

## *Food for thought:*

Diet quality, the  
microbiome and  
mental health



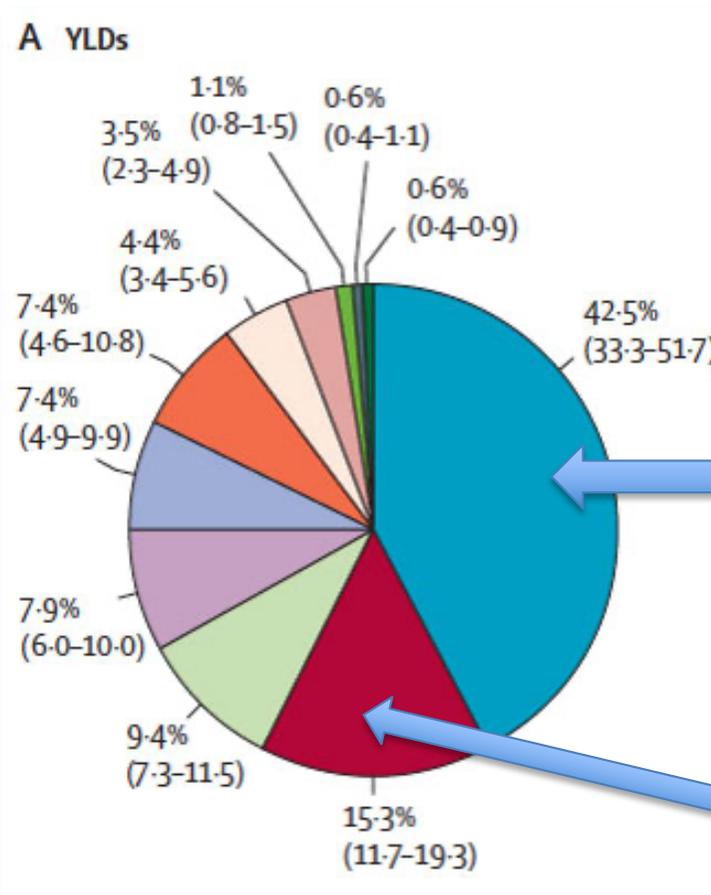
with **Prof. Felice Jacka**  
& **Kathleen Alleaume**

**FREE WEBINAR**



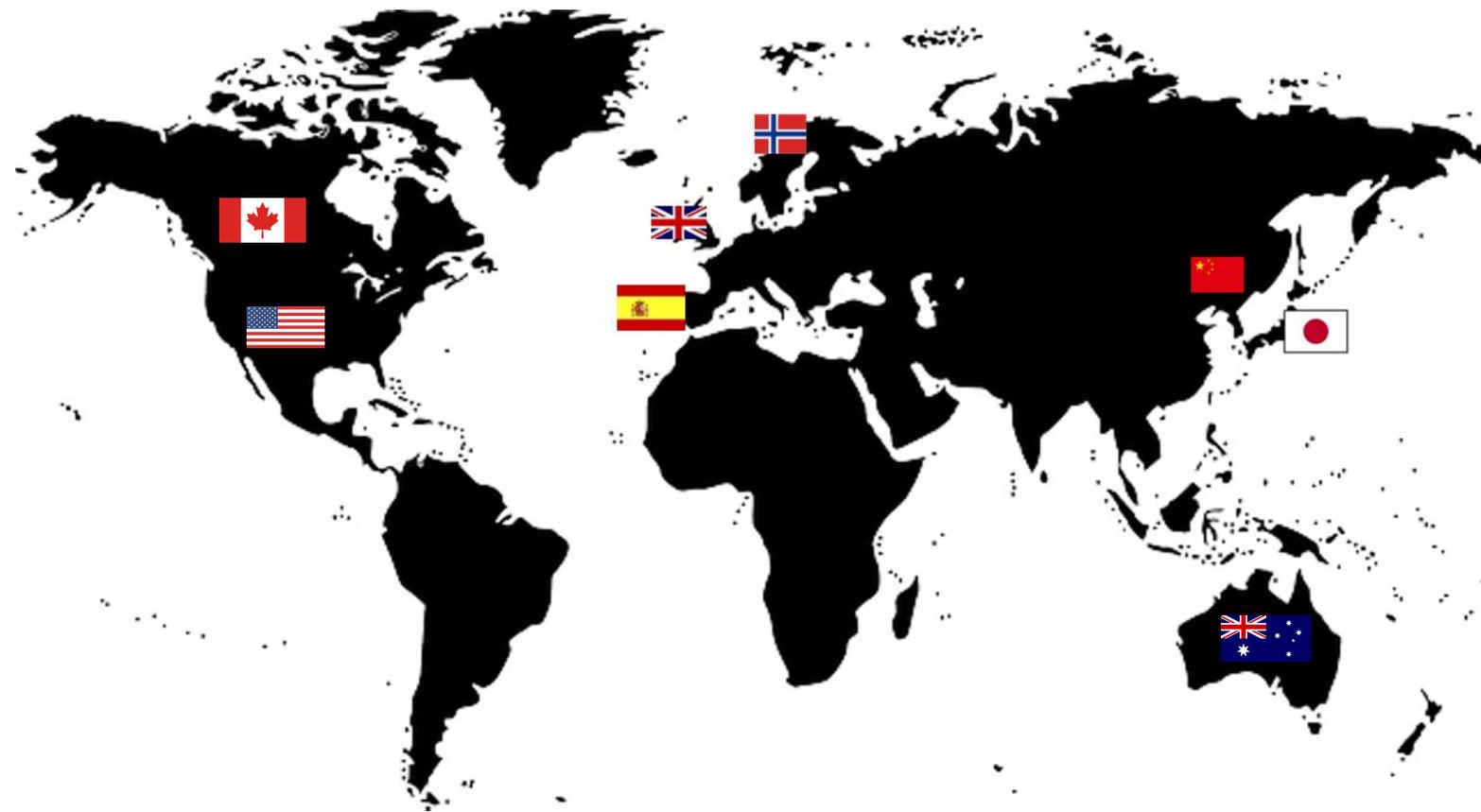


# Mental Health



Unipolar depression

Anxiety disorders



# Diet and Depression in Adulthood



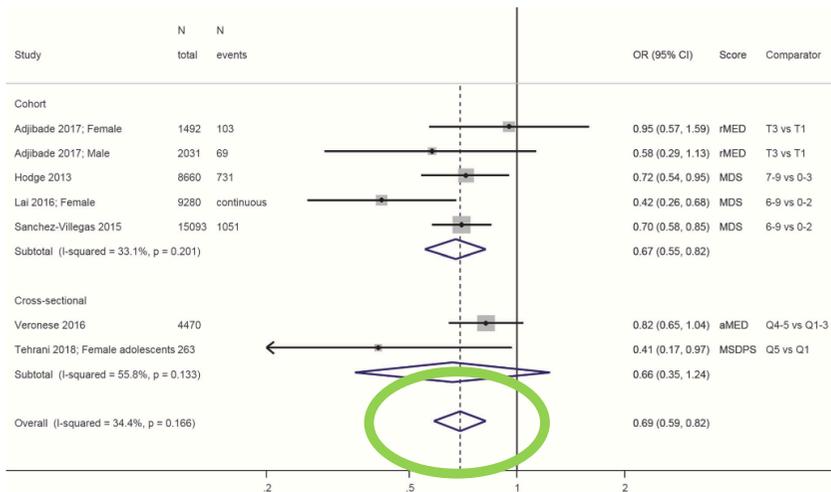
Molecular Psychiatry  
<https://doi.org/10.1038/s41380-018-0237-8>

REVIEW ARTICLE

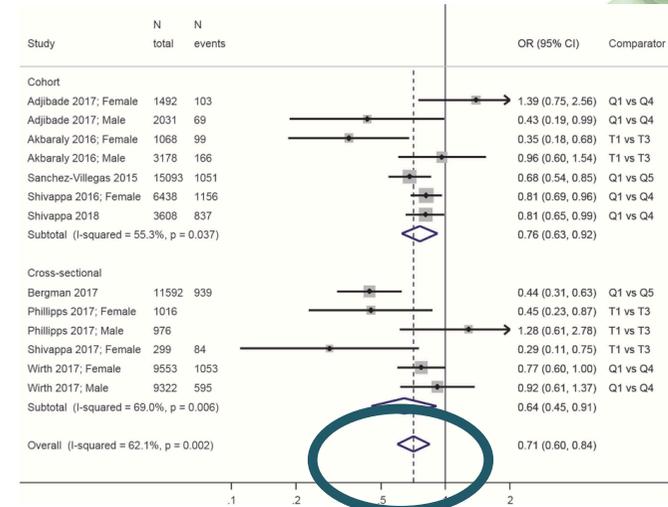
## Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies

Camille Lassale<sup>1,2</sup> · G. David Batty<sup>1</sup> · Amaria Baghdadli<sup>3,4</sup> · Felice Jacka<sup>5</sup> · Almudena Sánchez-Villegas<sup>6,7</sup> · Mika Kivimäki<sup>1,8</sup> · Tasnime Akbaraly<sup>1,3,9</sup>

Received: 10 May 2018 / Revised: 26 July 2018 / Accepted: 2 August 2018  
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**Fig. 1** Meta-analysis of studies investigating the association between a traditional Mediterranean diet and depressive outcomes. Estimates are ORs, RRs or HRs of depression for people with highest adherence compared to lowest adherence (categories or quantiles specified). MDS Mediterranean diet score, rMED relative MDS, aMED alternative MDS, T tertile, Q quintile



**Fig. 4** Meta-analysis of studies investigating the association between the Dietary Inflammatory Index DII and depressive outcomes. Estimates are ORs, RRs, or HRs of depression for people with lowest adherence compared to highest adherence (categories or quantiles specified). T tertile, Q5 quintile, Q4 quartile

Decreased incidence of depression:  
**Adherence to a Mediterranean diet: 0.67**  
 (95% CI 0.55–0.82)  
**Lower Dietary Inflammatory Index: 0.76**  
 (95% CI 0.63–0.92).

Lassale et al. *Molec Psychiat.* 2018.



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# Diet and Mood in Adolescents



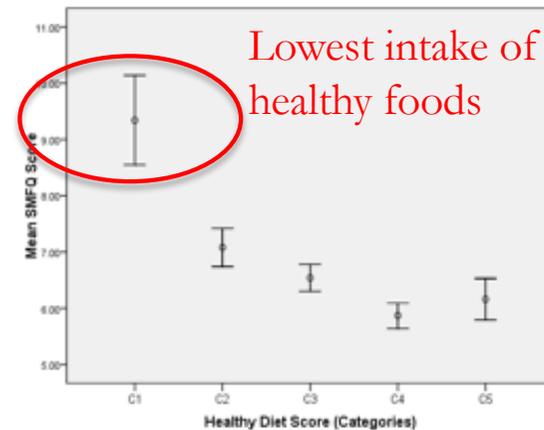
## Associations between diet quality and depressed mood in adolescents: results from the Australian Healthy Neighbourhoods Study

Felice N. Jacka, Peter J. Kremer, Eva R. Leslie, Michael Berk, George C. Patton, John W. Toumbourou, Joanne W. Williams

Healthy Neighbourhoods Study

n = 7114

Age 10 - 14 years



# Diet and Mental Health in Early Life



**NEW RESEARCH**

**Maternal and Early Postnatal Nutrition and Mental Health of Offspring by Age 5 Years: A Prospective Cohort Study**

Felice N. Jacka, Ph.D., Eivind Ystrom, Ph.D., Anne Lise Brantsaeter, Ph.D., Evalill Karevold, Ph.D., Christine Roth, M.Sc., Margaretha Haugen, Ph.D., Helle Margrete Meltzer, Ph.D., Synnve Schjolberg, M.A., Michael Berk, Ph.D.



Impact of early life nutritional exposures extends from physical to mental health

# Dietary improvement as a treatment strategy in major depression: the SMILES trial

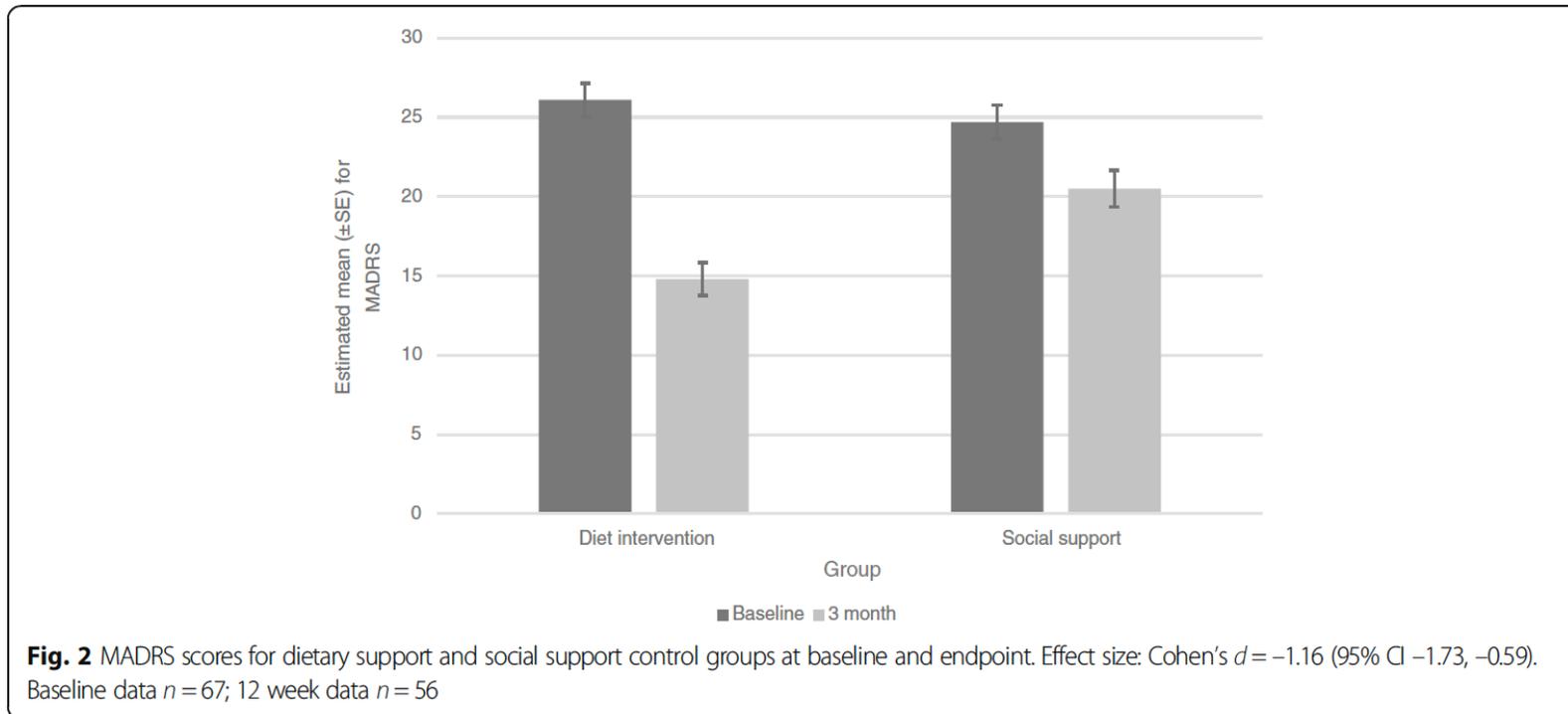




Protein	AND	Cereals and Starchy Vegetables	AND	Vegetables
<b>Tinned sardines</b> 		with <b>wholegrain biscuits</b> 		plus <b>avocado, tomato and cucumber</b> 
<b>Tinned salmon</b> 		with <b>tinned chickpeas</b> 		and <b>salad</b> 
<b>Tinned tuna</b> 		plus <b>instant brown or basmati rice</b> 		with <b>tinned corn, peas and beetroot</b> 
<b>Egg</b> 		on <b>wholemeal toast</b> 		with <b>avocado, tomato and mushrooms</b> 
<b>Supermarket rotisserie chicken (skin removed)</b> 		with <b>couscous</b> 		and <b>frozen vegetables</b> 

# Results

- ✓ **Significantly greater improvement in MADRS in ModiMed group** between baseline and 12 weeks vs controls,  $t(60.7) = 4.38, p < .001$
- ✓ The effect size for difference = Cohen's  $d$  of  $-1.16$  (95% CI  $-1.73, -0.59$ ),



# Dietary adherence



## ModiMed Diet score

greater increase in score in Med diet group than controls ( $p < 0.001$ )  
36 at baseline, 55 at 12 weeks

## Food groups

- ↑ 1.2 serves wholegrain/d (1 slice bread or ½ cup rice)
- ↑ 0.5 serves fruit/d (1/2 apple or 1 plum)
- ↑ 0.4 serves olive oil/d (1/2 tbsn)
- ↑ 1.1 fish/week (110g cooked fish)
- ↓ 21.8 serves/ week (1 serve = can coke, 2 scoops ice cream, 2 slices salami, 2-3 sweet biscuits, 1 doughnut)

Every 10% increase in dietary adherence there was 2.2 score improvement in MADRS

# Whole Diet-Focused Treatment



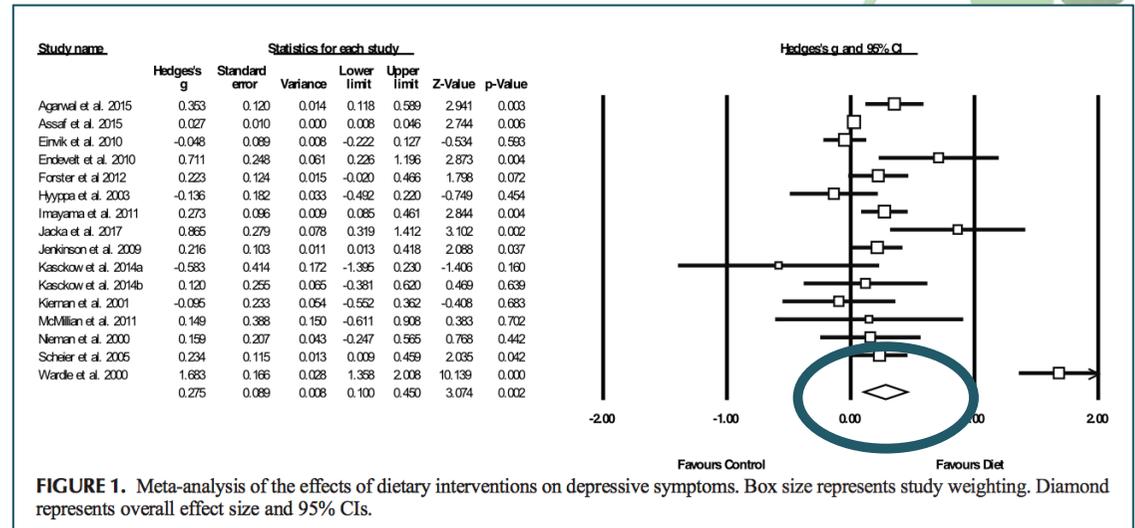
**SYSTEMATIC REVIEW/META-ANALYSIS**

**OPEN**

**The Effects of Dietary Improvement on Symptoms of Depression and Anxiety: A Meta-Analysis of Randomized Controlled Trials**

Joseph Firth, PhD, Wolfgang Marx, PhD, Sarah Dash, PhD, Rebekah Carney, PhD, Scott B. Teasdale, PhD, Marco Solmi, MD, Brendon Stubbs, PhD, Felipe B. Schuch, PhD, André F. Carvalho, MD, Felice Jacka, PhD, and Jerome Sarris, PhD

Psychosomatic Medicine  
(2019)



- N=16 RCTs with 45,826 participants
- Dietary interventions significantly reduced depressive symptoms
- No effect was observed for anxiety (but few studies)
- Greater benefits in females for both depression and anxiety



# Diet Quality and Brain Plasticity



Jacka et al. *BMC Medicine* (2015) 13:215  
DOI 10.1186/s12916-015-0461-x

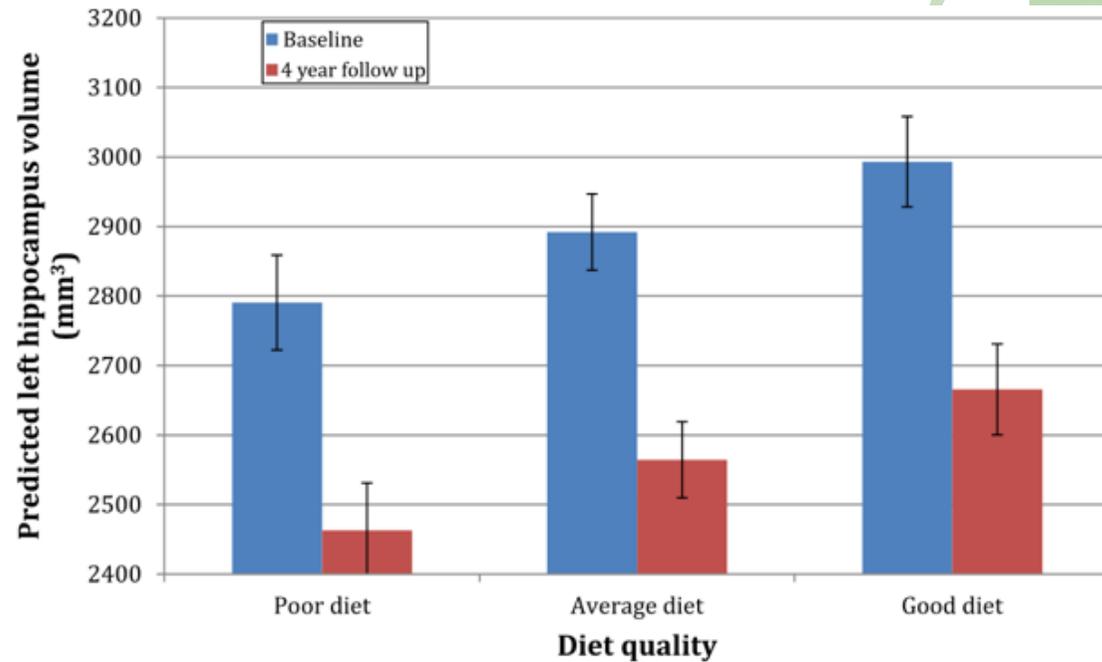
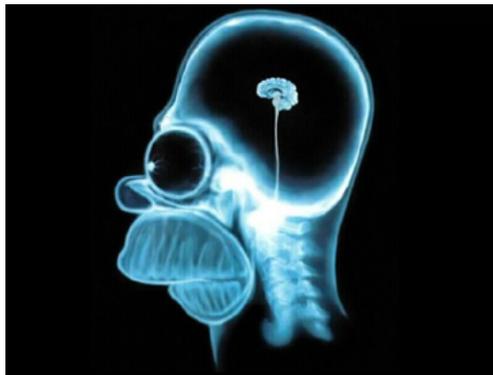
BMC Medicine

RESEARCH ARTICLE Open Access

Western diet is associated with a smaller hippocampus: a longitudinal investigation

Felice N. Jacka<sup>1,2,3,4\*</sup>, Nicolas Cherbuin<sup>5</sup>, Kaarin J. Anstey<sup>5</sup>, Perminder Sachdev<sup>6</sup> and Peter Butterworth<sup>5</sup>

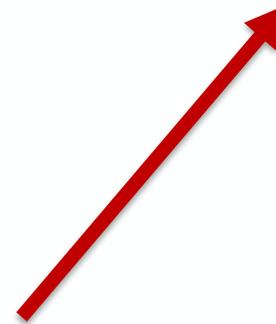
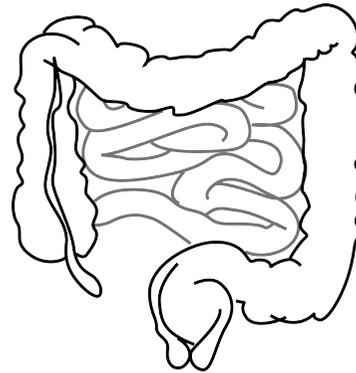
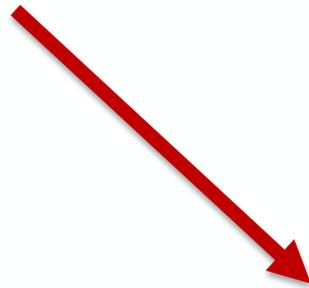
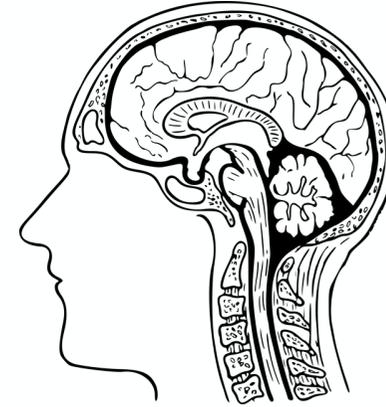
CrossMark



**Personality and Total Health Through Life**  
study: n = 255; aged 60 – 64 years;  
4 years follow-up

Jacka et al. 2015 *BMJ Medi*

A DEAKIN IDEA





## **Biological dysregulation associated with depression:**

- Inflammatory and oxidative stress (cytokines, C-reactive protein, ROS)
- Metabolic (insulin resistance, metabolic syndrome)
- HPA axis (cortisol)
- Neurotransmitter/neuropeptide (dopamine, serotonin, GABA, BDNF)

**Each modified by gut microbiota**

# Gut ↔ brain – how?



**Short Chain Fatty Acids (SCFAs) – eg. butyrate, acetate, propionate:**

- directly signal to cells through surface G protein–coupled receptors (GPCRs);
- affect gene transcription, including epigenetic mechanisms (acetylation, deacetylation of histone proteins)

# SCFAs



- **SCFAs have immunomodulatory properties** Furusawa (2013)  
*Nature*; Smith (2013) *Science*
- **SCFAs affect gut–brain hormonal communication** Wren et al. (2007)  
*Gastroenterology*
- **SCFAs regulate the synthesis of gut-derived 5-HT from enterochromaffin cells** Yano et al. (2015) *Cell*

## Short Chain Fatty Acids (SCFAs) – Butyrate

- Butyrate is energy source for colonocytes
- Butyrate regulates neutrophil function and migration, and has anti-inflammatory properties
- Butyrate is also important for maintaining the intestinal barrier by increasing the number of tight junctions within the epithelial layer of the colon



*Nicholson JK et al. Host-gut microbiota metabolic interactions. **Science** (2012)*

# Main factors influencing microbiota



Age

Medication  
use

**Diet**

Geography

Infection

Stress

# Diet and the Human Gut Microbiome: An International Review

Annette S. Wilson<sup>1</sup> · Kathryn R. Koller<sup>2</sup> · Matsepo C. Ramaboli<sup>3</sup> · Lucky T. Nesengani<sup>3</sup> · Soeren Ocvirk<sup>1,4</sup> · Caixia Chen<sup>1</sup> · Christie A. Flanagan<sup>2</sup> · Flora R. Sapp<sup>2</sup> · Zoe T. Merritt<sup>2</sup> · Faheem Bhatti<sup>1</sup> · Timothy K. Thomas<sup>2</sup> · Stephen J. D. O'Keefe<sup>1,3</sup>

- the fermentation of carbohydrate residues, namely fiber, releases metabolites that not only provide food for the colonic epithelium, but also exert a remarkable variety of regulatory effects on colonic mucosal inflammation and proliferation
- high fiber intakes provide high rates of butyrogenesis, **which exceed the metabolic requirements of the colonic mucosa and enter the blood stream** to exert epigenetic and immunomodulatory effects on other organs in the body
- based on nearly 135 million person-years of data from 185 prospective studies and 58 clinical trials with 4635 adult participants, comparing the highest dietary fiber consumers with the lowest, found a 15–30% lower rate in all-cause and cardiovascular-related mortality, in addition to a lower incidence and mortality in colorectal and breast cancer, coronary heart disease, stroke, and type 2 diabetes

## ARTICLE

Received 23 May 2014 | Accepted 20 Jan 2015 | Published 28 Apr 2015

DOI: 10.1038/ncomms7342

# Fat, fibre and cancer risk in African Americans and rural Africans

Stephen J.D. O'Keefe<sup>1</sup>, Jia V. Li<sup>2</sup>, Leo Lahti<sup>3,4</sup>, Junhai Ou<sup>1</sup>, Franck Carbonero<sup>5,†</sup>, Khaled Mohammed<sup>1</sup>, Joram M. Posma<sup>2</sup>, James Kinross<sup>2</sup>, Elaine Wahl<sup>1</sup>, Elizabeth Ruder<sup>6</sup>, Kishore Vipperla<sup>1</sup>, Vasudevan Naidoo<sup>7</sup>, Lungile Mtshali<sup>7</sup>, Sebastian Tims<sup>3</sup>, Philippe G.B. Puylaert<sup>3</sup>, James DeLany<sup>8</sup>, Alyssa Krasinskas<sup>9</sup>, Ann C. Benefiel<sup>5</sup>, Hatem O. Kaseb<sup>1</sup>, Keith Newton<sup>7</sup>, Jeremy K. Nicholson<sup>2</sup>, Willem M. de Vos<sup>3,4,10</sup>, H. Rex Gaskins<sup>5</sup> & Erwin G. Zoetendal<sup>3</sup>



- Animal proteins and fats 2-3 times higher in Western diet
- Carbohydrates and fibre far higher in African diet
- Profound differences in gut microbiota composition

African Americans switched to a high fibre/low fat diet for 2 weeks = significant reductions in mucosal inflammation and biomarkers of cancer risk (Africans switched to Western diet showed the opposite)

# Dramatic Increase in Allergic Disease since 1980

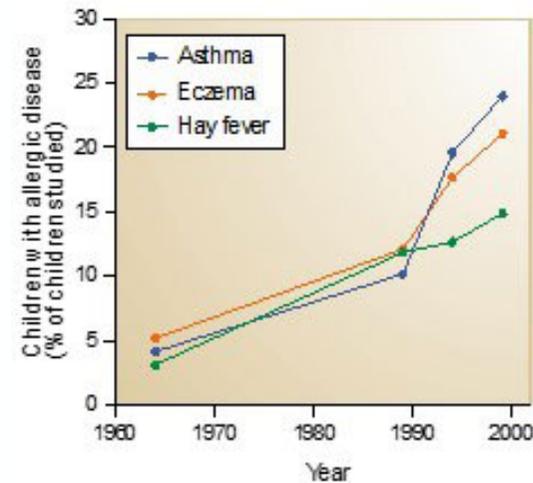
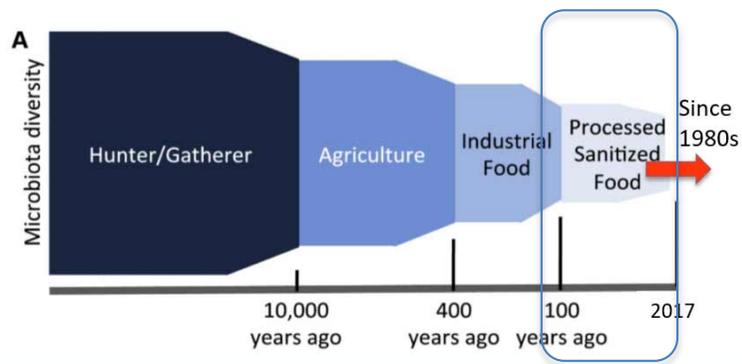


Figure 2 | The increase in the prevalence of asthma, eczema and hay fever since 1964. The results of four cross-sectional surveys of school children aged 9–12 years in Aberdeen, United Kingdom, between 1964 and 1999 are

# LETTER

doi:10.1038/nature12820

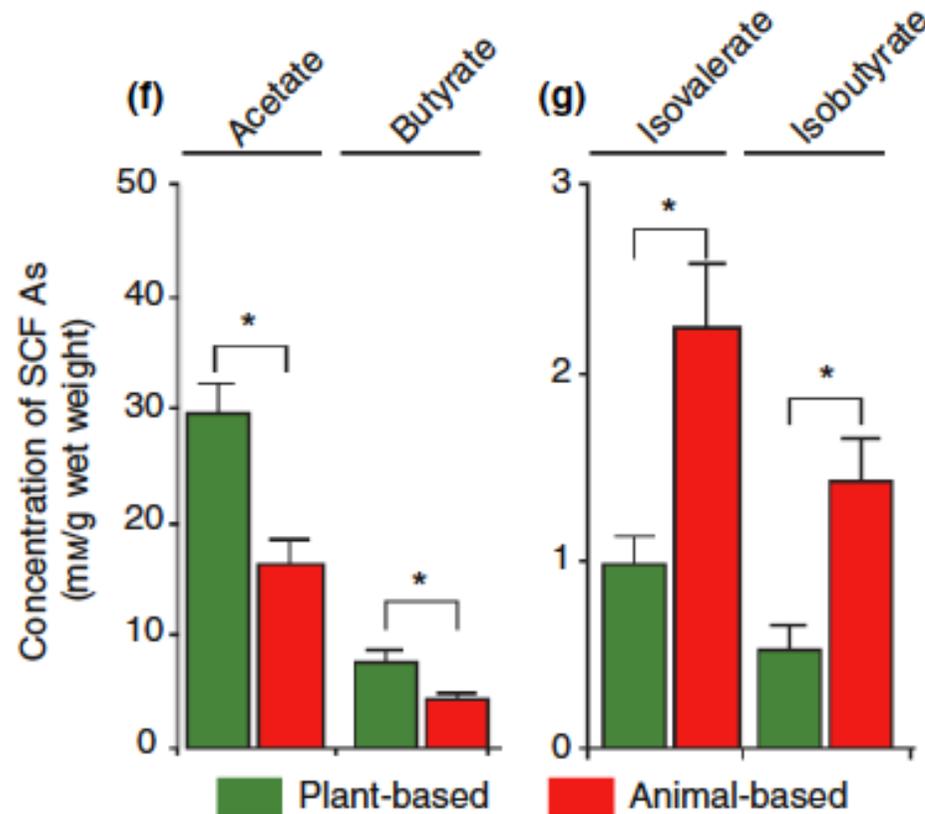
## Diet rapidly and reproducibly alters the human gut microbiome

Lawrence A. David<sup>1,2†</sup>, Corinne F. Maurice<sup>1</sup>, Rachel N. Carmody<sup>1</sup>, David B. Gootenberg<sup>1</sup>, Julie E. Button<sup>1</sup>, Benjamin E. Wolfe<sup>1</sup>, Alisha V. Ling<sup>2</sup>, A. Sloan Devlin<sup>4</sup>, Yug Varma<sup>4</sup>, Michael A. Fischbach<sup>4</sup>, Sudha B. Biddinger<sup>2</sup>, Rachel J. Dutton<sup>3</sup> & Peter J. Turnbar<sup>1</sup>

‘plantbased diet’ = grains, legumes, fruits and vegetables or  
‘animal-based diet’ = meats, eggs and cheeses

- N=10 (21–33 years)
- Consumed for five days
- Cross-over design

*Microbiota returned to baseline within 3-days post-dietary intervention*



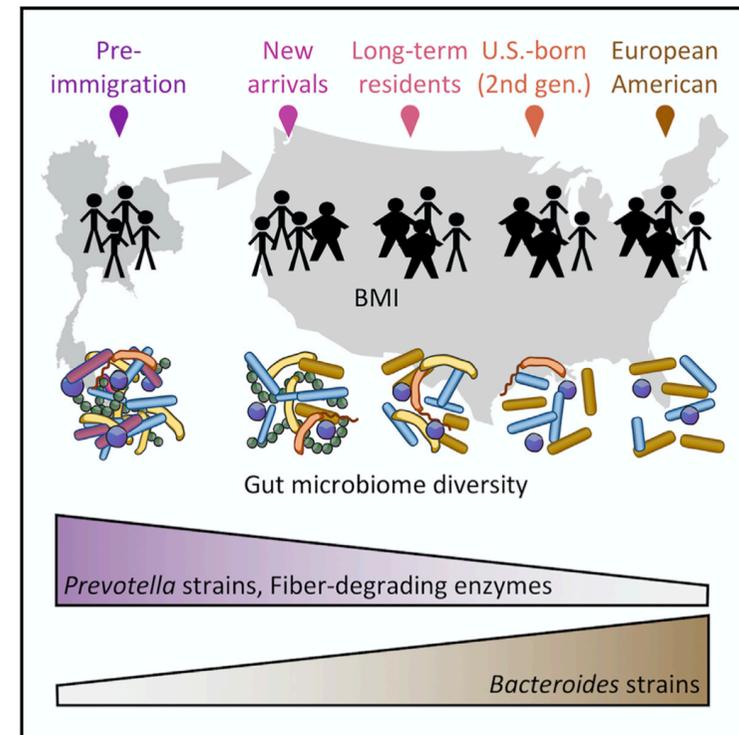
David et al. Nature (2014)

A DEAKIN IDEA

## US Immigration Westernizes the Human Gut Microbiome

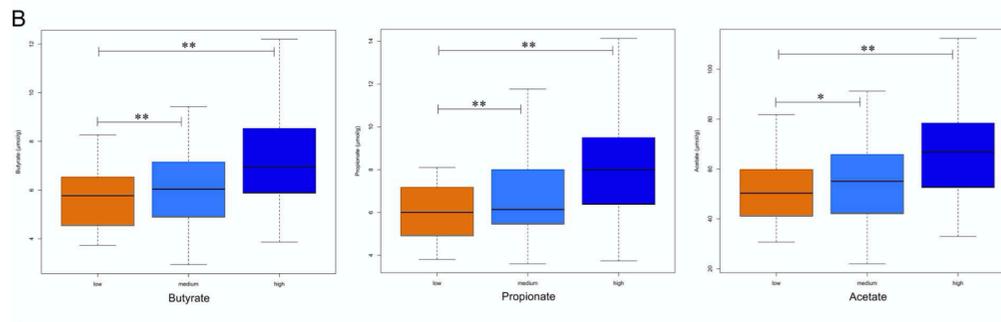


- US immigration is associated with loss of gut microbiome diversity
- US immigrants lose bacterial enzymes associated with plant fiber degradation
- Bacteroides strains displace Prevotella strains according to time spent in the USA
- Loss of diversity increases with obesity and is compounded across generations



# High-level adherence to a Mediterranean diet beneficially impacts the gut microbiota and associated metabolome

Francesca De Filippis,<sup>1</sup> Nicoletta Pellegrini,<sup>2</sup> Lucia Vannini,<sup>3,4</sup> Ian B Jeffery,<sup>5,6</sup> Antonietta La Storia,<sup>1</sup> Luca Laghi,<sup>3,4</sup> Diana I Serrazanetti,<sup>4</sup> Raffaella Di Cagno,<sup>7</sup> Ilario Ferracino,<sup>8</sup> Camilla Lazzi,<sup>2</sup> Silvia Turroni,<sup>9</sup> Luca Coccolin,<sup>8</sup> Patrizia Brigidi,<sup>9</sup> Erasmo Neviani,<sup>2</sup> Marco Gobbetti,<sup>7</sup> Paul W O'Toole,<sup>5,6</sup> Danilo Ercolini<sup>1</sup>



- 153 individuals habitually following omnivore, vegetarian or vegan diets (Italian)
- The majority of vegan (88%) and vegetarian subjects (65%) and 30% of omnivore subjects had a high adherence to the MD
- The faecal levels of SCFAs strongly correlated with the consumption of fruit, vegetables, legumes, and fibre
- By contrast, valerate and caproate concentrations were linked to consumption of protein- rich animal foods and fat
- Urinary TMAO levels were significantly lower in vegetarian and vegans (TMAO a potential risk factor for cardiovascular disease)
- The higher the adherence to the MD, the lower the measured TMAO level, even in the omnivores

# High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health<sup>1-4</sup>



*Wendy R Russell, Silvia W Gratz, Sylvia H Duncan, Grietje Holtrop, Jennifer Ince, Lorraine Scobbie, Garry Duncan, Alexandra M Johnstone, Gerald E Loble, R John Wallace, Garry G Duthie, and Harry J Flint*

- N=17 Obese men
- (1) high-protein and moderate-carbohydrate diet (HPMC) (4 weeks)
- (2) high-protein and low carbohydrate diet (HPLC) (4 weeks).
- (Prior to intervention: weight maintenance diet (7 days))

## **Results**

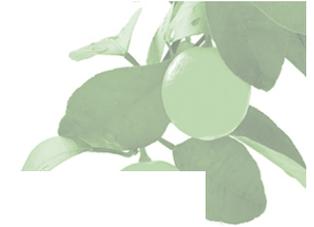
- Higher protein intakes increased the protein fermentation in the colon
- Compared with the maintenance diet, the HPMC and HPLC diets resulted in increased proportions of branched-chain fatty acids and concentrations of phenylacetic acid and N-nitroso compounds (cancer-related)
- HPLC diet decreased the proportion of butyrate-producing bacteria and butyrate in faeces
- HPLC diet greatly reduced concentrations of fibre-derived, antioxidant phenolic acids

## Substituting whole grains for refined grains in a 6-wk randomized trial favorably affects energy-balance metrics in healthy men and postmenopausal women<sup>1-3</sup>

*J Philip Karl,<sup>4</sup> Mohsen Meydani,<sup>4</sup> Junaidah B Barnett,<sup>4</sup> Sally M Vanegas,<sup>4</sup> Barry Goldin,<sup>5</sup> Anne Kane,<sup>5</sup> Helen Rasmussen,<sup>4</sup> Edward Saltzman,<sup>4</sup> Pajau Vangay,<sup>6</sup> Dan Knights,<sup>7</sup> C-Y Oliver Chen,<sup>4</sup> Sai Krupa Das,<sup>4</sup> Satya S Jonnalagadda,<sup>8,9</sup> Simin N Meydani,<sup>4</sup> and Susan B Roberts<sup>4\*</sup>*

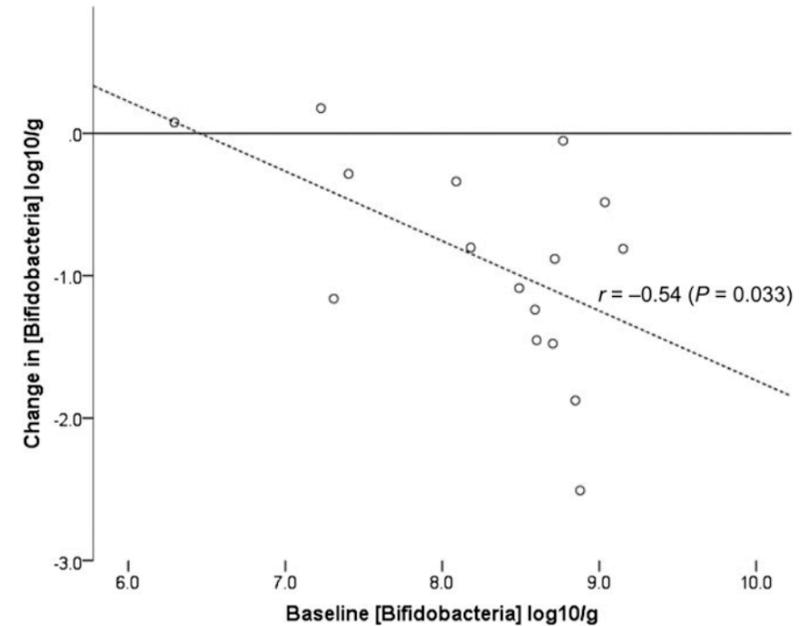
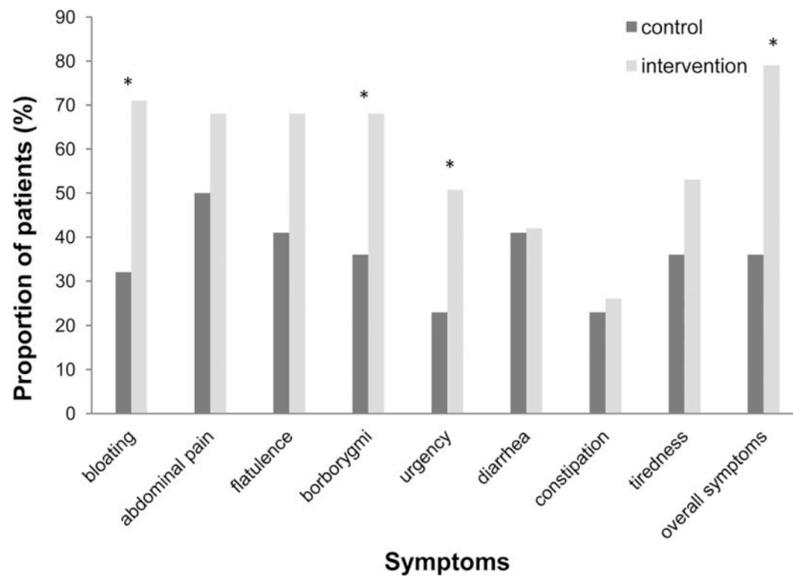


- Wholegrain diet vs refined grain diet – (6 weeks after 2-week run-in period)
- N=81
- Randomized, controlled, parallel, feeding study (provision of all foods)
- WG resulted in approx. 100-kcal/d energy deficit (primarily attributable to a greater energy excretion in stool)
- Higher stool short-chain fatty acid concentrations in the WG than in the RG
- Relative abundance of *Enterobacteriaceae* (proinflammatory taxa) decreased and butyrate-producing *Lachnospira* and *Roseburia* increased in the WG compared within the RG group



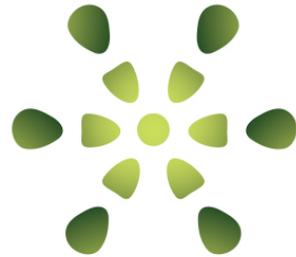
# Fermentable Carbohydrate Restriction Reduces Luminal Bifidobacteria and Gastrointestinal Symptoms in Patients with Irritable Bowel Syndrome<sup>1-4</sup>

Heidi M. Staudacher,<sup>5,6</sup> Miranda C. E. Lomer,<sup>5-7</sup> Jacqueline L. Anderson,<sup>5</sup> Jacqueline S. Barrett,<sup>8</sup> Jane G. Muir,<sup>8</sup> Peter M. Irving,<sup>5,7</sup> and Kevin Whelan<sup>5\*</sup>



**FIGURE 2** Baseline fecal bifidobacteria concentration in IBS patients compared with change in bifidobacteria concentration after 4 wk of fermentable carbohydrate restriction. \*Pearson correlation coefficient =  $-0.54$ ,  $P = 0.033$ . IBS, irritable bowel syndrome.

[www.foodandmoodcentre.org.au](http://www.foodandmoodcentre.org.au)



# FOOD & MOOD

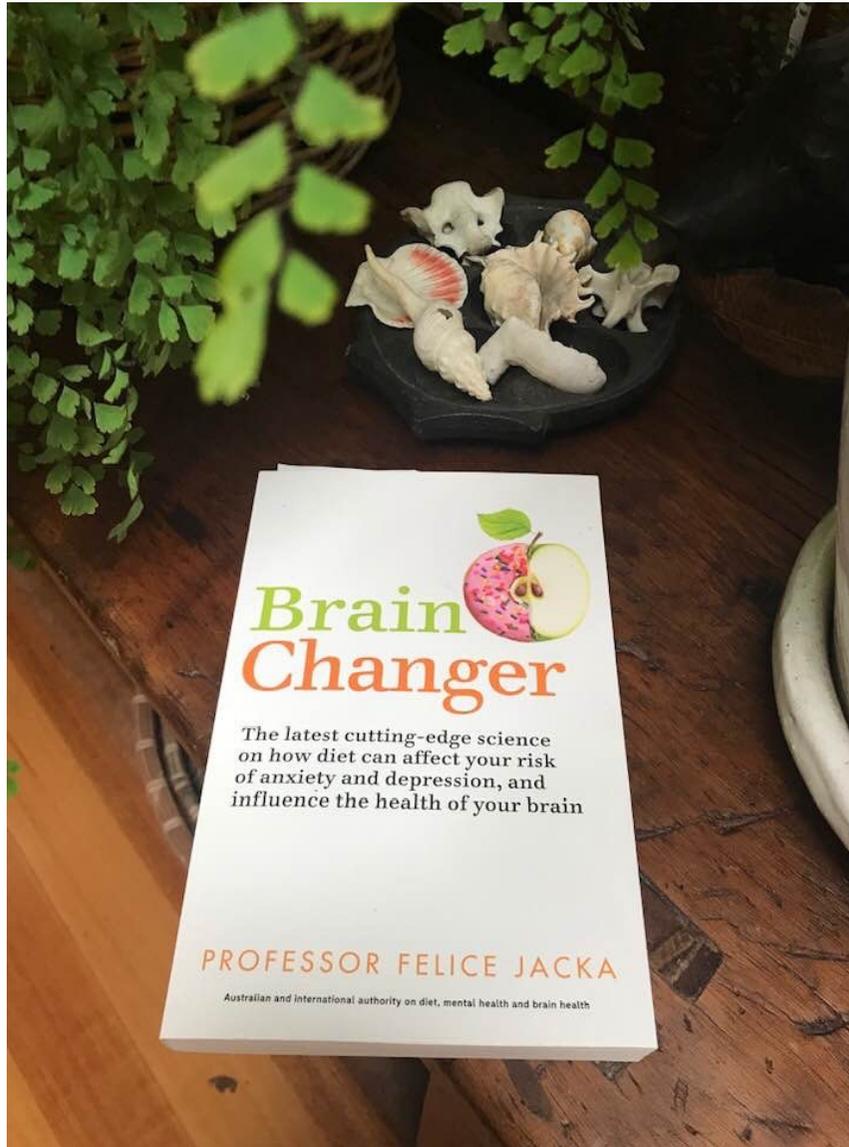
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## CENTRE

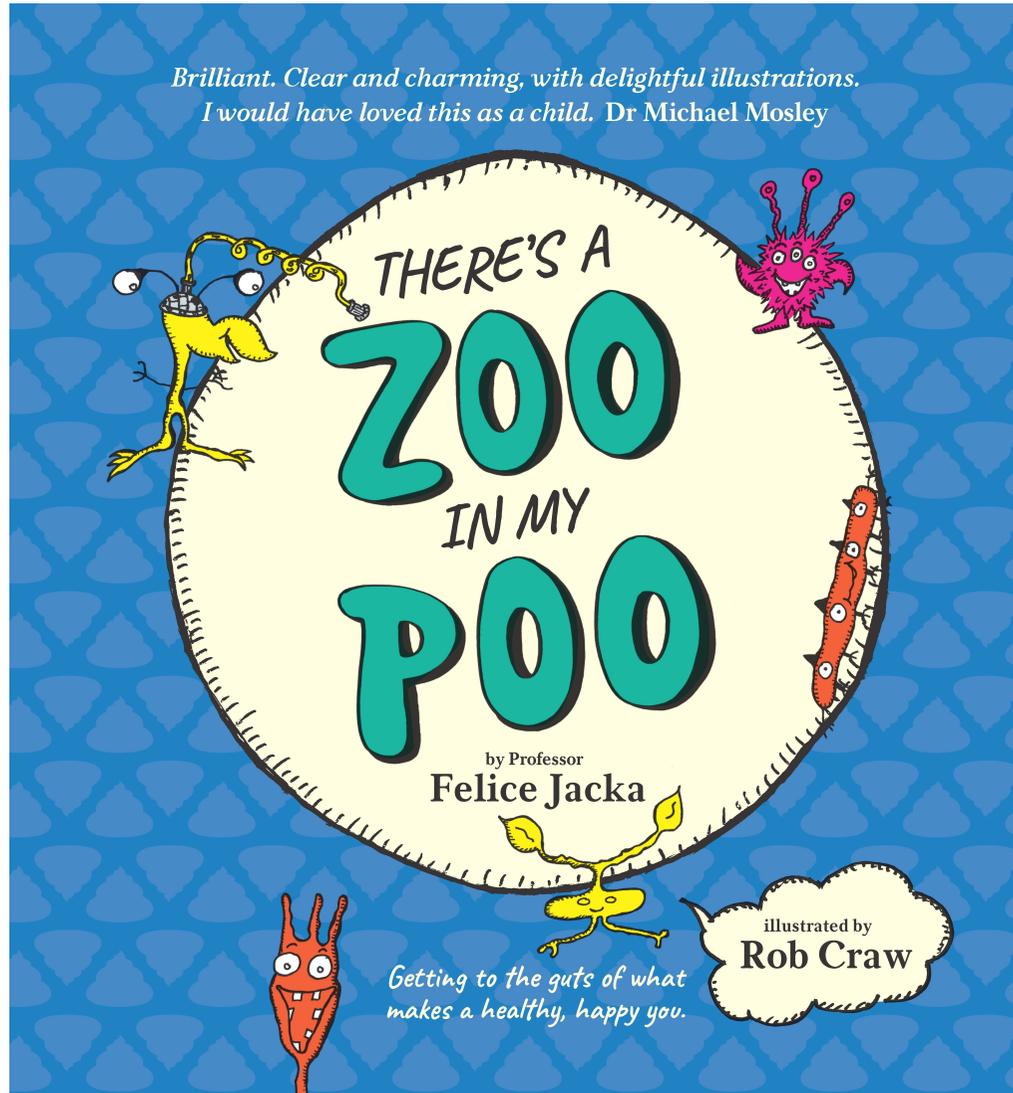
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A **DEAKIN** IDEA





Pan Macmillan Press  
February 2019



*Brilliant. Clear and charming, with delightful illustrations.  
I would have loved this as a child.* Dr Michael Mosley

THERE'S A  
**ZOO**  
IN MY  
**POO**

by Professor  
**Felice Jacka**

illustrated by  
**Rob Crow**

*Getting to the guts of what  
makes a healthy, happy you.*

Pan Macmillan Press  
August 2020

# Acknowledgements

## Postdoctoral

Dr Anu Ruusunen  
Dr Tetyana Rocks  
Dr Wolfgang Marx  
Dr Erin Hoare  
Dr Amy Loughman  
Dr Heidi Staudacher

## PhD Students

Samantha Dawson  
Claire Young  
Amelia McGuinness  
Hajara Aslam  
Sara Campolonghi  
Meg Hockey  
Jessica Davis  
Jessica Green  
Melissa Lane  
Gina Howland  
Madi West  
Samantha Collins



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**IMPACT**

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HEALTH AND CLINICAL TRANSLATION

