



 **Detailed Study Notes**

**Nicole Lippman-Barile, PhD**  
**Diet & Depression:**  
**What Do We Actually Know?**



## ***Table of Contents***

- [Introduction to this Episode](#)
- [Connection to Previous Episodes](#)
- [Effect Sizes: Opie Systematic Review](#)
- [Predictors of Success in Depression Research](#)
- [Behavioral Activation](#)
- [Implications of BA for Evaluating Nutrition Interventions](#)
- [Firth et al.- Meta Analysis of RCTs](#)
- [Are The Benefits in Diet Trials Actually Down to Diet?](#)
- [SMILES Trial](#)
- [SMILES: Expectation Bias & Other Issues](#)
- [AMMEND Study](#)
- [Final Thoughts to Consider](#)

## ***Introduction to this Episode***

Depression is a common disorder and is a leading cause of disability worldwide. Depression results from a complex interaction of social, psychological, and biological factors.

Diet has been one area that has been suggested in playing a role; from potential for exacerbating symptoms to being a treatment. And while some associations have been noted, many claims far exceed what (little) evidence exists.

Online it is common to see people claiming certain diets can treat depression or that certain foods will improve outcomes. However, does the evidence match such claims?

In trials that have been published on diet-depression, there has been considerable media attention and fanfare around some results. For example, the SMILES trial published out of Australia. However, some have raised considerable concerns about the interpretation of such findings.

In this episode, clinical psychologist Dr. Nicole Lippman-Barile is on the podcast to discuss what we currently know about diet and depression, what issues exist with current studies, and why many nutrition-mental health studies are being incorrectly interpreted.

## ***Connection to Previous Episodes***

### **#463: Do Vegan Diets Cause Depression?**

- In this episode, the Sigma team explores the question: “Do vegan diets increase the risk of depression?”
- In this episode, we explore the evidence from two ends:
  - 1) research related to the proposed mechanisms by which a vegan diet could cause problems.
  - 2) outcome data looking at the impact of such diets.
- [Click here](#) to go to the episode page.

### **#421: Brendon Stubbs, PhD – The Research on Depression & Physical Activity**

- Dr. Brendon Stubbs, PhD, is a Senior Clinical Lecturer and researcher at King's College London, conducting research in physical activity & mental health.
- He has published over 650 academic papers in several leading journals across multiple scientific fields.
- He has also informed policy guidelines in the UK, Europe and the World Health Organization.
- [Click here](#) to go to the episode page.

### **#422: Psychobiotics – Can Probiotics Improve Mood-related Disorders?**

- In this episode the Sigma team discuss the research looking at 'psychobiotics'; i.e. probiotics that have health impacts on those with psychiatric disorders or symptoms.
- They discuss the origins of the research, the gut-brain axis, mechanisms by which gut microbiota could impact mood, and then the human trials to date that have examined probiotics' effects on mood, anxiety, depression, bipolar disorder and other outcomes.
- [Click here](#) to go to the episode page.

### **#438: Diet, Brain Health & Cognitive Function**

- In this episode we took a look at the published data on how brain health is impacted by a variety of nutrients, foods and dietary patterns, including: vitamin D, omega-3 fatty acids, B vitamins, caffeine, flavonoids, coffee and green leafy vegetables.
- [Click here](#) to go to the episode page.

## Effect Sizes: Opie Systematic Review

**Paper:** [Opie et al., 2015 - The impact of whole-of-diet interventions on depression and anxiety: a systematic review of randomised controlled trials](#)

### Quick Overview

- Systematic review of randomised controlled trials of dietary interventions that used depression and/or anxiety outcomes
  - Seventeen studies met eligibility criteria and were included.
- Studies were classified into three categories in relation to their results:
  - those with statistically significant improvements in depression/anxiety outcomes, compared with the comparator group
  - those with non-significant improvements in depression/anxiety outcomes, compared with the comparator group
  - those with significantly worse scores, compared with the comparator group
- Compared with a control condition, almost half (47 %) of the studies observed significant effects on depression scores in favour of the treatment group.

### Magnitude of Effect

- As a general rule of thumb, effect sizes in nutrition could be thought of as:
  - 0.1 = negligible
  - 0.2 to 0.4 = small to modest effect size
  - 0.5 to 0.7 = moderate effect size
  - > 0.8 = large effect size
- In the Opie systematic review the reported effect size ranged from **0.19 to 2.02**.
  - So going from 0.19 to 2.02 is an enormous swing
  - This indicates that there is quite substantial variability in the magnitude of effect
  - The huge variance may be explained by factors beyond diet (discussed more in these notes)

### Role of Intervention Deliverer

- Of the studies reviewed and there were 17 reporting depression
- 85% of those studies had a positive outcome when the intervention was delivered by a professional.
- But in studies delivered by others (e.g. postdoc or layperson), 44% of studies had no difference between intervention and control group.

## **Predictors of Success in Depression Research**

- The Therapeutic Alliance
  - The relationship/rapport between the patient and the professional/practitioner.
- Intervention Intensity
  - By "intensity" in this context, we mean the number of contacts a participant or patient has with a practitioner.
  - One of the strongest predictors of beneficial outcomes in participants was the intensity of the intervention ([Amati et al., 2018](#)).
- Social support and social functioning
  - Having social support is a more important factor than socio-economic status alone ([Amati et al., 2018](#)).
- Previous successful treatment
  - This suggests that relapse should not be a contraindication for treatment.

## **Behavioral Activation**

- **Behavioral activation (BA)** is a third generation behavior therapy for treating depression.
  - It has evidence for being effective in treating depression ([Ekers et al., 2014](#)), with the greatest effects being in cases of mild to moderate depression.
- The [Beck Institute](#) describes BA as: *"getting clients more active and involved in life by scheduling activities that have the potential to improve their mood."*
- BA emerged from CBT, after some suggested that the benefits of CBT were solely down to the 'behavioral' aspect, with little to none from the 'cognitive' aspect.
  - So it's a strictly behavioral approach to treating depression
- This behavioral theory of depression can be thought of as:
  - Depression was caused by low rates of "response contingent positive reinforcement"
    - a depressed person's environment is basically devoid of opportunities for a person to experience positive reinforcement.
  - Things that allow us to receive positive reinforcement are things that also allow us to feel a sense of mastery and a sense of pleasure.
- So basic idea of behavioral activation in practice is:

- Getting a person oriented towards the understanding that your behaviors affect your thoughts, they affect how you feel, they affect your future.
- Bringing awareness to behaviors. E.g.,:
  - How do you feel when you do this?
  - How do you feel before you do this?
  - What's your thought process like?
- Finally, helping someone increase engagement in these adaptive behaviors
- Magnitude of that effect is greater in mild to moderate depression.

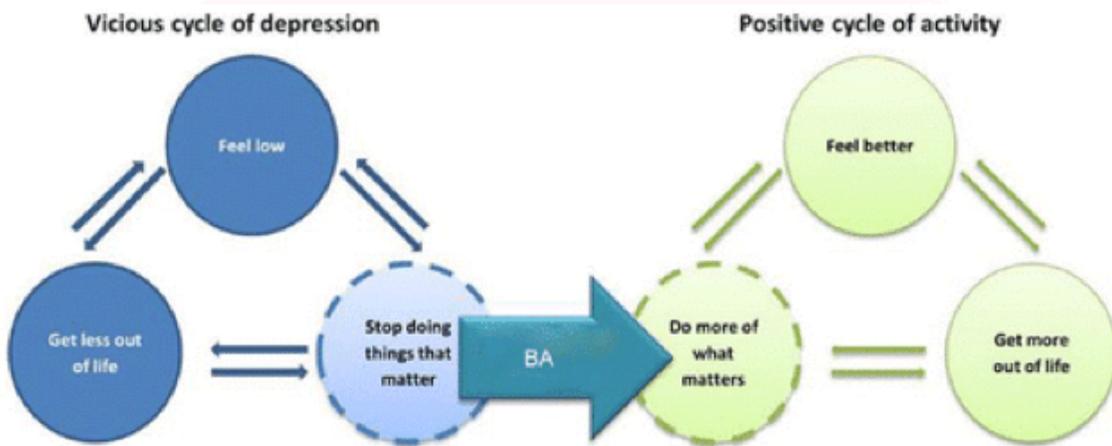


Image from [positivepsychology.com](http://positivepsychology.com)

## ***Implications of BA for Evaluating Nutrition Interventions***

- If someone is told to change their diet in a certain way (e.g. eat more greens, omega-3, etc.), this potentially could end up being a form of behavioral activation.
  - And so we must ask: is the change we're observing down to the dietary change or simply due to the action acting as behavioral activation?
- Example:
  - Someone with depression is told to start cooking for themselves at home.
  - Even if they just take that action, regardless of the content of the food, they're now engaging in an adaptive behavior on a regular basis.
  - Not only are they cooking for themselves regularly and trying to stick to that, the dietitian (or whoever is also administering the instructions and treatment) is also problem solving with them, such that they adhere to this protocol as best as possible.
  - Dr. Lippman-Barile makes the argument that in such a case you're actually doing behavioral activation.
    - That's the form of treatment that the person is doing regardless of the diet that you're actually getting a person to eat.

## Firth et al. - Meta Analysis of RCTs

**Paper:** [Firth et al., 2019 - The Effects of Dietary Improvement on Symptoms of Depression and Anxiety: A Meta-Analysis of Randomized Controlled Trials](#)

- Included 16 RCTs of dietary interventions
  - 15 of those were in **non-clinically depressed** participants
  - Only 1 study (SMILES) was in individual with clinical depression diagnosis
- Total sample size= 45,800 people
- Studies were on dietary pattern interventions
  - so these were not manipulating a single nutrients or macronutrients
- Reported effect size of 0.28 (compared to the control)
  - I.e., small to modest effect size range.

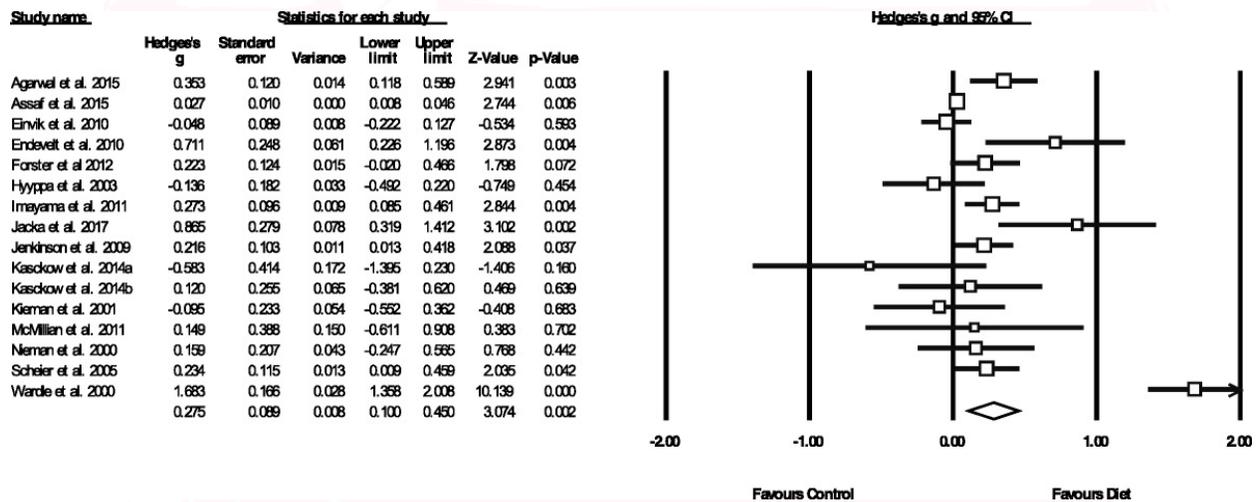


Figure taken from: [Firth et al., Psychosomatic Medicine 81\(3\):p 265-280, April 2019.](#)

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### Key Aspect:

The key thing highlighted in the episode about this MA was the differences we see when looking at whether the dietary intervention group was compared to an *active* control or an *inactive* control...

## Key Aspect of this MA

- **Active control** = where the control group aren't changing their diet, but are still getting some other active aspect of the intervention
  - For example, the control group is doing an exercise regime but making no dietary change, while the intervention group are making dietary changes plus exercising.
- **Inactive control** = is where the placebo or control group are literally just being told "carry on with your habitual diet routine".
- So in this MA, when we look at interventions that were compared to active or inactive controls, we see very different effect sizes:
  - The effect size versus an **active** control was 0.17 (i.e., a pretty negligible effect size)
  - The effect size versus an **inactive** control was 0.30 (i.e. still in the small to moderate range, but getting close towards moderate effect size).
- From this we can see that the level of "intervention" in a control group (i.e., whatever that control group is doing) is influencing the outcome.
- Therefore it's likely that diet is possibly having exaggerated effect sizes in certain contexts.
- And actually in terms of if we were trying to isolate the independent effects of diet, it really may not be that much of a significant factor relative to other of these behaviors and otherwise we're talking about.

	Sample		Meta-Analysis				Heterogeneity		
	Studies	Diet/Control, n/n	Hedge's g	95% CI	p	Q	p	I <sup>2</sup>	
Main analysis	16	18,746/27,080	0.275	0.100 0.450	.002	141.4	<.01	89.39	
High-quality studies	11	18,567/26,902	0.321	0.116 0.526	.002	131.08	<.01	92.37	
Diet versus active control	10	1027/921	0.174	0.012 0.335	.035	22.8	.007	60.56	
Diet versus inactive control	10	18,022/26,297	0.308	0.017 0.599	.038	115.9	<.01	92.24	
Nonclinical depression	15	18,715/27,055	0.246	0.070 0.423	.006	132.69	<.01	89.4	
Diet + exercise versus exercise alone	2	139/137	0.265	0.030 0.500	.027	0.008	.928	0.000	
<b>Comparative subgroup analyses for depression outcomes</b>									
Aim: improving nutrition	9	560/610	0.365	-0.024 0.753	.066	71.9	<.01	88.9	
Aim: reducing % fat intake	4	17,601/26,307	0.477	0.069 0.884	.022	53.1	<.01	94.35	
Aim: inducing weight loss	4	585/483	0.212	0.087 0.338	.001	2.21	.529	0.00	
Nutrition professional	12	18,618/26,890	0.329	0.124 0.535	.002	136.83	<.01	91.96	
No nutrition professional	4	128/190	0.124	-0.124 0.371	.328	3.487	.322	13.961	
>75% female sample	8	17,706/26,314	0.195	0.055 0.336	.007	18.97	.008	63.10	
>75% male sample	4	366/362	-0.208	-0.449 0.033	.091	5.17	.160	41.93	
100% female sample	6	17,739/26,141	0.164	0.019 0.310	.027	18.97	.008	63.10	
100% male sample	3	353/352	-0.176	-0.427 0.074	.168	5.17	.16	41.93	

Figure taken from: [Firth et al., Psychosomatic Medicine 81\(3\):p 265-280, April 2019.](#)

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## Are The Benefits in Diet Trials Actually Down to Diet?

- As discussed in relation to the Firth et al. meta-analysis, it seems that diet interventions that show benefit, may be having their effect sizes exaggerated, because of aspects of the intervention that have nothing to do with the specific foods being eaten.
  - And the Firth et al. MA is useful for showing this difference between active and inactive controls.
- So if we're trying to isolate the **independent effects of diet**, then it doesn't look like diet as having any sort of particularly important effect.
- So can we actually attribute the reported effect sizes in diet intervention studies down to the specific diet or diet recommendations?
- Consider:
  - People are trying to make a causal inference that the reason that there is this effect on depression outcomes is because of the dietary treatment.
  - **But** we know that there are factors like:
    - number of practitioner contacts
    - the therapeutic alliance
    - the expertise or experience of the professional delivering the intervention
    - simply making a change that someone perceives to be positive is itself going to potentially be improving mood.
- So when diet is compared to an active control (i.e. something that is having an effect), is the “diet” intervention actually having an impact independent of the dietary changes?
  - i.e. is it just the behaviors that they're doing and receiving some sort of positive effect?

## SMILES Trial

**Study:** [Jacka et al., 2017 - A randomised controlled trial of dietary improvement for adults with major depression \(the 'SMILES' trial\)](#)

- 12 week randomized control trial
- Participants with moderate to severe depression
- Looking at an adjuvant dietary intervention.
  - So participants were either engaged in therapy and/or on pharmacotherapy for their symptoms.
- Diet intervention = modified Mediterranean diet.
- In the intervention group, the participants received **seven individual dietary support sessions** that were an hour long, delivered by an accredited practicing dietician.
  - Weekly sessions for the first month
  - Then biweekly sessions thereafter for the remainder of the intervention.
- Initial sessions focus on the diet: getting participants confident that they could execute the diet and adhere to it.
- But then the subsequent sessions used [Motivational Interviewing](#) techniques and also encourage the participants to set personalized goals.
  - *“MI is a collaborative, goal-oriented style of communication with particular attention to the language of change. It is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person’s own reasons for change within an atmosphere of acceptance and compassion.”* ([Miller & Rollnick, 2013, p. 29](#))
- The **comparison control group** were given social support, specifically a **‘befriending’** protocol.
  - Befriending = neutral topics are discussed with participants, with the aim being to retain that neutrality in the conversation.
- And over the course of 12 weeks, the **between group difference was an effect size of 1.16.**
  - That's an enormous effect size for either a nutrition or psychotherapy intervention.
- It's instructive to note that **the control group** themselves still had an effect size that is **greater** than the average effect size in cognitive behavioral therapy interventions, in antidepressant interventions, and drug trial placebo comparisons!

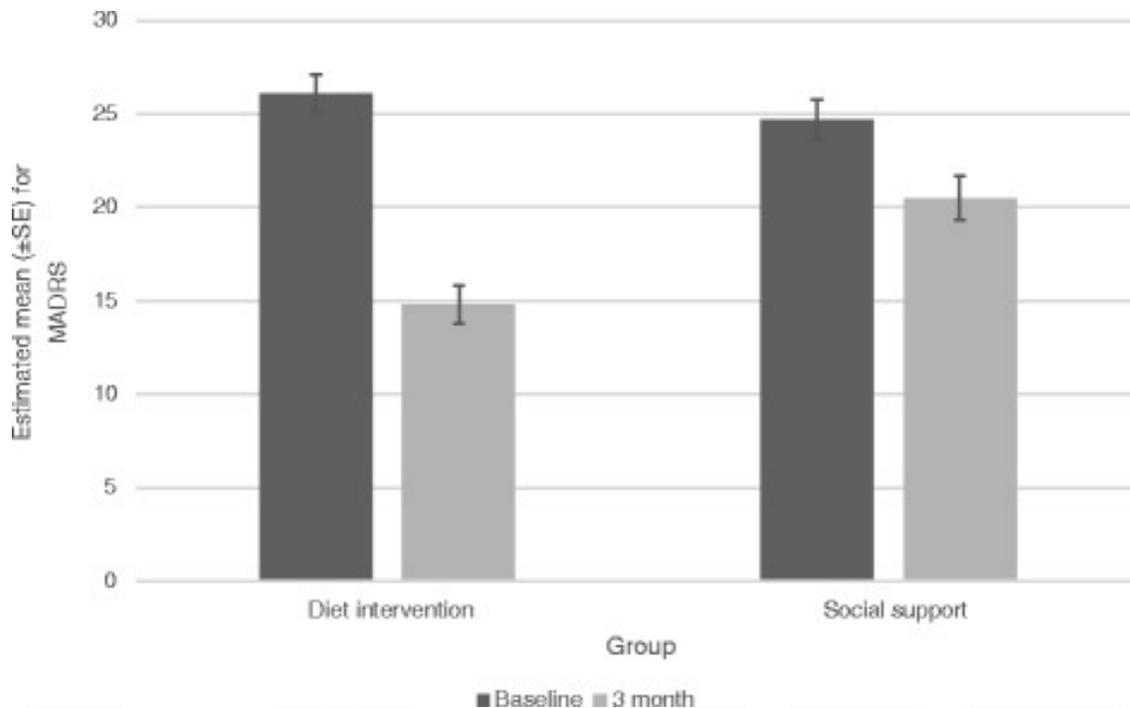


Figure from: [Jacka et al., BMC Med. 2017 Jan 30;15\(1\):23.](#)

## SMILES: Expectation Bias & Other Issues

- One issue to consider here was the language used in recruitment and in delivery of the intervention.
- This could create an expectation bias or expectation effect.
- And a group at Leiden University in the Netherlands, raised concerns related to recruitment of the SMILES trial.
  - [Molendijk et al. comment: [The SMILES trial: do undisclosed recruitment practices explain the remarkably large effect?](#)]
- For example, on the recruitment web page, you could see such statements as:
  - "Bananas look like a smile, but can also help you smile because they contain tryptophan, which is a mood stabilizer"
  - "Banana, Brazil nuts, broccoli: they all have something in common apart from starting with the letter B. They all contain nutrients which can stabilize mood"
  - "The fear that we are eating our way to depression is prompting governments to take action"
- And that was accompanied by testimonials, including *"the solution to my depression is good quality food"*
- This creates the potential for an enormous level of expectation to be created by someone with moderate to severe depression.

## **AMMEND Study**

**Study:** [Bayes et al., 2022 - The effect of a Mediterranean diet on the symptoms of depression in young males](#)

- "AMMEND: A Mediterranean Diet in MEN with Depression" study
- A 12-wk, parallel-group, open-label, randomized controlled trial
- Aimed to assess the effect of a Mediterranean diet in the treatment of moderate to severe depression in young males (18–25 y).
- Befriending therapy was chosen for the control group.
- The primary outcome measure was the Beck Depression Inventory Scale—version II (BDI-II) and secondary outcome was quality of life (QoL).
- 72 participants completed the study.
- After 12 weeks, the mean change in BDI-II score was significantly higher in the MD group compared with the befriending group at week 12 (mean difference: 14.4; 95% CI: 11.41, 17.39).
- The mean change in QoL score was also significantly higher in the MD group compared with the befriending group at week 12 (mean difference: 12.7; 95% CI: 7.92, 17.48).
- However this trial exhibited all the same issues as outlined for SMILES and other studies of this nature.
- Results were being put down to dietary changes, when the actual changes may not have been what was leading to symptom improvements.

## ***Final Thoughts to Consider***

- In the rhetoric around nutritional psychology and psychiatry, it seems that often the enthusiasm far outpaces the evidence.
- And it's important to temper that expectation.
- We need to stop using causal language in describing these outcomes of these interventions.
- When we synthesize the evidence and we end up with this small to modest effect size that could be explained by some other factors, then people really should be pulling back on the enthusiasm for saying that *“if you improve your diet it will improve your mental health”*.

