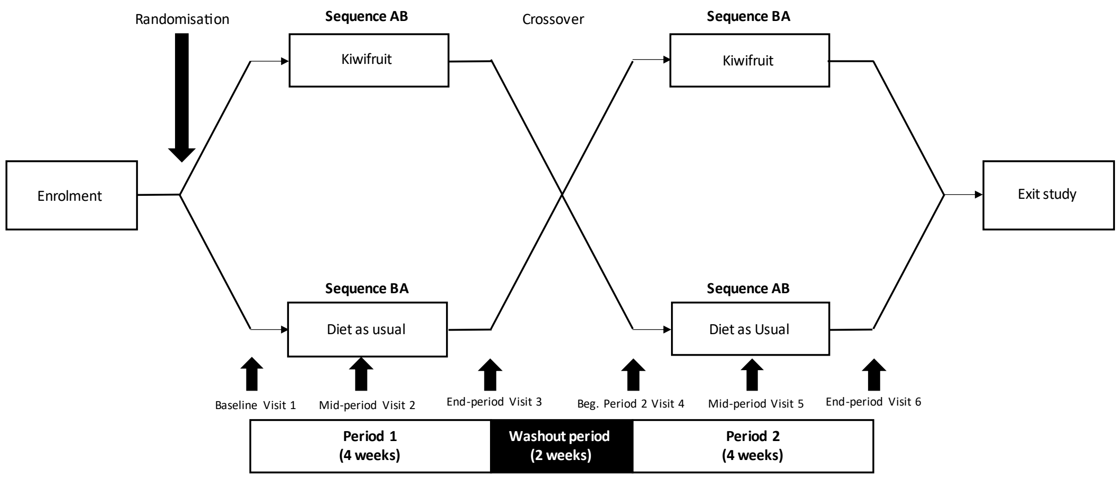
The Gold Kiwifruit and Psychological Health (GoKiPH) trial (Australian New Zealand Clinical Trials Registry: ACTRN12622000259741p) was a two-period, non-blinded crossover trial with participants randomised to a counter-balanced sequence. Participants consumed 2 SunGold kiwifruit daily or their typical diet for four weeks, with a two-week washout between periods (Figure 5). There were no changes to study protocol after trial commencement.

5.4.2 Participants

Eligibility criteria are detailed in Table 9. Participants aged between 18 - 60 years old with mild to moderate mood disturbance were recruited through the Commonwealth Scientific and Industrial Research Organisation (CSIRO) Research Clinic in Adelaide, Australia, from June to October 2022. The study was advertised on the CSIRO Facebook page and Research Clinic website.

Figure 5

Schematic Overview of GoKiPH Trial



5.4.3 Procedure

After responding to study advertisements, interested applicants were directed through a two-stage screening process that incorporated a medical screening questionnaire followed by a telephone-delivered assessment of mood (Kessler Psychological Distress Scale, K10;

Kessler et al., 2002). Participants attended six, fortnightly, in-clinic visits. Participants were remunerated AUD$40 per visit on a pro rata basis (maximum remuneration $AUD 240) for their participation. At each visit, participants provided a fasting blood sample, completed psychometric and gastrointestinal symptom questionnaires and basic anthropometric measures were documented.

Table 9

GoKiPH Study Eligibility Criteria.

Inclusion Criteria	Exclusion Criteria
Males and females aged 18-60 years	Allergy/intolerance to kiwifruit and/or latex
Non-smoker (within 6 months of baseline visit)	Recent smoker or NRT* (within 6 months)
Scores in the *mild* (20-24) to *moderate* (25-29) ranges on the Kessler Psychological Distress Scale at phone screening	Taking vitamin C supplements (within 3 months of baseline)
Willing to provide written informed consent	Previous or current diagnosis of Diabetes Mellitus, Bleeding Disorders, iron deficiency or hypo-/hyperthyroidism
Able to access own email address/service	Needle phobia or fainting due to fear of needles
Fluent in English	Taking prescription medication for gastrointestinal conditions (within 3 months of baseline)
	Initiation of, or alteration to, a course of anti-depressant, anxiolytic or antipsychotic (within 6 months of baseline)
	Received an investigational drug (within 3 months of baseline)
	Currently enrolled in any other dietary study or previously enrolled in a dietary intervention study at CSIRO involving kiwifruit

*NRT: nicotine replacement therapy.

At the first and second visits during the kiwifruit intervention period, participants received a two-week supply of SunGold kiwifruit, along with instructions on storage, consumption and disposal of unused fruit. They were also provided with a compliance and health log to record consumption and adverse events. Participants were asked to provide a photographic record of any unused study product at the completion of the intervention period. Participants were instructed to consume their usual diet during the two-week washout period.

5.4.4 Intervention

Participants consumed two Zespri SunGold kiwifruit (‘Zesy002^{TM}, *Actinidia chinensis* var. *chinensis*) daily for 28 days. Participants consumed the kiwifruit at a time of their choosing, either both in a single sitting or separately throughout the day (i.e., one at a time). Participants were instructed to store the kiwifruit in domestic refrigeration to maximise ripeness, and to remove the skin prior to eating (consume the flesh only).

5.4.5 Outcome Measures

5.4.5.1 Profile of Mood States Short Form (POMS-SF). The POMS-SF (McNair & Heuchert, 2005) is a self-report measure that contains a list of 35 mood-related adjectives. Respondents are asked to indicate the degree to which each item reflected their experience during the preceding seven-day period. Items are rated on a five-point Likert-type scale ranging from 0 (not at all) to 4 (extremely). The mood-related items reflect six factors of tension-anxiety, depression-rejection, anger-hostility, vigour-activity, fatigue-inertia, and confusion-bewilderment. A total mood disturbance (TMD) score is calculated by subtracting the value of the vigour-activity sub-scale from the sum of the remaining five sub-scales (minimum score -20 to maximum score 100) with higher scores indicating greater mood disturbance (Cronbach’s α = 0.87-0.92).

5.4.5.2 Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS). The WEMWBS (Tennant et al., 2007) is a 14-item scale that measures subjective wellbeing and psychological functioning in the previous two-week period. The positively worded statements such as feeling good about myself, thinking clearly, and feeling relaxed, are rated on a Likert-type scale ranging from 1 (none of the time) to 5 (all of the time). The 14 items are summed to produce a total wellbeing score (minimum score 14 to maximum score 70) with higher scores reflecting greater levels of wellbeing (Cronbach α = 0.89).

5.4.5.3 Subjective Vitality Scale (SVS). The six-item version of the SVS (Bostic et al., 2000) assesses feelings of subjective vitality and includes statements that ask respondents about their feelings of feeling energised, looking forward to each day and feelings of aliveness. Each positively worded statement is rated on a seven-point Likert scale from 1 (not at all true) to 7 (very true) with all items summed to produce a total vitality score (minimum score 6 to maximum score 42) with higher scores reflecting greater vitality (Cronbach α = 0.85).

5.4.5.4 Gastrointestinal Symptom Rating Scale (GSRS). The GSRS (Revicki et al., 1998) is a 15-item scale that asks respondents to rate the severity of common gastrointestinal symptoms such as heartburn, bloating and constipation during the preceding seven-day period on a seven-point Likert scale from 1 (no discomfort at all) to 7 (very severe discomfort). The 15 items reflect five domains (abdominal pain, reflux syndrome, diarrhoea syndrome, indigestion syndrome and constipation syndrome) of gastrointestinal symptoms with higher scores indicating greater symptom severity (Cronbach α = 0.61-0.83).

5.4.5.5 Blood Plasma Vitamin C Analysis. Participants fasted for a minimum of 10 hours prior to providing a sample at in-clinic appointments conducted between 7.30 a.m. and 9.00 a.m. on the morning of their appointment. A 5mL blood sample was drawn directly into a lithium heparin tube, wrapped in foil to protect the sample from light and placed on ice while awaiting collection. Once collected, samples were frozen and stored at temperatures below -18°C while awaiting analysis. After thawing for analysis, 100µL of Precipitant P was combined with 100µL serum and mixed for 30 seconds on a vortex mixer prior to incubation for 10 minutes at 4°C. The sample was subsequently centrifuged for 10 minutes at 10,000x g, and the vitamin C content of a sample (20μL) of the resulting supernatant was determined by high performance liquid chromatography using ultra-violet detection (Pullar et al., 2018b).

5.4.6 Sample Size

It was determined that a sample size of $N = 60$ participants would be required for a repeated-measures model assuming a small within-between interaction effect ($\eta^2 = 0.02$) with 80% power ($\alpha = 0.05$). Using a crossover design, this number is reduced by 50%, thus requiring a minimum sample size of $N = 30$ to power the study. A previous clinical trial that used an identical intervention as well as primary mood outcome measures and vitamin C analysis reported an attrition rate of 7% (equivalent to $n = 2$ in the present trial), albeit in a non-mood-disturbed sample (Conner et al., 2020). An additional 10% attrition ($n = 4$) was apportioned to allow for dropouts given the mood-disturbed population the trial was seeking to recruit, thus requiring a sample size of $n = 36$.

5.4.7 Randomisation, Allocation and Blinding

Participants were block randomised to sequence in a 1:1 allocation using a computer-generated algorithm by a co-author (IZ). The lead researcher (MB) was responsible for enrolling and assigning participants to sequence. Researchers and participants were unblinded to sequence allocation and the intervention.

5.4.8 Data Analysis and Statistical Methods

Statistical analyses were performed using R version 2023.6.1.524 (RCoreTeam, 2023). In the event of missing data for the psychological (POMS-SF, SVS & WEMWBS) and gastrointestinal (GSRS) questionnaires, these were replaced using the intra-individual scale mean when at least 50% of scale items were completed (Mainzer et al., 2021). Missing data were mainly due to dropout ($n = 3$; $n = 1$ sequence AB, $n = 2$ sequence BA; see Figure 5), which all occurred by week 2. Missingness on individual scales across the sample ($n = 26$) did not exceed 15% (minimum 3% to maximum 14%). A mixed effects linear regression model was adopted for primary and secondary outcomes to estimate change in the outcome variable under kiwifruit supplementation and diet as usual conditions. Using the LMER function within the LME4 package in R (Bates et al., 2015), models were specified to include main effects for sequence allocation, treatment, time, and a treatment*time interaction. In addition, two random effects specifications were compared to identify the optimal model for the primary outcome (TMD) and included: 1) model with random intercepts for each participant (1|SubjectID); and 2) a model permitting variation of the treatment effect across subject/sequence combinations (Treatment|SubjectID:Sequence). The model permitting differential effects across participant/sequence combinations performed statistically better (chi-square = 11.73, df = 2, $p = .002$) and was retained for all subsequent models.

5.4.9 Statement of Ethics

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures were approved (Ethics ID: 2022_008_HREC) by the Executive of the CSIRO Health and Medical Research Ethics Committee (CHMHREC). The CHMHREC is a National Health and Medical Research Council Registered Human Research Ethics Committee (Registration: EC00187). The trial was prospectively registered with the Australian and New Zealand Clinical Trial Registry (Trial ID: ACTRN12622000259741p). All participants provided written informed consent.

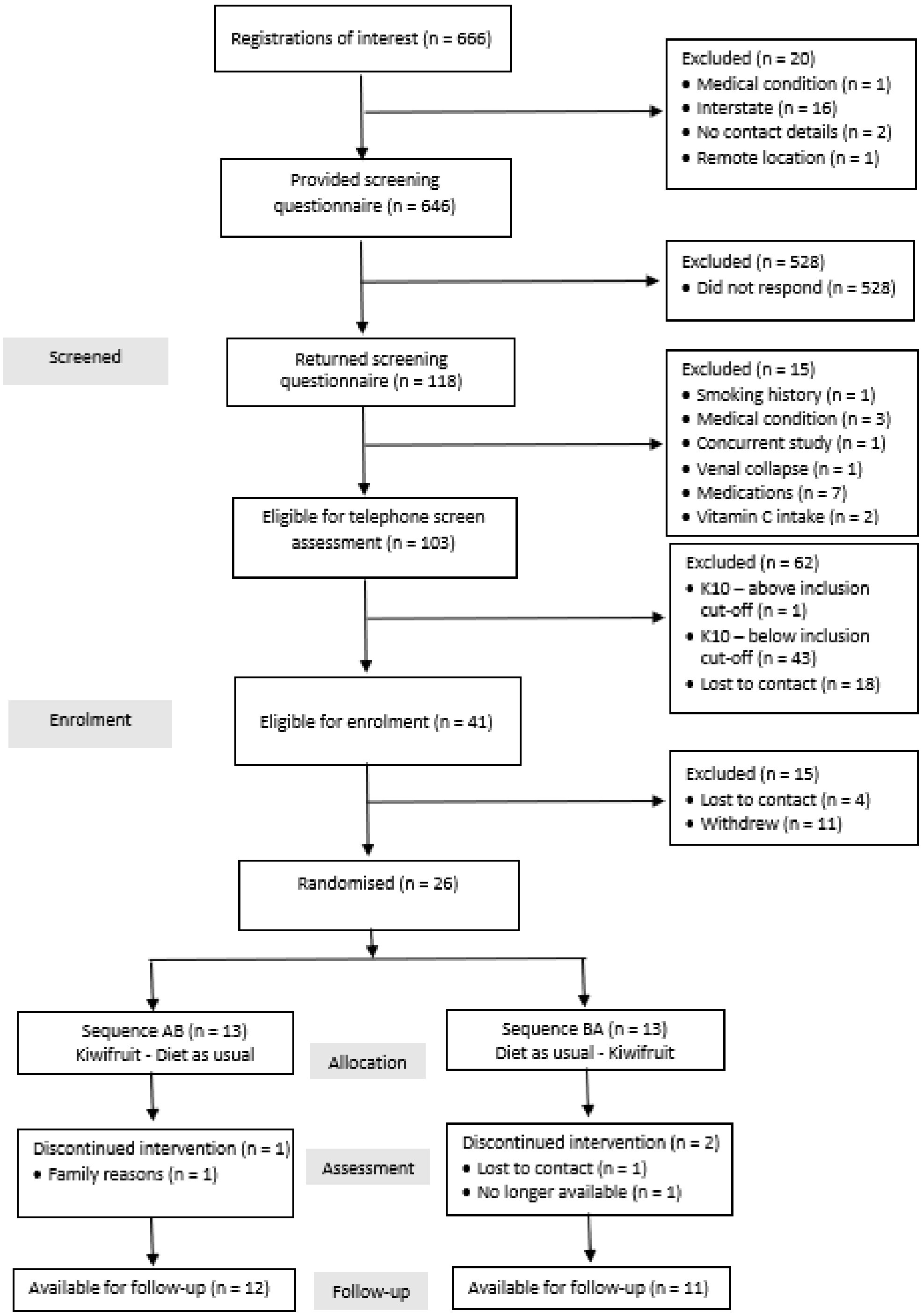
5.5 Results

5.5.1 Recruitment

The study received a considerable amount of interest (Figure 6) and 18% (118 of 666) of applicants who expressed an interest in participation returned the medical screening questionnaire. Fifteen applicants (13%) were excluded based on medical eligibility criteria.

Figure 6

CONSORT Flowchart of Movement of Participants Through Screening, Enrolment, Allocation and Follow-up



Forty-four (43%) of the remaining 103 applicants were excluded following psychological screening and a further 18 (18%) were lost to contact. Fifteen (37%) of the remaining 41 applicants either withdrew (n = 11) or were lost to contact (n = 4), leaving 26 participants eligible for enrolment.

5.5.2 Participant Characteristics

Twenty-six participants were sequentially enrolled in the trial between June and October 2022 with n = 13 participants allocated to each sequence. Three participants withdrew from the study. One participant (sequence AB) withdrew after the second visit citing family health issues; and two participants from sequence BA withdrew after completing the baseline visit (lost to contact n = 1, and work commitments n = 1). The mean age of the kiwifruit and diet as usual conditions were not dissimilar. The sample was predominantly female (≥ 75%) and the mean BMI was in the overweight range (25.0 - 29.9; Table 10). The two conditions were moderately mood-disturbed on a scale from -20 to 100, with higher scores indicating greater mood disturbance.

The mean blood plasma vitamin C concentration indicated the two conditions were vitamin C-replete at baseline. The mean wellbeing scores were moderate with higher scores indicating greater wellbeing (minimum 14 to maximum 70), as was the mean vitality score with higher scores reflecting greater vitality on a scale from six to 42. Gastrointestinal symptom ratings for each group were considered low on a scale from 15 - 95 with higher scores indicating greater symptom severity.

Table 10

*Baseline Characteristics for Kiwifruit and Diet as Usual Conditions**

	Kiwifruit (n = 24)	**Diet as usual (n = 25)**
Female (%)	18 (75%)	19 (76%)
Age	36.8 (11)	36.3 (11.2)
BMI	29.1 (8.4)	29.9 (8.1)
POMS-SF TMD	27.6 (13.5)	21.7 (17.5)
Vitamin C^	57.9 (27.3)	54.4 (20.6)
WEMWBS	42.1 (5.7)	43.8 (7.4)
SVS	22.5 (6.2)	23.5 (6.9)
GSRS	26.6 (7.7)	25.0 (7.6)

*Means (SD) unless stated. ^µmol/L. BMI = Body Mass Index (kg/m^2); POMS-SF TMD = Profile of Mood States - Short Form Total Mood Disturbance; WEMWBS = Warwick-Edinburgh Mental Wellbeing Scale; SVS = Subjective Vitality Scale; GSRS = Gastrointestinal Symptom Rating Scale

5.5.3 Adverse Events and Compliance

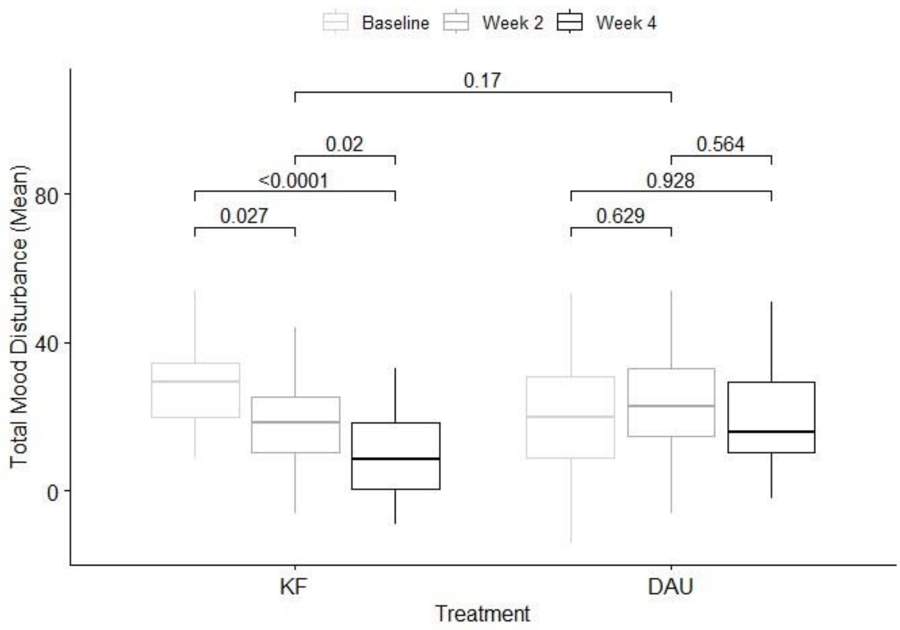
No serious adverse events were recorded. One participant reported flatulence and mild bloating that persisted for three weeks during the kiwifruit intervention however, this did not affect participation or compliance. Phlebotomy staff were unable to draw blood from one participant on two occasions, and on a single occasion for a second participant. Compliance with study product consumption was high (n = 26, 97%) and did not differ between sequences ($p > 0.05$).

5.5.4 Primary Outcome - Total Mood Disturbance

Linear mixed effects models for primary and secondary outcomes are presented at Table 11. The model examining the effect of the intervention on total mood disturbance showed a significant time effect, $F(2, 112.88) = 7.96$, $p < .001$, but not a significant overall treatment effect, $F(1, 114.17) = 3.34$, $p = .07$. However, the interaction between treatment and time was significant, $F(2, 112.87) = 9.52$, $p < .001$. As shown in Figure 7, mean total mood disturbance scores reduced significantly at week 2 and week 4 in the kiwifruit condition. Scores for the DAU period did not change significantly across timepoints.

Figure 7

Mean Difference (SE bars) in Total Mood Disturbance at Week 2 and Week 4 for Kiwifruit (KF) and Diet as Usual Condition (DAU)



5.5.5 Secondary Outcomes

Regarding plasma vitamin C, results showed a significant time effect, $F(2, 83.28) = 5.39$, $p = .006$, and a significant overall treatment effect, $F(1, 23.03) = 18.92$, $p < .001$. The interaction between treatment and time was significant, $F(2, 83.42) = 3.91$, $p = .02$. As evident in Figure 8(A), mean vitamin C concentration increased significantly at week 2 and week 4 in the kiwifruit condition. Mean vitamin C levels for the DAU period did not vary considerably across timepoints.

Results for wellbeing showed a significant effect of time, $F(2, 112.20) = 4.40$, $p = .015$, and a significant overall treatment effect, $F(1, 85.98) = 4.12$, $p = .05$. There was a significant interaction between treatment and time, $F(2, 112.19) = 6.16$, $p = .003$. Mean wellbeing scores did not increase significantly at week 2 but were significantly increased at week 4 in the kiwifruit condition. Mean wellbeing scores did not change significantly across timepoints (Figure 8(B)).

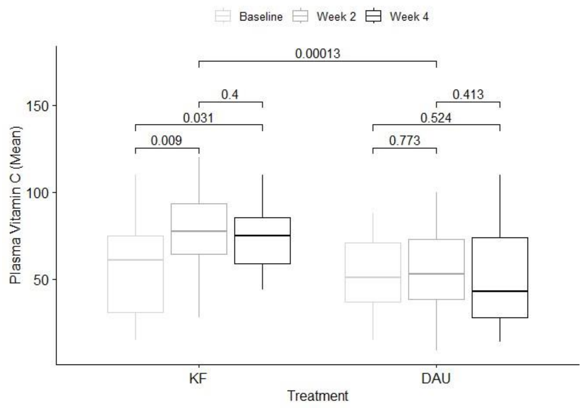
With regard to vitality, the results showed a significant time effect, $F(2, 112.45) = 4.44$, $p = .014$, and a significant overall interaction between treatment and time, $F(2, 112.45) = 5.94$, $p = .004$. However, there was not a significant overall treatment effect, $F(1, 93.59) = 1.60$, $p = 0.21$. As seen in Figure 8(C), there was a significant increase in vitality scores at week 4 but not at week 2 in the kiwifruit condition. Vitality scores did not differ significantly across timepoints in the DAU period.

In relation to gastrointestinal symptoms, the model showed a significant time effect, $F(2, 90.60) = 4.36$, $p = .016$, and a significant interaction between treatment and time, $F(2, 90.60) = 6.83$, $p = .002$. However, there was not a significant overall treatment effect, $F(1, 22.98) = 1.0$, $p = 0.33$. As shown in Figure 8(D), mean gastrointestinal symptom ratings decreased significantly at week 2 and this was maintained at week 4 in the kiwifruit condition. Mean symptom ratings did not vary greatly across timepoints in the DAU period.

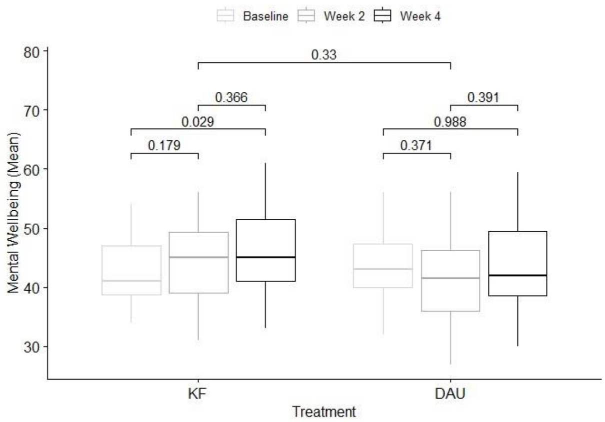
Figure 8

Mean Difference (SE bars) in Plasma Vitamin C (A), Wellbeing (B), Vitality (C) and Gastrointestinal Symptoms (D) at Week 2 and Week 4 for Kiwifruit (KF) and Diet as Usual Condition (DAU)

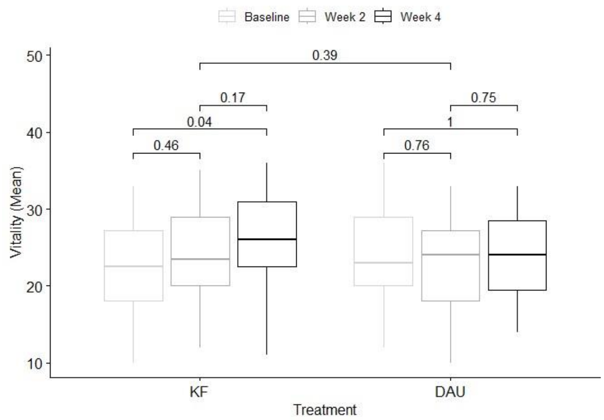
(A)



(B)



(C)



(D)

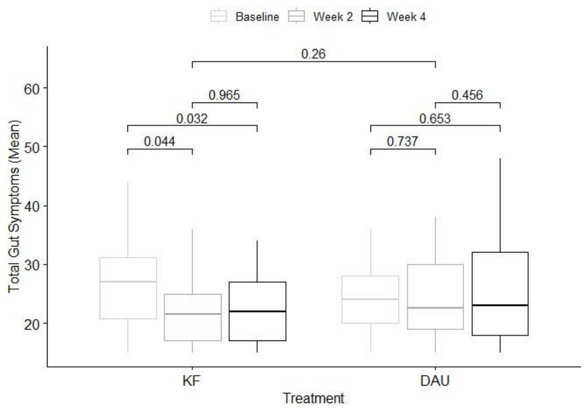


Table 11

*Linear Mixed Effects Models for Primary and Secondary Outcomes for Sequence, Treatment, Time and Treatment*Time Interaction*

Model	**TMD**			**Plasma vC**			**SVS**			**WEMWBS**			**GSRS**		
	β	CI	*p*	β	CI	*p*	β	CI	*p*	β	CI	*p*	β	CI	*p*
Sequence															
AB	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BA	12	3.6, 21	.007*	2.3	-11, 16	0.7	-4.7	-9.1,-0.39	.034*	-6.3	-11, -2.0	.006*	1.1	-3.8, 6.0	0.6
Treatment															
Kiwifruit	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
DAU	-6.9	-13,-0.92	.024*	-2.7	-14, 9.1	0.7	1.4	-.35, 3.1	0.12	1.7	-0.36, 3.8	0.10	-2.1	-5.1, 0.90	0.2
Time															
Week 2	-8.9	-15,-2.9	.004*	23	11, 34	<.001*	1.3	-0.38, 3.0	0.13	2.5	0.46, 4.5	.017*	-4.3	-6.6, -1.9	<.001*
Week 4	-18	-24, -12	<.001*	17	6.0, 29	.003*	3.9	2.2, 5.7	<.001*	4.2	2.2, 6.3	<.001*	-4.6	-7.0, -2.3	<.001*
Treatment*Time															
DAU*Week 2	12	3.4, 20	.006*	-19	-35, -3.0	.02*	-1.8	-4.3, 0.58	0.13	-4.5	-7.4, -1.6	.003*	3.7	0.36, 7.0	.03*
DAU*Week 4	19	10, 27	<.001*	-20	-36, -4.0	.015*	-4.3	-6.7, -1.8	<.001*	-4.4	-7.3, -1.5	.003*	6.2	2.8, 9.5	<.001*

TMD = Total Mood Disturbance; vC = vitamin C; SVS = Subjective Vitality Scale; WEMWBS = Warwick-Edinburgh Mental Wellbeing Scale; GSRS = Gastrointestinal Symptom Rating Scale; CI = Confidence interval; DAU = Diet As Usual. *significant at $p = 0.05$

5.6 Discussion

This two-period, non-blinded randomised crossover trial investigated the potential for daily consumption of two SunGold kiwifruit to support psychological health through increased vitamin C intake in mood-disturbed adults. Importantly, there were no serious adverse events reported during the trial and the intervention was well tolerated. Consuming two SunGold kiwifruit daily for 28-days was associated with a significant reduction in mood disturbance compared to usual diet. Results for the secondary outcomes of blood plasma vitamin C concentration, wellbeing, vitality and gastrointestinal symptoms all reflected that the mean change in scores were significantly greater during the kiwifruit period compared to diet as usual.

Results indicate that increased vitamin C concentrations from SunGold kiwifruit consumption may be a significant factor in supporting improvements in mood, wellbeing and vitality in the mood-disturbed sample. Of interest, the improvements in gastrointestinal functioning offer the possibility of an additional kiwifruit-mediated pathway toward improved psychological health. The present results are supported by previous clinical trials that found similar associations between gold kiwifruit consumption and psychological wellbeing, albeit in young adults with sub-optimal vitamin C concentrations (Carr et al., 2013a; Conner et al., 2020). In recruiting a mood-disturbed sample of 18 - 60-year-olds however, the present trial extends that body of work to include a cohort that arguably stands to receive greater benefit than non-mood disturbed populations (Firth et al., 2019). Likewise, results for gastrointestinal functioning reflect previous work that SunGold kiwifruit consumption was associated with reductions in gastrointestinal symptoms in healthy and clinical samples (Bayer et al., 2022b; Eady et al., 2019; Eady et al., 2020). Acknowledging the associations between gastrointestinal functioning and mood disorders (Appleton, 2018), the present trial augments this work by providing preliminary evidence for SunGold kiwifruit to improve mood through a reduction in gut symptom severity.

Notwithstanding the contribution of vitamin C to improved psychological health in the present trial, other nutrients in SunGold kiwifruit may have contributed to the observed improvements. SunGold kiwifruit contain relatively high concentrations of vitamin E, potassium, folate and dietary fibre, all of which are associated with improved mental health outcomes. For example, vitamin E is recognised for its antioxidant and anti-inflammatory actions and its important role in the modulation of depressive symptomatology (Manosso et al., 2020). Diets high in potassium are associated with greater vigor, reduced mood disturbance and improved mood (Torres et al., 2008), and dietary folate intake has been associated with lowered risk of developing depression and reduced depression severity (Jacka et al., 2012; Kendrick et al., 2008). Dietary fibre is associated with positive modulation of gut microbiota, which has been implicated in the pathogenesis of depression (Marx et al., 2021). The pathway between gut microbiota and depression is thought to be partly explained by the metabolism of tryptophan, an amino acid found in SunGold kiwifruit (Drummond, 2013) and recognised for its role in serotonin production (Tveden-Nyborg, 2021).

The association between diet quality and mental health is well-established (Dawson et al., 2016). Results from observational and clinical trials have consistently demonstrated that healthy dietary patterns, such as the Mediterranean diet, characterised by high intake of fruits, vegetables, wholegrains, legumes, seafood, nuts, seeds and olive oil, while being low in sugar, red meat, and processed and refined foods (Bayes et al., 2022), are associated with reduced risk of depression (Lassale et al., 2019; Marx et al., 2017) and reduced depressive symptoms in depressed populations (Firth et al., 2019). Dietary patterns such as the MDP have produced small yet significant reductions in depression severity in clinical populations There is almost universal consensus in the nutritional psychiatry field that further research is required to distil the constituents and mechanisms of action of dietary interventions to develop more targeted and cost-effective treatments and importantly, to conceive low-intensity treatments that offer self-agency to individuals with mental health conditions (Ceolin et al., 2022; Firth et al., 2019).

The present research demonstrated the potential for a simple, single-food intervention to reduce mood disturbance and improve positive affective states such as vitality and wellbeing in a mood-disturbed population. Furthermore, numerous barriers exist that would challenge the capacity of many individuals to adopt and adhere to a healthy dietary pattern to support their psychological health. These include perceptions of increased cost, food literacy, extra time and effort in meal preparation and family food preferences (Scannell et al., 2020). Factors such as low self-efficacy, reduced motivation and lack of social support often experienced by depressed populations represent additional barriers to adopting a healthy diet (Barre et al., 2011). Thus, our study provides fresh insight into the potential for a nutrient-dense fruit to positively influence psychological health through multiple pathways and importantly, aligns with the World Health Organisation's (WHO) call for lifestyle-based interventions such as diet to constitute a first-line intervention for mental health disorders (Burrows et al., 2022).

5.6.1 Study Limitations

Study findings must be interpreted with consideration to the following limitations. First, although the study examined the influence of vitamin C on psychological health, vitamin C concentration was not an eligibility criterion. It was subsequently identified that the mean vitamin C concentration of the kiwifruit and diet as usual conditions (M / SD = 57.9 µmol/L / 27.3 µmol/L, and 54.4 µmol/L / 20.6 µmol/L, respectively) were toward the lower end of the adequate to saturating status range (i.e., 50 - 75 µmol/L; Rowe & Carr, 2020). Increasing vitamin C intake beyond saturation status has little, or no effect on tissue concentration (Carr & Frei, 1999), thus creating a potential ceiling effect on mood outcomes in the present sample.

Second, other nutrients found in SunGold kiwifruit (e.g., vitamin E, potassium, folate and dietary fibre) with established associations with mental health outcomes (Koopman et al., 2017; Maes et al., 2000; Opie et al., 2017) were not measured and their relative contribution remains unquantified. This does not preclude however, that the observed improvements in mood outcomes are the direct result of vitamin C or that other nutrients in the kiwifruit acted either alone or synergistically to affect improvements. For example, vitamin C from gold kiwifruit supports the bioavailability of iron (Beck et al., 2011), a trace element associated with mood outcomes and considered essential for serotonin synthesis (Beard, 2003; Młyniec et al., 2014). Furthermore, it is understood that vitamin E and vitamin C act synergistically to ameliorate oxidative stress, a potential mechanistic pathway in mental health disorders (Marx et al., 2021).

Third, as is common in clinical nutrition research when examining whole foods or whole-of-diet interventions, blinding of participants and researchers is difficult, if not impossible (Weaver & Miller, 2017). The present study was not immune to these challenges and participants and researchers remained aware of allocation, intervention and study methodology. Fourth, the sample in the present trial was predominantly female (~ 75%) and it has been reported that female participants tend to report greater psychological benefit from dietary interventions compared to all-male samples (Firth et al., 2019). Gender-specific factors cited to explain this difference include sex differences in metabolism and body composition and socio-cultural differences in expectations regarding diet that predispose females to be more likely to adopt health behaviors compared to males (Firth et al., 2019). Additionally, females exhibit a greater dose-response bioavailability of vitamin C than males (Carr & Rowe, 2020). Noted gender differences in dietary intake and behavior (Kiefer et al., 2005), mood disorders (Piccinelli & Wilkinson, 2000) and iron bioavailability (Berthou et al., 2022) may further limit generalisability of findings.

Finally, the mean baseline gastrointestinal symptom rating of the kiwifruit and diet as usual conditions (*M / SD* = 26.6 / 7.7, and 25 / 7.6, respectively) were in the lowest quartile (possible score range 15 - 95), suggesting a mild symptom profile. This may have introduced a floor effect on symptom reduction. SunGold kiwifruit-delivered dietary fibre may have conferred broader effects on gut health by increasing the diversity of dietary fibre ingested compared to a single-fibre supplement. This is supported by previous findings that noted SunGold kiwifruit consumption resulted in fewer side effects and greater symptom reduction than a dose-matched single dietary fibre supplement (Bayer et al., 2022b; Eady et al., 2019). Notwithstanding the threat of a floor effect, participants reported significant reductions in gastrointestinal symptom severity. Acknowledging the established associations between mood disturbance and gastrointestinal symptoms (Van Oudenhove et al., 2016), the improvements in psychological wellbeing may have been informed by dietary fibre-induced gastrointestinal symptom reduction rather than from increased vitamin C intake.

5.6.2 Study Attributes

The primary strength of this study was the decision to recruit adults with mild to moderate mood disturbance. Current clinical treatment guidelines recommend dietary interventions as one component of lifestyle-based treatment protocols for adults with sub-clinical depression (Marx et al., 2023b). Previous kiwifruit trials examining mood did not select participants based on mood status. Thus, the present work provides valuable new information on the benefits of a whole food dietary intervention for psychological health. The use of validated measures of mood, wellbeing, vitality and gastrointestinal functioning in addition to objective measurement of vitamin C concentration at regular intervals across the trial further strengthens results. Screening for conditions that might affect vitamin C bioavailability (e.g., smoking) and excluding individuals with alterations in dose or class of pharmacological agent in the lead-up to the trial to avoid the potential for baseline mood to be affected by any changes were additional assets. The crossover design was chosen as it served to reduce the sample size required along with the added advantage of each participant acting as their own control. Although considered *a priori* as negligible, any potential carryover effect from vitamin C intake during the kiwifruit intervention were controlled for by setting the length of the washout period in line with depletion and repletion kinetics of vitamin C (Blanchard, 1991). Recruitment and retention difficulties for studies involving mood-disturbed individuals are well-documented (Hughes-Morley et al., 2015), however, the low drop-out rate and substantial interest in the study reflect positively on the study design. Highlighting the relatively benign nature and low risk of the intervention, SunGold kiwifruit was well-tolerated, and no study product-related serious adverse events were reported.

5.6.3 Directions for Future Research

The aim of the present trial was to examine the potential for SunGold kiwifruit to support psychological health in an at-risk population, namely, adults with mild to moderate mood disturbance. Targeting this population is of particular importance given that dietary interventions, and in particular single food interventions, represent a relatively low-risk, low-intensity preventative measure that can either form part of a clinician-delivered treatment program or as a self-management approach for reducing symptoms of depression (Firth et al., 2019).

Larger randomised controlled trials with more diverse mental health, cultural, age and socio-demographic profiles are warranted. Recruiting a population-representative gender balance would support generalisation of results and would help determine the optimum nutrient intake to prevent or reduce depressive symptoms and support the development of gender-individualised dietary interventions. For example, future SunGold research could target at-risk populations likely to benefit from increased intake of specific nutrients in SunGold kiwifruit in longitudinal studies (i.e., increased folate and vitamin C intake to reduce the incidence of perinatal depressive symptoms). To the extent possible, incorporating study design features that achieve full, or at least partial blinding of participants and researchers would substantiate findings. Lastly, future research that identifies the individual components or micronutrient interactions that mediate the relationships between dietary intake and psychological health will contribute to the field and provide a greater understanding of the role of dietary interventions in the treatment of mental health conditions.

5.7 Conclusions

The present trial provides preliminary evidence that SunGold kiwifruit consumption improves mood, wellbeing, vitality and gastrointestinal functioning, as well as vitamin C status, in mood-compromised adults. These findings build upon the small but growing body of work uncovering the mood-enhancing properties of SunGold kiwifruit. Importantly, the present study demonstrated these effects in mood-disturbed participants, adding further weight to the potential benefits of dietary interventions, such as kiwifruit, for reducing mood symptoms. Emerging evidence suggests that while dietary interventions can realise small but significant reductions in depression symptoms in non-clinical populations, larger effects are observed in populations with higher baseline symptoms of depression (Marx et al., 2021). Given the growing recognition of the benefit to psychological health from dietary interventions and the need to provide alternate or adjuvant options in the clinical and public policy space, the nutrient dense SunGold kiwifruit offers an appealing, nutritious and affordable pathway to positive psychological health.

Chapter 6: General Discussion and Research Conclusions

6.1 Overview

The overarching aim of this thesis was to examine the potential for kiwifruit to support psychological health and wellbeing. Kiwifruit are a nutrient-dense fruit with recognised benefits to nutritional status as well as digestive, metabolic and immune health (Richardson et al., 2018). In addition to substantial quantities of vitamin E, dietary fibre, potassium and folate, gold kiwifruit has exceptionally high levels of vitamin C, an essential micronutrient implicated in numerous biological pathways including those involved in mood regulation (Pullar et al., 2018a). Gold kiwifruit consumption has been associated with improved mood, increased feelings of vitality and greater wellbeing in otherwise healthy adults aged 18 - 35 years with sub-optimal vitamin C concentrations (< 50 µmol/L; Conner et al., 2020). However, there is limited knowledge of the potential benefit of gold kiwifruit consumption for mood and psychological health in other populations despite indications that those with greater mood disturbance received an enhanced benefit (Carr et al., 2013a).

The initial aim of the present research was to undertake a literature review of the existing work regarding kiwifruit consumption and psychological health to identify gaps in the literature. Emerging from the findings of the literature review, a small feasibility trial was undertaken to determine the practicability of running a subsequent larger trial with the defined population of interest, namely, adults with sub-optimal vitamin C status and mild to moderate mood disturbance. The recruitment challenges and results of the feasibility trial informed the design and methodology of the final study of this thesis, namely, a randomised, two-period crossover trial that delivered a gold kiwifruit intervention to otherwise healthy adults with mild to moderate mood disturbance. The present studies contribute to the nascent research and importantly, provide a novel contribution to the field by recruiting from a population not previously studied and one that is well-placed to receive clinical and nutritional benefit.

6.2 Summary and Significance of Key Findings

Study 1 was a rapid review of the literature seeking to identify intervention trials that incorporated whole kiwifruit supplementation (green or gold) and included mood-related psychological constructs such as depression, wellbeing, vitality, or mood disturbance as the primary outcomes of interest. The review resulted in the identification of two randomised trials that satisfied the search terms. In short, the studies reported that gold kiwifruit consumption was associated with improved mood, wellbeing and vigour and reduced fatigue in adults aged 18 - 35 years with sub-optimal vitamin C status (Carr et al., 2013a; Conner et al., 2020). The former trial was a parallel-arms design in which young adult males were randomised to consume either half or two gold kiwifruit daily for six-weeks with a five-week lead-in period. Conner *et al.* (2020) conducted a randomised, placebo-controlled, three-arm trial with a two-week lead-in, four-week intervention and two-week washout.

Study 1 identified a critical gap in the research space. The two studies had recruited participants based on sub-optimal vitamin C concentrations, but mood status did not feature in the study selection criteria. Critically, evidence from observational and supplementation studies have reported that high vitamin C status was associated with elevated mood and conversely, that inadequate vitamin C status was associated with impaired mood states (Appel et al., 2008; Pullar et al., 2018a). The study by Carr *et al.* (2013a) reported results of an exploratory analysis that found participants (n = 8) with higher-than-average baseline mood disturbance experienced significantly greater improvements in mood compared to participants with lower-than-average baseline mood disturbance. This finding was the catalyst for the decision to examine the effect of a gold kiwifruit intervention on adults with sub-optimal vitamin C status and mild to moderate mood disturbance in Study 2. The significant contribution of Study 1 was to synthesise the existing literature, identify a critical gap that warranted further investigation, and contribute to the design and implementation of Studies 2 and 3 with regard to the choice of kiwifruit cultivar, dose-rate and duration of intervention period.

The purpose of Study 2 was to determine the feasibility of being able to recruit, assess and follow-up a cohort of adults aged 18 - 60 years with sub-optimal vitamin C status (> 23µmol/L to < 50 µmol/L) in conjunction with mild to moderate mood disturbance. Secondary outcomes assessed the potential for SunGold kiwifruit to support psychological health through improved vitamin C status. The findings suggested that a larger randomised trial was feasible; however, modifications to study protocols would be necessary to avoid issues with study recruitment as well as compliance with a weekly smartphone-delivered mood assessment measure. Although the final sample (n = 4) was too small to permit traditional statistical analysis; visual analysis of individual plots suggested SunGold kiwifruit was linked with increased vitamin C status and potentially reduced mood disturbance scores in all participants.

The existing literature had examined the effect of gold kiwifruit consumption on psychological health in a defined population of New Zealand adults aged 18 - 35 years with sub-optimal vitamin C status (Carr et al., 2013a; Conner et al., 2020). Study 2 extended this research in a number of directions. First, Study 2 broadened the eligible age range to encompass adults aged 18 - 60 years. Second, participants were recruited from a community sample and not from tertiary institution environments. Third, Study 2 extended the eligibility criteria to include adults with mild to moderate mood disturbance, and fourth, it undertook all of these extensions within an Australian context. Furthermore, Australian nutrition surveys do not typically collect data on vitamin C status or intake, so the prevalence of sub-optimal vitamin C status in the Australian population remained unquantified. Global reviews have indicated a lower prevalence of vitamin C deficiency in high-income countries compared to low- and middle-income countries and found that certain groups (i.e., those with low socio-economic status in high-income countries) are at greater risk of deficiency (Rowe & Carr, 2020). There were no previous studies identified that provided epidemiological information on the prevalence of vitamin C deficiency in Australian populations. The closest approximation in terms of socio-cultural and economic profile was an observational study of healthy, middle-aged New Zealand adults (n = 404) that reported 62% of the cohort had sub-optimal vitamin C concentrations (Pearson et al., 2017). Study 2 also attempted to recruit from a population (i.e., adults with mild to moderate mood disturbance) associated with greater recruitment and retention challenges (Hughes-Morley et al., 2015).

Study 2 makes a significant contribution to the nutritional psychiatry research space in two respects. First, it examined the effects of a vitamin C-rich fruit on both biochemical (vitamin C status) and psychological (mood) outcomes in vitamin C- and mood-compromised adults. Second, it informed the design and implementation of a larger, randomised trial that ultimately contributes to a greater understanding of the role of dietary interventions in supporting psychological health.

Study 3 was a randomised crossover trial that sought to overcome some of the limitations of the existing research into kiwifruit consumption and psychological health. First, previous research had recruited 18 - 35-year-olds, thus, there was limited generalisability to other age cohorts and in particular, to age cohorts associated with higher prevalence rates of MDD (i.e., 35 - 60-year-olds; Arias de la Torre et al., 2021). Second, existing work had not recruited a population with mild to moderate mood disturbance; and third, neither study had assessed gastrointestinal functioning, a potential confound that might contribute to improved depressive symptomatology from increased dietary fibre intake following kiwifruit consumption. Study 3 found that consuming two SunGold kiwifruit daily for 28-days was associated with improved psychological health as indicated by decreased mood disturbance and improved wellbeing and vitality compared to diet as usual. The observed reductions in gastrointestinal symptom severity and concomitant mood improvements following SunGold kiwifruit consumption adds a novel contribution to the existing research that suggest an indirect pathway to improved psychological health through increased dietary fibre intake from SunGold kiwifruit.

The results of Study 3 are in line with previous research and provide significant new contributions to the literature. Study 3 expands on the exploratory analysis of participants with higher-than-average mood disturbance conducted by Carr *et al.* (2013a) by specifically targeting mood-disturbed adults, a cohort that arguably stands to receive greater benefit from an intervention targeting improved psychological health. Furthermore, Study 3 overcomes some of the limitations of previous research by recruiting a community-based sample from a broader age-range with mild to moderate mood disturbance. The study also makes a substantial contribution to our understanding of the potential mood-enhancing properties of individual foods that form part of a broader healthy dietary pattern with established benefits to psychological health in clinical and sub-clinical populations (Jacka et al., 2017; Sánchez-Villegas et al., 2013). For example, fruit consumption is considered an integral component of a healthy dietary pattern, yet to date, trials delivering whole-of-diet interventions have not examined the efficacy of individual foods or food groups. Swapping out discretionary foods for healthy foods was highlighted as a strength of the SMILES trial (Jacka et al., 2017) and SunGold kiwifruit are an excellent candidate for such strategies. Self-perceived barriers toward adherence to a whole-of-diet approach include suitability and taste, affordability, additional time/effort, food literacy, cooking skills and family food preferences (Scannell et al., 2020). The self-perceived ability to successfully adhere to a whole-of-diet approach is reported as another disadvantage. For example, over one-third of participants (*n* = 147, 40%)

in the Scannell *et al.* (2020) survey described the MDP as either too restrictive or overly difficult to follow. Adults with MDD or mild to moderate mood disturbance are likely to face the additive challenge of mental health-related barriers to implementing a whole-of-diet change such as low motivation, low self-efficacy, depleted energy for food-related activities (i.e., cooking and shopping), decreased concentration (Opie et al., 2018) and the recognised interplay between depression and an unhealthy lifestyle including poor diet (Rahe & Berger, 2016). Thus, the present research provides a valuable contribution to the extant nutritional psychiatry literature and endorses SunGold kiwifruit not so much as way to get a 'foot in the door', but as a way to get 'fruit in the fridge' as a starting point to building healthy dietary patterns in clinically and mild to moderately depressed populations.

6.3 Clinical and Theoretical Implications

The results of the three studies described in this thesis have important clinical and theoretical implications. The review of the literature in Study 1 highlighted the growing interest and emerging research examining nutrient intake and dietary interventions and the potential for whole food-delivered nutrients to enrich nutrient status and psychological health. Study 2 revealed some of the challenges associated with undertaking research within a discrete population with poor nutrient status and illustrated the value of feasibility trials in maximising the success of future large-scale clinical studies. Study 3 found that SunGold kiwifruit consumption substantially increased vitamin C intake and conferred benefits to psychological health through reduced mood disturbance and improved wellbeing and vitality in mild to moderately depressed adults. The predominant clinical implication across all three studies is the potential utility of a single, whole food to deliver benefits to psychological health as a stand-alone vector or as an integral component of a larger healthy dietary pattern.

More recently, the focus of nutritional psychiatry research has shifted from examining single nutrient or single foods to whole-of-diet interventions (e.g., MDP) for the prevention and treatment of mental health conditions (Jacka, 2017). While this redirection has obvious merit, numerous barriers exist outside of an intervention trial that would challenge the capacity of many individuals to adopt and adhere to a healthy dietary pattern to support their psychological health. These include perceptions of increased cost, extra time and effort in meal preparation and food preferences of other household members (Scannell et al., 2020). Factors such as low self-efficacy, reduced motivation and lack of social support often experienced by depressed populations represent additional barriers to adopting a healthy diet (Barre et al., 2011). Thus, from a clinical perspective, Studies 2 and 3 provide clinicians with evidence that a single food item can deliver meaningful improvements to psychological health that can be presented to clients as an achievable, low-intensity self-care strategy for mental health. When viewed through a behavioural activation lens, a low-intensity treatment goal such as adding a SunGold kiwifruit to the usual diet represents an affordable and achievable goal that would directly influence physiological and psychological health. This could contribute to a sense of accomplishment, increased self-mastery and autonomy; direct the individual toward a structured, healthier lifestyle (Soucy Chartier & Provencher, 2013); and build further self-efficacy for adherence to other healthy nutrition behaviour (Cuadrado et al., 2018).

The finding that consumption of SunGold kiwifruit was associated with self-reported improvements in gastrointestinal health has important clinical implications. Consumption of SunGold kiwifruit has previously been associated with improvements in physiological markers of gastrointestinal function (Bayer et al., 2022b; Eady et al., 2020). Findings augment the existing body of work and confirm that, similar to green kiwifruit, SunGold kiwifruit is a safe and well-tolerated intervention for supporting gut motility and health. From a clinical perspective, high dietary fibre and high fruit intake has been associated with decreased odds of depression (Gangwisch et al., 2015; Matison et al., 2021) and it has been proposed that their ability to modulate gut microbiota and increase brain-derived neurotrophic factor levels directly influences mood (Dalile et al., 2021). Thus, Study 3 has important clinical implications with respect to the potential benefits to psychological health from improved gastrointestinal functioning following increased dietary fibre intake from SunGold kiwifruit.

An important theoretical implication of the present work is to inform and augment the existing research surrounding the efficacy of dietary interventions in the prevention and treatment of depression and other mental health conditions. There is a clear need to establish causal relationships between dietary patterns and the risk of mental health conditions, and to determine how best to incorporate dietary interventions within mental health care (Firth et al., 2020). Additionally, there is a need to examine the role of dietary interventions as a depressive prophylaxis for populations asymptomatic or currently in remission. The support base for the efficacy of dietary interventions in the treatment of depression is currently rated as low but with good acceptability (e.g., practicability, risk-benefit ratio, applicability to the population; Marx et al., 2023a). This rating is based on a small (n = 4) pool of RCTs demonstrating moderate to large effect sizes but with a high risk of bias. Studies 2 and 3 offer critical new findings to augment the extant literature regarding diet, nutritional intake and psychological health. Specifically, the results accord with current guidelines for nutrition interventions that emphasise that the intake of nutrient-dense foods may be efficacious in reducing depressive symptoms (Marx et al., 2023a). Of particular importance, the current studies advance evidence for the efficacy of a nutrient-dense fruit delivering substantial amounts of vitamin C to reduce depressive symptomatology in a population at risk of developing a mood disorder. If the present findings are replicated in subsequent large-scale studies, SunGold kiwifruit could be included in future clinical guidelines as a ‘superior’ food for mental health as part of a lifestyle-based dietary intervention.

From a practical perspective, Study 2 highlighted the challenges associated with recruiting from a narrow population stratum not previously studied. The prevalence of sub-optimal vitamin C status in Australian adults remained unquantified prior to recruitment. Including vitamin C status as an eligibility criterion precluded a substantial number of applicants from enrolling in the study. Linking vitamin C status with mild to moderate mood disturbance as eligibility criteria further narrowed the recruitment pool. Study 2 also reinforced the value of the feasibility trial as an essential prerequisite to inform the design and success of larger clinical studies or definitive RCTs seeking to investigate the impact of novel interventions in populations with atypical recruitment and retention difficulties or examining an existing intervention with the potential for novel outcomes.

The clinical implications of Studies 2 and 3 extend beyond the treatment room. Nutritional psychiatry research is currently limited by a lack of studies investigating dietary interventions. Identifying effective adjuvant treatments for mild to moderate mood disturbance is critical. Individuals with mild to moderate mood disturbance utilise health care services to a greater extent than clinical populations (Rodríguez et al., 2012) and as many as 20% will go on to develop clinical depression (Kroenke, 2017). Preventative psychological interventions (e.g., CBT, problem-solving therapy, interpersonal therapy) have been shown to reduce the incidence of depression by a clinically relevant 21% compared to control interventions (van Zoonen et al., 2014). However, the research that has examined the relative cost-effectiveness of preventative interventions for depression is limited. An analysis by Mihalopoulos *et al.* (2011) reported on an individual and a group-based psychological intervention for the prevention of depression in adults with sub-clinical depression and noted an incremental cost-effectiveness ratio of AUD$8,600- and AUD$20,000-per-DALY-prevented, respectively. The interventions were described as ‘good value for money’ and it was estimated that the individual and group therapy would avert 2,600 and 1,700 DALYs, respectively. The individual therapy (Willemse et al., 2004) was a minimal-contact model that incorporated two visits to a Psychologist, a self-help CBT manual and six short follow-up phone calls over two months. The study reported that 12% of the therapy group and 18% of the control group (care as usual) had depression at 12-months follow-up (p = 0.032). Although a brief psycho-bibliotherapy intervention is not directly comparable to a single food dietary lifestyle-based intervention, they share features such as reduced interaction with mental health services, the promotion of self-care and self-management principles and lowered financial burden compared to traditional psychological interventions. The application of a low-intensity, self-managed dietary intervention that reduces incidence of depression is likely to support tangible reductions in the mental health burden at the individual, societal and health-system levels, in addition to informing public health policy and dietary guidelines.

A clinical and real-world implication of Study 3 relates to the 'bang for your buck' offered by SunGold kiwifruit. The relationships between diet quality, mental health and socio-economic disadvantage have been extensively examined. Although reverse causation has not been ruled out (i.e., poor diet can both precede and succeed depression), associations between healthy dietary intake and reduced odds of depression have been consistently reported (Matison et al., 2021), and socio-economic status has been reported to mediate the relationship between consumption of an unhealthy western dietary pattern and depressive symptoms (Jacka et al., 2014). Consuming a healthy diet is considered more expensive than consuming an unhealthy one (Darmon & Drewnowski, 2015; Rao et al., 2013). Perhaps reflecting this, it has been reported that Australian adults with low socio-economic status consume between 15% - 50% less fruit than adults of high socio-economic status (Lee & Lewis, 2021). Although the term has no established medical definition (Gupta & Mishra, 2021), kiwifruit have been described as a *superfood* (Sanz et al., 2021) due to the abundance of nutrients and bioactive compounds and the associated psycho-physiological health-promoting properties. The findings of all three studies in this thesis suggest that SunGold kiwifruit can deliver a cornucopia of nutrients in a single fruit that could be promoted as a first-choice food in the fruit-spending budget of consumers.

By identifying and introducing a minimally effortful whole food intervention with proven efficacy in reducing mood disturbance and improving wellbeing and vitality in adults with mild to moderate mood disturbance, there is an opportunity to integrate such treatments into health promotion and prevention efforts as well as self-help resources, dietary guidelines, treatment resources for clinicians and public education programs at relatively low cost with maximal population reach. This is particularly critical on two counts. First, advocating for SunGold kiwifruit as a ready-for-implementation, evidence-based lifestyle intervention with mental health-enhancing properties would substantially reduce the average 17-year gap between the discovery of scientific advancements and their implementation in real-world settings (Zullig et al., 2023). Secondly, the current mental health services model in Australia is failing to satisfy demand for psychological services (Vacher et al., 2023) with wait times of up to three months and a recent workforce survey noting that one-third of Psychologists reported they were unable to accept new referrals due to workload (APS Workforce Survey, 2022). The three studies herein provide one such example of an accessible, affordable, low-risk, low-intensity self-help dietary intervention with demonstrated efficacy that can be adopted across multiple intervention touchpoints and populations.

6.4 Strengths

The present research possesses a number of strengths that support conclusions and future research directions. Dietary intake is now recognised as a modifiable risk factor in the prevention and treatment of depression (O’Neill et al., 2022). Current treatment guidelines recommend dietary interventions as part of multi-modal lifestyle-based intervention treatment protocols for adults with sub-clinical depression (Marx et al., 2023b). Accordingly, the principal strength of this thesis was the decision to recruit adults with mild to moderate mood disturbance a cohort which, based on a meta-analysis of RCTs examining the effect of vitamin C supplementation on mood status (Yosaee et al., 2021), and the results of Carr *et al.* (2013a) were most likely to receive benefits to psychological health from a kiwifruit intervention.

A particular strength of the thesis was the stepwise progression across the three Studies. Study 1 identified a critical gap in the literature which informed the development of the feasibility trial (Study 2), which subsequently provided valuable direction for a larger trial (Study 3) in terms of eligibility criteria, participant burden and other methodological issues. Strict inclusion criteria were a strength of all three studies in this thesis. The use of rigorous study selection criteria, multiple databases, co-author (x3) consensus and library resources to formulate search terms were a strength of Study 1. Similarly, Studies 2 and 3 incorporated strict inclusion criteria that screened for conditions that might affect vitamin C bioavailability (e.g., smoking and vitamin supplement use) and excluded participants with any changes to dose or class of anti-depressant in the three months preceding the trial. This latter exclusion criterion was designed to limit the extent to which recent changes to psychopharmacological treatment that might have promoted changes to symptomatology encroached on trial timelines, thus contaminating results. The strict selection criteria of Study 2 (i.e., sub-optimal vitamin C and mild to moderate mood disturbance) and subsequent recruitment challenges provide valuable information for future research projects regarding difficulties that might be experienced in recruiting this population.

The duration of the intervention and crossover periods and the intervention dose-rate were strengths of Study 3. The four-week duration of the intervention period was chosen as it was, a) identical to that used by Conner *et al.* (2020) and, b) had proven to be of sufficient length to establish reliable indices of change in plasma vitamin C and psychological health.

Likewise, the two-week crossover period was considered appropriate to account for treatment and carryover effects and was aligned with established vitamin C pharmacokinetics (Blanchard, 1991). The choice of trial design and methodology of Study 3 is reinforced by the low dropout rate, negligible adverse events and tolerability of the intervention. Thus, these trial outcomes can inform further research and provide leverage for future study protocols.

A strength of Studies 2 and 3 was the use of validated measures of mood, wellbeing and gastrointestinal function. The psychometric screening measures used in Study 2 (DASS-21; Lovibond & Lovibond, 1995) and Study 3 (K10; Kessler et al., 2002) are well-established, validated screeners for psychological distress and symptoms of depression and anxiety in clinical settings and population-based surveys (Andrews et al., 2003; Lovibond & Lovibond, 1995; Staples et al., 2019). Where possible, outcome assessment measures used in Studies 2 and 3 were identical to those used in the two trials identified in Study 1 (Carr et al., 2013a; Conner et al., 2020). This included validated measures that examined positive affective states such as vitality, vigour and wellbeing in addition to measures of negative affective states such as depressed mood and anxiety. A frequent limitation of meta-analyses is the heterogeneity in how outcomes are measured (O'Neill et al., 2022; Walker et al., 2008). The present research made a deliberate attempt to support the synthesis of trial data into future systematic reviews or meta-analyses to provide greater clarity to researchers and clinicians regarding the efficacy of SunGold kiwifruit interventions on psychological health.

The frequent mechanistic assessment of vitamin C was a notable strength of Studies 2 and 3. A common limitation in nutrition studies has been the over-reliance on subjective measures of dietary intake such as food frequency questionnaires and the lack of biological assessment of nutrient status (O'Neill et al., 2022). For example, food frequency questionnaires and dietary surveys are subject to error from person-specific or intake-related biases (Bingham et al., 2002). The inclusion of objective nutrient biomarkers has been recommended to strengthen the quality of nutrition research findings (O'Neill et al., 2022) and this has been lacking in previous vitamin C supplementation studies (Lykkesfeldt & Poulsen, 2010). Additionally, the two studies were the first to use a validated measure of vitality, a psychological construct not previously assessed in a nutrition intervention in adults with mild to moderate mood disturbance.

6.5 Limitations

Findings of the present research must be considered with regard to the following limitations. Participant recruitment strategies for Study 2 and Study 3 relied on a discrete cohort. Participants were almost exclusively recruited via advertisements placed on the CSIRO website and Facebook page. A bulk mail-out to an existing CSIRO volunteer database was also used as part of the recruitment drive in Study 2. It is commonly accepted that clinical trial volunteers tend to be well-educated and have a higher socio-economic status compared to the general population (Young et al., 2020). Furthermore, the "healthy enrolee effect" in nutrition trials is well-documented and describes the phenomena whereby participants are more likely to be health-conscious, self-motivated individuals consuming nutrient-rich diets and are less likely to have low nutrient status (Lykkesfeldt, 2020). The studies did not collect information on education or socio-economic status and, other than an objective measure of plasma vitamin C, we did not assess overall nutrient status. The issue of self-selection bias remains a threat. The decision to recruit from the CSIRO online portals and volunteer database recruited participants with an existing interest in research or the subject matter, who were seeking to improve their health from involvement in the studies. Furthermore, it is possible that we recruited participants who had been involved in multiple previous CSIRO trials. All of the above selection issues resulted in the recruitment of individuals not necessarily representative of the general population, thus limiting the generalisability of results.

Almost without exception, whole food nutrition intervention trials face the challenge of expectation bias due to issues with blinding participants and researchers to condition and masking trial objectives. The present research was not immune to these challenges and results must be considered with that in mind. A placebo condition (an inert tablet designed to match the vitamin C supplement in appearance and flavour) was incorporated into the three-arm trial identified in Study 1, although this only achieved single-blinding between the supplement and placebo conditions and not the kiwifruit condition (Conner et al., 2020). Although identified *a priori* that the inclusion of a placebo condition would have strengthened the findings of Studies 2 and 3, this was not possible within the pragmatic restrictions of the present iPhD. Furthermore, a placebo condition would be extremely difficult to achieve, as it would need to be identical in form, appearance, sensory experience and satiety effect to a kiwifruit while being devoid of nutrients. However, the presence of a placebo effect in the present studies should not negate its potential benefits. Placebo effects of non-pharmacological treatments in clinical trials in mental health are well-documented with lower baseline depression symptomatology, as was the case in the present research, associated with a stronger placebo response (Weimer et al., 2015). Notwithstanding any improvements to psychological outcomes from a placebo effect, the gains in vitamin C and broader nutrient status from SunGold kiwifruit may have contributed to mood improvements over and above any placebo-induced benefits whilst potentially contributing other psychological or physiological health benefits.

A limitation of Studies 2 and 3 is that objective nutrient assessment was restricted to vitamin C. SunGold kiwifruit contain relatively high concentrations of other nutrients such as folate, vitamin E and dietary fibre, that may have contributed to the observed effects. Low folate intake has been identified as a risk factor for depression and associated with increased depression severity (Opie et al., 2017). Vitamin E demonstrates neuroprotective properties and low vitamin E status has been linked to depression (Maes et al., 2000). Dietary fibre intake supports a balanced gut microbiota, considered an important modulatory pathway in psychological health (Koopman et al., 2017). SunGold kiwifruit contain tryptophan, a precursor for serotonin (Islam et al., 2016; Sivakumaran et al., 2018) and increased dietary intake of tryptophan has been associated with reduced depression symptomatology and improved positive affect (Lindseth et al., 2015). The interactions or synergistic effects between micronutrients are largely unquantified and may have informed results. For example, vitamin C supports vitamin E bioavailability, and has a well-established role in dietary iron absorption, the neuro-bioavailability of which is associated with depression (Berthou et al., 2022).

Studies 2 and 3 found that improvements in mood and psychological health were associated with reductions in gastrointestinal symptom severity. Although this is not necessarily a limitation of the studies *per se,* it limits the extent to which the observed improvements in psychological outcomes can be attributed solely to increased vitamin C intake. The present work is consistent with previous findings that indicated SunGold kiwifruit-delivered dietary fibre significantly reduced gastrointestinal symptoms ratings in gut-healthy and gut-compromised individuals (Bayer et al., 2022b; Eady et al., 2019; Eady et al., 2020), however these trials did not assess mood. Other studies (Gearry et al., 2022), albeit involving green kiwifruit, have reported improvements in IBS-related quality of life constructs such as sadness, loss of enjoyment, helplessness and social isolation, all of which are associated with MDD (Marx et al., 2023b). With regard to mood-related outcomes from increased dietary fibre intake, a meta-analysis of RCTs (k= 10, n = 740) reported that dietary fibre supplementation (not via whole food) did not improve depressive symptoms compared to controls (Aslam et al., 2023). This is at odds with the small but significant inverse association between food-delivered dietary fibre intake and depressive symptoms reported in observational trials (Aslam et al., 2023). It is possible that the SunGold-delivered dietary fibre conferred broader effects on gut health by increasing the diversity of dietary fibre ingested compared to a single-fibre supplement and that participants experienced improve mood outcomes as a result of reduced symptom severity. This is supported by some of the previous work with SunGold that found kiwifruit-delivered dietary fibre resulted in fewer side effects and greater symptom reduction than a dose-matched single dietary fibre supplement (Bayer et al., 2022a; Eady et al., 2019). Study 2 and Study 3 did not specifically recruit for gastrointestinal symptom severity and the mean baseline gastrointestinal symptom ratings in Study 3 were in the lowest quartile, suggesting a mild symptom profile for the sample. This may have introduced a floor effect and limited the generalisability of findings. Additionally, the inclusion of an objective assessment of gastrointestinal functioning would have strengthened findings and provided insights into any underlying physiological features influencing gut motility and health (Grønlund et al., 2018).

An important limitation of all three studies is sample size and sample characteristics. Although it had been identified *a priori* that there was limited research examining the relationships between kiwifruit consumption and psychological health, the findings of Study 1 are limited by the small sample size ($n = 2$) and heterogeneity between the two studies. The small sample size of Study 2 ($n = 4$) restricted data analysis to visual inspection of data plots only, thus limiting the causal conclusions of findings. In terms of sample characteristics, females were overrepresented in Studies 2 and 3 (100% and ~ 75%, respectively). Gender differences in metabolism, vitamin C pharmacokinetics, iron bioavailability and eating behaviours limit the generalisability of findings. Compared to males, females attain significantly higher vitamin C concentrations relative to intake (Carr & Lykkesfeldt, 2023) and possess greater knowledge and awareness of nutrition compared to males (Kiefer et al., 2005). Additionally, Studies 3 and 4 occurred during the COVID pandemic and the degree to which localised short-term lockdowns and travel restrictions, and negative health effects of COVID symptoms from infection might have informed psychological outcomes during the trials is undetermined and these factors present a potential confound to trial results.

Another limitation concerns the eligibility criteria adopted in Study 3. Vitamin C status was not used as an inclusion criterion, and this limits the generalisability of findings. A common design limitation in nutrition trials is to recruit participants with adequate nutrient status of the nutrient under examination (Morris & Tangney, 2011). The mean vitamin C concentration at the commencement of the kiwifruit intervention period in Study 3 (n = 24, M = 57.9 μmol/L, SD = 27.3 μmol/L) was adequate (> 50 μmol/L; Lykkesfeldt & Poulsen, 2010). Although there was a significant increase from baseline scores for psychological outcomes (e.g., mood disturbance, wellbeing and vitality) following kiwifruit consumption, recruiting a cohort of participants with sub-optimal vitamin C status (> 23 μmol/L to < 50 μmol/L) may have returned even greater improvements in psychological health than otherwise observed. The planned sub-analysis of participants with sub-optimal baseline vitamin C could not be undertaken due to insufficient numbers however, this should be considered in future research where applicable.

One final limitation of Studies 2 and 3 is the failure to account for the effects of participant attributions/beliefs or behavioural activation. It is possible that the observed improvements in psychological health are unrelated to kiwifruit and may be a product of intrinsic factors. Considered alongside Deci and Ryan's self-determination theory (Deci & Ryan, 2012), participants' intrinsic motivation for engaging in the studies (e.g., volunteering to advance scientific research or adopting a healthy dietary behaviour to improve wellbeing) could elicit feelings of interest, enjoyment, competency or self-autonomy and promote 'flow'

(Reiss, 2004). Viewed through a behavioural activation lens, aside from the potential benefits a participant might receive from the act of engaging in a healthy, enjoyable behaviour (SunGold kiwifruit anyone?), initiating new, self-perceived healthy behaviours might boost levels of positive affect, thereby decreasing depressive symptoms (Soucy Chartier & Provencher, 2013). From a self-efficacy viewpoint, Studies 2 and 3 required participants to self-monitor their dietary behaviour by completing a compliance record sheet that recorded the daily consumption of the study product. Reviewing one's own successful performance of a dietary goal, in this instance consuming two kiwifruit per day, could boost an individual's sense of mastery, subsequently leading to enhanced self-efficacy (Prestwich et al., 2014). Behaviours such as self-monitoring, action planning and time management, namely, all behaviours that participants may have initiated to achieve compliance with study directions, are strong predictors of self-efficacy (Annesi & Vaughn, 2017). Furthermore, nutrition behaviour is predicted by self-efficacy to the extent that an individual's perception that they can successfully adhere to a dietary intervention, in the present case a relatively simple addition to the diet of two kiwifruit per day, informs more healthy nutrition behaviour (Cuadrado et al., 2018). The diet as usual condition used in Study 3 would not account for these factors.

6.6 Future Research Directions

Research regarding the role of kiwifruit in supporting psychological health is in its infancy. Although there are no studies involving clinically depressed adults in SunGold research, and a dearth of the same in the nutritional psychiatry literature more generally, future research should build on the foundational work herein by conducting larger, randomised controlled trials in both clinical and sub-clinical populations. Recruiting community-sampled, mild to moderately depressed cohorts from broad socio-cultural and socio-demographic strata would support generalisability of future findings. It would also serve to augment the more substantive volume of work that has demonstrated improved depressive symptomatology from dietary interventions in sub-clinical populations (Firth et al., 2020; Yosaee et al., 2021). Targeting mild to moderately mood-disturbed populations is of particular importance given that dietary interventions, and in particular single food interventions, represent a relatively low-risk, low-intensity preventative measure that can either form part of a clinician-delivered treatment program or as a self-management approach for reducing symptoms of depression (Firth et al., 2019).

Future research should examine the role of gender differences in responses to dietary interventions. Studies using predominantly (> 75%) female samples reported significant benefits to psychological health from dietary interventions compared to trials with primarily male samples (Firth et al., 2019). Gender differences in nutrition knowledge and expectations regarding diet, differences in metabolic responsivity to diet, and mood disorder prevalence have been posited as contributors to the observed differences in psychological health outcomes (Firth et al., 2019). Additionally, females exhibit a greater dose-response bioavailability of vitamin C than males (Carr & Rowe, 2020). Examining these gender differences would help determine the optimum nutrient intake to prevent or reduce depressive symptoms in clinical and sub-clinical populations and support the development of gender-individualised dietary interventions. For example, future SunGold research could target at-risk populations likely to benefit from increased intake of specific nutrients in SunGold kiwifruit in longitudinal studies (i.e., increased folate and vitamin C intake to reduce the incidence of perinatal depressive symptoms).

An important future direction for nutrition research is to conduct large, blinded RCTs across diverse populations and settings. Future research endeavours should consider the following measures to maximise trial robustness and generalisability of findings. Research staff collecting primary outcome measures (e.g., psychological assessments and blood serum collection) could be blinded to the interventions, which could be coded in a manner that also blinds statisticians to intervention assignment (Weaver & Miller, 2017). The duration of the intervention must be of sufficient length to observe a meaningful effect on outcome measures while balancing the need for high compliance and low drop-out. As shown in Studies 2 and 3, the duration of the intervention (28-days) was sufficient to observe meaningful indices of change in nutrient and psychological outcome measures, and there was high compliance and minimal dropout. As previously noted, the decision to recruit participants with sub-optimal vitamin C status and mild to moderate mood disturbance contributed to recruitment difficulties in Study 2. Maintaining these important eligibility criteria while maximising sample size could be accomplished through a multi-site trial. This would require the sample size to be large enough to expose any site-by-treatment interaction but would provide the ability to generalise findings to different populations (Feaster et al., 2011).

A critical issue to address in future nutrition research examining vitamin C is to recruit participants with appropriate baseline characteristics. A comprehensive review of the vitamin C supplementation literature considered it "imperative" that, due to the substantial variations in vitamin C bioavailability, hypovitaminosis C (< 23 µmol/L) be set as an inclusion criteria in order to maximise the possibility of observing a treatment effect (Lykkesfeldt & Poulsen, 2010). The upper threshold for sub-optimal vitamin C (50 µmol/L) was the eligibility criteria for Studies 2 and 3, which was in line with those used in Carr *et al.* (2013a) and Conner *et al.* (2020; < 50 µmol/L and < 40 µmol/L, respectively). Results showed that 42% of applicants screened for vitamin C status in Study 2 recorded vitamin C concentrations ≤ 50 µmol/L. Similarly, 42% of participants in Study 3 recorded vitamin C status below 50 µmol/L at the baseline visit. This was slightly higher than reported by Carr *et al.* (2013a) and Conner *et al.* (2020; 27% and 25%, respectively) and is possibly a reflection of vitamin C dose-concentration relationships relative to age (Carr & Lykkesfeldt, 2023). Although the standard suggested by Lykkesfeldt and Poulson is scientifically rigorous, Studies 2 and 3 would have both been $n = 1$ had they adopted the sub-optimal threshold as an eligibility criteria. A caveat to Lykkesfeldt and Poulson's hypovitaminosis C imperative however, is that recruiting participants with a nutrient status below a certain threshold can limit the generalisability of findings (Weaver & Miller, 2017). Considering the present work, this may raise an ethical dilemma whereby this would preclude participants with sub-optimal vitamin C status (> 23 μmol/L and < 50 μmol/L) who might otherwise benefit from the intervention. Future research will need to remain cognisant of this threat to recruitment and findings. Studies that recruit based on hypovitaminosis C would need to amass a large enough pool of applicants to accommodate screening attrition rates; or, if recruiting based on sub-optimal concentrations, recruit a large enough sample to allow for a sub-group analyses. This would help to account for the established dose-dependency pharmacokinetics and subsequent variability in vitamin C concentrations at below-saturation levels (Conner et al., 2020; Lykkesfeldt & Poulsen, 2010).

There is a pressing need for future nutrition research to include mechanistic assessment of nutrient markers in addition to vitamin C. Including other objective assessments such as neuroimaging and biomarkers of particular neurotransmitters (e.g., serotonin) should also be considered in future research. The relationship between dietary nutrient intake and psychological health is complex and there are numerous potential mechanisms of action and biological pathways through which SunGold kiwifruit might exert positive effects on psychological health. Kiwifruit contain a range of micronutrients and bioactive compounds with known association with psychological health such as vitamins C and E, folate, potassium, tryptophan, serotonin and dietary fibre (Bender et al., 2017; Briguglio et al., 2018; Ding & Zhang, 2022; Lydiard, 2001). It is also likely that the synergistic cooperativity between dietary micronutrients and other bioactive compounds in kiwifruit (e.g., vitamins C and E) would potentiate the positive effects on mood outcomes (Shahidi et al., 2021). If we are to identify the mechanisms of action of dietary interventions on psychological health, then concomitant mechanistic assessment of multiple nutrient biomarkers is essential. A previous study that examined gold kiwifruit and psychological health did not observe any association between increased vitamin E intake and mood outcomes, however vitamin E was assessed by food diary only rather than objective measures (Carr et al., 2013a). The same study did assess dietary iron intake mechanistically but found no association between iron intake and mood, however, this was likely due to participants' baseline iron status being within normal limits. These two examples highlight, a) the value of including mechanistic observation of nutrient status; and b) the critical need to recruit participants with appropriate baseline characteristics.

The evidence to support the role of dietary interventions and nutrition in adults with clinical and sub-clinical depression continues to build (Eliby et al., 2023; Nicolaou et al., 2020). Likewise, our understanding of the complex interplay between dietary intake and the numerous biological pathways through which diet could credibly influence psychological health is growing. Future SunGold research, and nutrition research in general, must conduct RCTs in defined populations such as individuals with clinical depression and mild to moderate mood disturbance; those with a previous history of depressive episodes but currently asymptomatic; and individuals at greater risk of depression (e.g., somatic conditions such as gastrointestinal disorders, substance abuse). The interaction between dietary interventions and psychopharmacological agents has not been examined in detail and is an area that warrants investigation (Firth et al., 2019). Similarly, the relationship between dietary interventions, the gut microbiota and psychological health are yet to be fully explored. For example, dietary fibre intake modulates gut microbiota (Dalile et al., 2021) leading to increased BDNF, a neurotrophin associated with the pathophysiology of depression (Lin & Huang, 2020). More generally, longitudinal studies are required to document the relative reduction in the risk of developing depression from nutritional interventions if nutritional psychiatry is to promote them as preventative treatments. These research opportunities present new and exciting challenges for the field of nutritional psychiatry. A greater understanding of the mechanisms of action and the putative causal factors of dietary interventions on psychological health can then be translated into individual prevention and treatment protocols and inform broader health policy and dietary guidelines.

6.7 Conclusion

SunGold kiwifruit are a nutrient-dense fruit considered exceptionally high in vitamin C and other bioactive compounds with known associations with symptoms of mood disorders such as depression. The present thesis adds to existing research and demonstrates the benefits of SunGold kiwifruit consumption on psychological health in adults with mild to moderate mood disturbance. Overall, the results of the present research program are consistent with previous findings involving gold kiwifruit (Carr et al., 2013a; Conner et al., 2020) and reflect the broader evidence base that supports the use of dietary interventions in the prevention and treatment of depression in clinical and sub-clinical populations (Eliby et al., 2023; Firth et al., 2020).

Given the complex interplay between dietary intake and the numerous biological pathways implicated in psychological health, elucidating the mechanisms of action of dietary interventions remains a considerable challenge for the field of nutritional psychiatry (Marx et al., 2021). The broad array of nutrients and bioactive compounds in foods and the synergistic cooperativity between micronutrients and individual biopsychosocial factors provide further challenges in the search for evidentiary proof of the pathways between diet and positive psychological health. The present thesis contributes new knowledge to the field regarding a food-ubiquitous micronutrient, vitamin C, delivered via SunGold kiwifruit. The results provide support for the consumption of SunGold kiwifruit to reduce symptoms of depression and improve psychological health in adults with mild to moderate mood disturbance.

Nutritional psychiatry is a rapidly growing field of research, and dietary interventions are now considered an integral component of lifestyle-based interventions for the prevention and treatment of depression (Marx et al., 2023a). Future directions could include SunGold kiwifruit interventions in clinical and at-risk populations. Given the growing recognition of the benefits of dietary interventions on psychological health and the need to translate evidence-based interventions into real-world applications, the nutrient dense SunGold kiwifruit offers an appealing, nutritious and efficacious pathway to improved psychological health.

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