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# Lifestyle modification and its impact on MS health outcomes.

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Neuroepidemiology Unit  
Centre for Epidemiology and Biostatistics  
Melbourne School of Population & Global Health





# The Neuroepidemiology Unit

- Melbourne School of Population and Global Health, Faculty of Medicine
- Set up in 2015 by Professor George Jelinek
- Over 40 peer reviewed publications from our flagship HOLISM study
- Many other publications from other NEU studies and collaborations
- Current collaborations across UK, Europe, USA and within Australia
- We aim to assess the role of lifestyle modification in MS





# Questions we are trying to answer



Which lifestyle factors are associated with better health outcomes?



Which lifestyle modifications are the most important?



Is it necessary to do all of them?



# What is lifestyle modification?

- Lifestyle modification involves **altering long-term habits and maintaining the new behaviour for months or years**. Lifestyle modification can be used to treat a range of diseases.

## NEU studies

### Lifestyle behaviours

- smoking
- diet
- physical activity
- vitamin D
- stress reducing activities

### Outcomes

- disability
- depression
- fatigue
- relapse rate
- quality of life

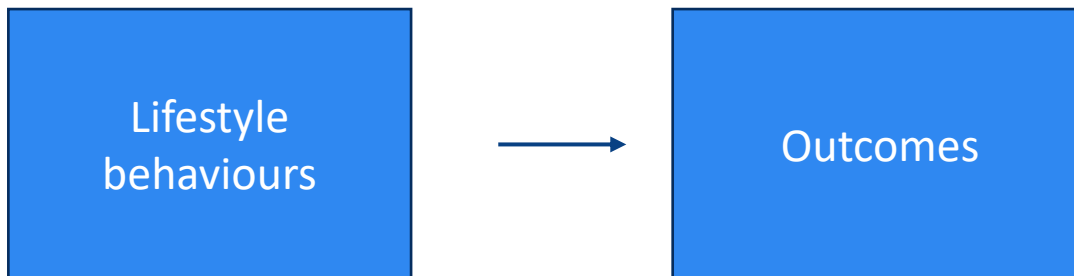
## OMS Program: 7 steps

- Eat well
- Sun and Vitamin D
- Exercise
- Meditate
- Medication
- Family members
- Change for life



# Background

Modification of lifestyle risk factors may represent potential points of intervention for improving health outcomes in people with MS





# Evidence

- Proving which interventions work is not easy
- Many types of evidence
- Each type of research comes with its own limitations
- Each piece of evidence forms part of the jigsaw of understanding the “truth”
- Is there anything such as proof?
- Is proof necessary?



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# Evidence – what types of studies?



## Observational studies



**Observe the effect** of a risk factor, treatment or other intervention in a population **without trying to change who is or isn't exposed to it**

Watching things unfold over time without intervening

# Observational studies–designs



## Cross sectional study

- Examines lifestyle and outcomes at one time point
- “snapshot”
- Cannot determine cause

## Longitudinal study

- Examines lifestyle and outcomes over time
- How these lifestyles affect rates of an outcome
- Can be **more confident of causal relationships**
- Prospective analysis looks at a behavior at one point and what happens in the future



# Evidence – what types of studies?



## Experimental studies



Where researchers **introduce an intervention** and **study the effects**.



Experimental studies are usually randomized, meaning the subjects are grouped by chance.



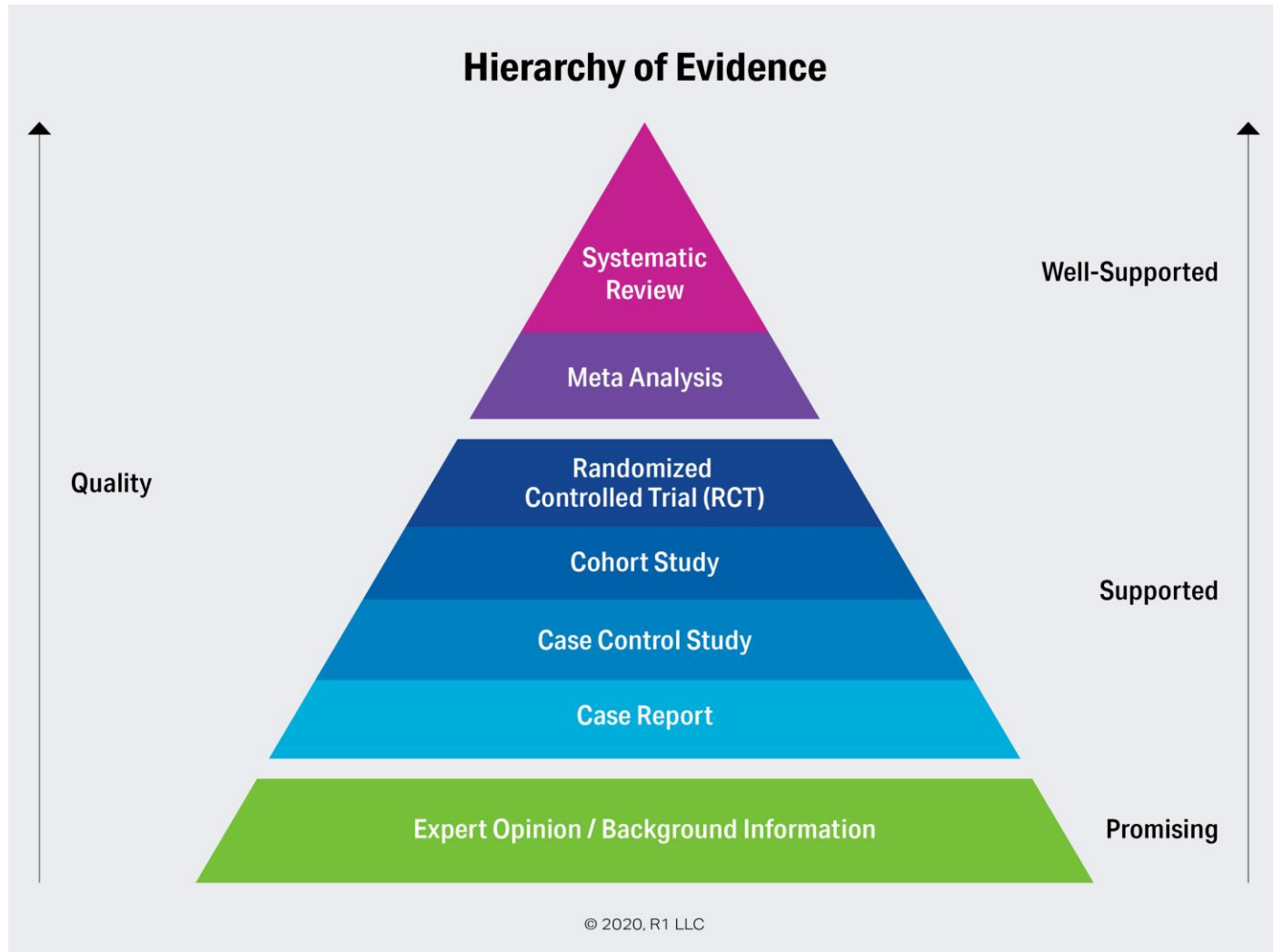
# Evidence

## Strengths and weaknesses

- Depends on the question
- Observational studies
  - only way to explore certain questions
  - results are open to dispute
  - “confounding biases”
- The RCT
  - “gold standard”
  - little is left to chance
  - time consuming, expensive
  - participant recruitment and retention



# The hierarchy of evidence





# The HOLISM study

Important study due to longitudinal nature  
7.5 years of data





## What is a healthy diet?

- Many ways of defining or measuring
- Diet habits questionnaire
- Describes diet quality

## Specifically

- High in fruit and vegetables, grains, pulses etc
- High in polyunsaturated fatty acids (flaxseed, oily fish)
- Low in dairy and meat and saturated fat
- Low in processed foods, sugars, empty calories

# Diet and disability, fatigue and relapse

- Better diet quality associated with less disability progression.
- Associations with relapse rate and fatigue only seen cross-sectionally

Outcome	Author	Study design	Result
<b>Disability</b>	Fitzgerald	Cross-sectional	Better diet associated with less disability
	Hadgkiss	Cross-sectional	Better diet associated with less disability
	Marck	Cross-sectional	No association
	Simpson-Yap	2.5-year prospective	Better diet associated with less disability
	Simpson-Yap	7.5-year prospective	Better diet associated with less disability
<b>Fatigue</b>	Fitzgerald	Cross-sectional	Better diet associated with decreased fatigue
	Hadgkiss	Cross-sectional	Better diet associated with decreased fatigue
	Marck	Cross-sectional	Trend towards better diet associated with decreased fatigue
	Simpson-Yap	2.5-year prospective	No prospective association
	Simpson-Yap	7.5-year prospective	No prospective association
<b>Relapse</b>	Fitzgerald	Cross-sectional	No association
	Weiland	Cross-sectional	Better diet weakly associated with decreased relapse rate.





# Diet and disability over time

- Examined baseline diet and risk of having increased disability at 7.5 years
  - High quality diet → less risk of increasing disability (33% less risk in top half diet quality)
  - Meat and dairy consumption → double risk of increasing disability
- Examined what happened if you changed your diet quality
  - **Decreased** their diet quality → 2.3-fold greater increase in disability
  - **Stopped** having a high diet quality → 42% greater increase their disability
  - Those **who started** or had a high quality → inverse trends with increasing disability



# Diet & quality of life and depression

- Diet quality associations with QoL and depression are substantiated in prospective results

Outcome	Author	Study design	Result
Depression	Marck	Cross-sectional	Better diet associated with decreased depression
	Taylor 2014	Cross-sectional	Better diet associated with decreased depression
	Taylor 2019	2.5-year prospective	Better diet associated with decreased depression
Anxiety	Marck	Cross-sectional	No association
Quality of life	Marck	Cross-sectional	Better diet associated with better physical & mental QoL
	Hadgkiss	Cross-sectional	Better diet associated with better physical & mental QoL
	Evers	Cross-sectional	Better diet associated with better physical & mental QoL, only among females
	Simpson-Yap	7.5-year prospective	Better diet quality associated with better physical & mental QoL



# Diet and depression

Baseline to 2.5 year follow up

• High diet quality, no meat or dairy intake → less depression

• Also

- vitamin D supplementation
- omega 3 supplementation
- regular exercise
- meditation at baseline

→ less depression 2.5 years later



# Diet and QoL

Baseline to 7.5 years follow up

- Baseline high diet quality → better physical-QoL
- Baseline meat consumption → lower physical-QoL
- Baseline dairy consumption → lower physical- and mental-QoL per year





# Benefits of “sticking” to a diet?

Two studies looking sticking with an MS specific diet

- Improved diet quality
  - Following any diet program → higher overall diet quality
  - Adherence to the OMS diet → highest diet quality.
  
- Improved health outcomes (not published)
  - Persistent-adherence to the OMS-diet → lower fatigue, disability and depression than both non- and partial (ceased)-adherence.



# The UK MS Register Diet Study

- University of Swansea, Imperial College London and Oxford Brookes University
- Data from UK MS Register
  - national survey of >2400 people
  - surveyed biannually since 2011
  - clinical, demographic and some lifestyle characteristics
- Large 120 question diet survey 2015-16, very intensive instrument
- We will same diet survey in 2022 and assess relationships of diet with outcomes over 10 years' follow-up
- Why?
  - Adding depth and breadth to current diet data
  - Potential for RCT



# Physical activity & disability

- Multiple cross-sectional studies show greater physical activity associated with less disability
- One prospective cohort study substantiates this, finding lower disability associated with greater physical activity

Author	Study design	Sample size	Measure	Result
Jelinek 2016	Cross-sectional	2,469	IPAQ	<ul style="list-style-type: none"> <li>• Moderate/high IPAQ associated with 55% and 93% lower frequencies of moderate and severe PDDS (both <math>p &lt; 0.001</math>)</li> </ul>
Marck 2014	Cross-sectional	2,232	IPAQ	<ul style="list-style-type: none"> <li>• Lower disability in those with higher physical activity (<math>p &lt; 0.001</math>)</li> </ul>
Motl 2013	2.5-year prospective cohort	269	Accelerometer	<ul style="list-style-type: none"> <li>• Lower disability as with higher physical activity (<math>p &lt; 0.05</math>)</li> </ul>
Marck 2022	Cross-sectional	3,112	IPAQ	<ul style="list-style-type: none"> <li>• Physical activity lower in those with severe vs mild disability (<math>p &lt; 0.001</math>)</li> </ul>
van Hijfte 2022	Cross-sectional	305	IPAQ	<ul style="list-style-type: none"> <li>• Inactive have 1.4 units higher MSSS (<math>p = 0.001</math>) but Active vs Minimally Active not different (<math>p = 0.91</math>)</li> </ul>



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# Physical activity & relapse

- Two cross-sectional studies evaluate relapse as outcome
- Both show greater physical activity associated with reduced relapse rate

Author	Study design	Sample size	Measure	Result
Grover 2015	Cross-sectional	13 MS	Godin Leisure-time	<ul style="list-style-type: none"> <li>• 50% lower relapse rate in those reporting strenuous physical activity, <math>p=0.035</math></li> </ul>
Marck 2014	Cross-sectional	2,232	IPAQ	<ul style="list-style-type: none"> <li>• 12-month relapse rate lower in those with higher physical activity (<math>p=0.009</math>)</li> </ul>





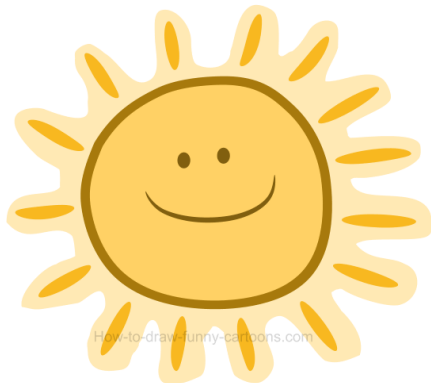
# Vitamin D & disability

- Fewer studies evaluating vitamin D and disability
- Mixed results
- One prospective study showing less disability with increasing vitamin D
- Possibly due to latitude, initial Vitamin D levels and routine supplementation
- Heterogeneity of methods tempers interpretation

Author	Study design	Measure	Result
Smolders 2008	Cross-sectional, n=267	Serum 25(OH)D Serum 1,25(OH) <sub>2</sub> D	• No association
Weinstock-Guttman 2011	Retrospective cohort, n=193	Serum 25(OH)D Serum 1,25(OH) <sub>2</sub> D	• No association
Ascherio 2018	Nested cohort study within Betaferon RCT, n=332	Deseasonalised 25(OH)D	• 50nmol/L increase in first 12 month 25(OH)D associated with 0.18 lower subsequent change in EDSS, p=0.19
Wesnes 2021	Prospective cohort study, n=88 RRMS	Deseasonalised 25(OH)D	• -0.45 lower 10-year EDSS progression per 18nmol/L 25(OH)D

# Vitamin D & relapse

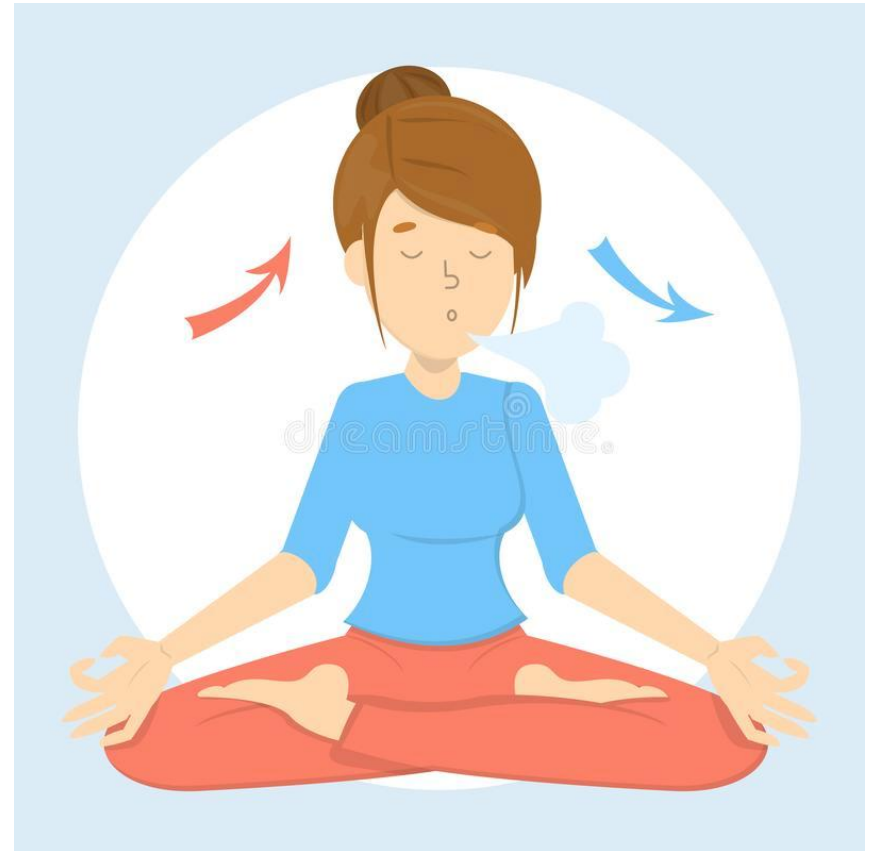
- Most prospective studies show beneficial relationship between vitamin D and reduced relapse rate



Author	Study design	Measure	Result
Smolders 2008	Cross-sectional, n=126	Serum Vitamin D	• No association
Mowry 2010	Prospective cohort study, 110 paediatric-onset MS	Deseasonalised 25(OH)D	• Higher vitamin D associated with lower relapse rate
Simpson 2010	Prospective cohort, n=145	10nmol/L serum 25(OH)D Monthly modeled 25(OH)D	• aHR=0.91, p=0.006 • aHR=0.88, p=0.001
Runia 2012	Prospective cohort study, n=73	Deseasonalised 25(OH)D	• Compared to 25(OH)D>100nmol/L, 25(OH)D<50nmol/L have RR=1.9, p=0.013
Ascherio 2014	Nested cohort study within Betaferon RCT, n=334	Deseasonalised 25(OH)D	• 50nmol/L increase in first 12 month 25(OH)D associated with 57% lower subsequent relapse rate (aRR=0.43, p=0.030)
Simpson 2018	Prospective cohort study, 279 FCD followed after referral first event	Deseasonalised 25(OH)D	• No association of baseline 25(OH)D with subsequent relapse risk

# Stress reducing activities

- One of our prospective HOLISM NEU papers over 2.5 to 7.5 years
- Meditation
  - reduces depression
  - increases mastery
  - once weekly as little as 20 mins





# So what does it all mean?



High quality diet is associated with improved health outcomes: disability, fatigue, depression and sometimes relapse rate

Vitamin D supplementation, non smoking, physical activity, stress reducing activities are all associated with improved outcomes

All health outcomes: QoL, disability, fatigue, depression and relapse rate are affected by some if not all behaviours in these large populations



# A whole of lifestyle approach: STOP-MS study

5-day residential group workshops, promoted the OMS program, commenced in 2002

6 workshops run between March 2012 and May 2013

3 years after attending the workshop, participants reported

- Improved physical and mental QOL
- A small decrease in disability
- Fewer had a relapse the preceding year
- Behaviours were maintained
- Medication use increased

Feasible and sustainable

# Some or all behaviours?



HOLISM study looking at individual lifestyle behaviours and QoL over 7.5 years.

- Engagement with **≥3 lifestyle behaviours** is associated with higher QoL.
- Optimal effects with **5 behaviours**
- Prospectively, **≥3** behaviours at 2.5-year, and **≥2** behaviours at 5- and 7.5-year led to higher mental QoL.
- Most likely driven by diet and physical activity

Suggestive that multiple healthy lifestyle recommendations should be encouraged and supported for MS management.



# MS type

NEU collaboration with the Accelerated Cure Project for Multiple Sclerosis, MA, USA. Using a large (1100) US population (iConquer MS database)

Looked at diet, supplements, wellness activities (mind/mind-body etc) and physical activity related to QoL cross sectionally

## Progressive MS

Various healthy diets → better mental and physical quality of life

Physical activity → better cognitive function and mobility and less depression and fatigue.

## RRMS

Wellness activities → improved cognitive function, social participation

Physical activity → higher mobility, positive mood, social satisfaction, lower anxiety, depression and fatigue and improved sleep



# What other outcomes and studies

- The NEU less common outcomes and study types
- Outcomes
  - Mastery: the extent to which an individual perceives their life circumstances as being under their control.
  - Engagement: the value of participation and belonging
- Study types
  - Qualitative interviews: talking directly to people and exploring experiences
  - Qualitative analysis of written answers
- Personal experience
- Collective experience

# Mastery

- Those with the highest mastery had
  - 90% less depression
  - 60% less fatigue
  - 77% fewer had severe disability
- Prospectively between 2.5 and 5 years, those in the top half of mastery had 70% less depression
- A protective relationship of mastery with depression was observed



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# Engagement

- Engagement with resources
  - improved QOL
  - lower rates of depression and fatigue
- Depression among workshop attendees half that of the whole sample.
- No engagement
  - 3 x fatigue
  - 10 x depression
  - lower physical and mental QOL
- Strongly support a role for engagement in resources promoting lifestyle modification.



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# Qualitative studies

Free text responses in baseline  
HOLISM survey regarding lifestyle  
modification

**Practical challenges**

**Physical / psychological barriers**

**Enablers of change**

**Experienced outcomes**

*I'm a firm believer in lifestyle changes and dietary changes however I have found it hard to implement. A bit contradictory I know! With three young kids I do seem to still put myself last despite my illness...there is never enough time in the day!!*

*I wouldn't be as determined an individual as I am if I hadn't been told of my diagnosis or experienced these symptoms...I can say that I would never have achieved what I have without them.*





# Personal experience

## OMS retreats/workshops

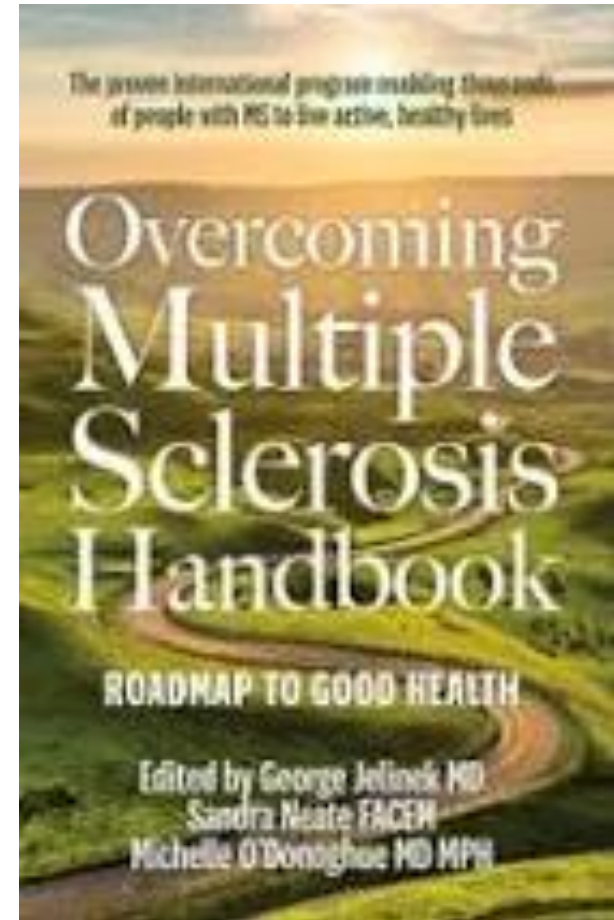
- 20 years
- 100s of participants
- Australia, NZ, Europe, UK
- Strong networks
- Social media groups
- Reunions
- Watched people over these years self-manage, develop their own expertise and frequently remain well.





# The Overcoming MS Handbook Roadmap to Good Health

- Edited by George Jelinek, Sandra Neate and Michelle O'Donoghue
- A range of topics including mental health, choosing your healthcare team, improving resilience, work, pregnancy and progressive MS





# The Overcoming MS Handbook Roadmap to Good Health

- Team of international experts, most with MS, on the OMS program, with particular expertise or experience
  - Neurologist: what is MS
  - Chef: diet
  - Psychiatrist: mental health
  - Psychologist: resilience
- Personal stories in each chapter
- Conversational companion to the other Overcoming MS books



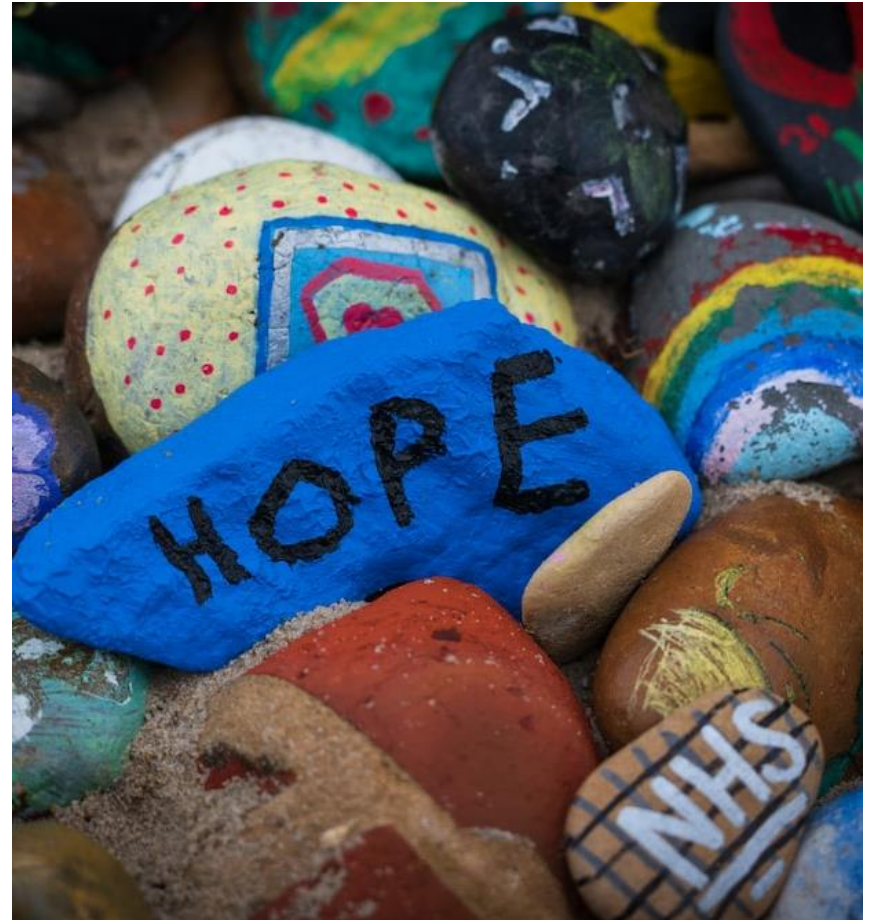


# What we're aiming for

- Build a picture of what lifestyle modification can do
- Help people with MS find confidence and empowerment through knowledge
- Provide people with MS with the tools to self-manage MS
- Live with hope based on evidence

Overcoming  
MS

Find hope,  
based on evidence







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