

Better Health Outcomes through Lifestyle: A Platform for Secondary and Tertiary Prevention of MS

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Content of this presentation

- Background
- Lifestyle factors and MS
 - Smoking, Alcohol, Diet and omega 3, Vitamin D, Exercise, and Stress reduction
- HOLISM study
 - Longitudinal observational study
- STOPMS lifestyle retreat study
 - Longitudinal follow up of lifestyle intervention
- Future directions
- Conclusion and discussion



Background – preventive medicine

The greatest
medicine of all
is to
teach people
how not
to need it.

- “**Preventive Medicine** focuses on the health of individuals, communities, and defined populations. Its goal is to protect, promote, and maintain health and well-being and to **prevent disease, disability, and death**” (American College of Preventive Medicine)
- **Primary prevention:** prevent disease or injury before it ever occurs.
- **Secondary prevention:** reduce the impact of a disease or injury that has occurred.
- **Tertiary prevention:** soften the impact of an ongoing illness /injury that has lasting effects.
- “Four of the most prominent chronic diseases (cardiovascular diseases, cancer, COPD and type 2 diabetes) are linked by common and **preventable biological risk factors**, notably high blood pressure, high blood cholesterol and overweight, and by related **major behavioural risk factors: unhealthy diet, physical inactivity and tobacco use.**” (WHO)



Background - MS

- MS aetiology
 - Genetic
 - Environmental factors

“modifiable environmental factors hold the key to preventing some 80% of cases”
Ebers, Lancet Neurology 2008
- MS disease course
 - Age onset
 - Environmental factors
- MS management
 - Important to prevent damage as reversing damage is more difficult
 - Medication
 - Modifiable lifestyle factors



Background - Overcoming Multiple Sclerosis

www.overcomingmultiplesclerosis.org

Home > About OMS > Who We Are

Who We Are
Mission
About Prof. Jelinek
Our Team

DONATE TODAY

Who We Are

OVERCOMING MULTIPLE SCLEROSIS

Overcoming Multiple Sclerosis promotes a program of diet and lifestyle management that has been shown to improve the health and lives of people with MS. Professor George Jelinek, who was diagnosed with MS in 1999, developed the rigorously researched OMS Recovery Program more than 15 years ago.

OMS is well established in Australia and New Zealand as a non-profit organization that accepts no funding from the pharmaceutical industry. In 2011, we founded a charity in the UK to increase awareness of OMS, with the aim of making our program and its benefits available to the more than 2.5 million people with MS around the world.

With the launch of our charities in the US, UK and Australia, OMS is becoming a truly global organization.

A little helping hand.
Help us raise awareness of the OMS Recovery Program and the research behind it, so that more people with MS can lead better, healthier lives.

Donate today

RECOVERING FROM MULTIPLE SCLEROSIS
GEORGE JELINEK — EDWIN LAM

OVERCOMING MULTIPLE SCLEROSIS
AN EVIDENCE-BASED GUIDE TO RECOVERY
PROFESSOR GEORGE JELINEK

OVERCOMING MULTIPLE SCLEROSIS





Modifiable lifestyle factor - smoking



- Smoking increases chance of developing MS (Hawkes, *Mult Scler*, 2007)
- Many studies suggest a clear role for smoking in disease progression (Healy et al. *Arch of Neurol*, 2009; Pittas, et al. *J of Neurol*, 2009)
- Smokers are more likely to have progressive disease, and to progress at an earlier age (Sundstrom et al. *Mult Scler*, 2008)
- Possible neurotoxic or immuno-modulatory effects of smoking (Kalra et al. *J pharmacol exp ther*, 2000; Freeman. *J R Soc Med*, 1988).
- Smoking is linked to an escape-avoidance coping response (Bricker et al. *Nicotine & tob res*, 2011).

Modifiable lifestyle factor - alcohol



- Few studies, no consensus yet
- Moderate alcohol use may have a neuro-protective effect (D'Hooghe, Exp rev neurotherap, 2012)
- A US survey has shown a dose response association for alcohol use and lower disability scores in people with RR and progressive MS (Goodin. Mult Scler. 1999)
- A “U-shaped” pattern of association between alcohol use was seen for disability in MS (Foster et al, J of Neuroimmunol, 2012).
- Benefits of moderate alcohol use in other chronic diseases (Arriola, Heart, 2010)
- Like smoking, hazardous alcohol use is linked to an escape-avoidance coping response (Cooper et al, J abnorm psychol, 1992).



Modifiable lifestyle factor – diet



- Associations between MS risk and diets high in saturated and low in polyunsaturated fats, vegetable protein and dietary fibre (Swank, New Engl J Med 1952; Agranoff, Lancet, 1974; Ghadirian, Int J Epidemiol, 1998; Zhang, Am J Epidemiol 2000)
- “What increases inflammation are hypercaloric Western-style diets, characterized by high salt, animal fat, red meat, sugar-sweetened drinks, fried food, low fiber...” (Ricio, ASN Neuro, 2015)
- Swank’s landmark study: longitudinal follow up of people with MS trialled on a very low saturated fat diet (Lancet 1990)
- RCT of a low fat diet plus fish oil showed relapse rate reduction, physical, and mental health improvements (Weinstock-Guttman, Leukot Essent Fatty Acids 2005)
- “*I propose a new framework for understanding MS as a dysfunction of the metabolism of lipids.*” Corthals, Q Rev Biol, 2011



Modifiable lifestyle factor - omega 3 supplements and fish consumption



- Omega 3 fatty acids have neuroprotective properties (Das, Nutrition, 2003; Zhang et al. Front Biosci 2011)
- Fish and omega 3 fatty acid consumption play a role in disease development and progression (Jelinek, Qual Prim Care, 2009).
- High doses of omega-3 modulated the immune response in people with MS (Gallai, J Neuroimmunol, 1995)
- More frequent fish consumption slows progression to disability (D'Hooghe et al, Eur J Neurol 2012)
- Intervention studies have not produced uniform results.



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Modifiable lifestyle factor - sunlight & vit



- Association of decreasing latitude (Simpson, J Neurol Neurosurg Psych 2011), recalled time in the sun during childhood, and solar skin damage relate inversely to incidence of MS (van der Mei, BMJ, 2003)
- Few studies about associations between latitude and disease course
- Strong seasonal variation in relapses: peaks in spring and troughs in autumn (Spelman, Anal Neurol 2014)
- Trials with vitamin D suggest a benefit: reduced conversion of optic neuritis to MS, and fewer lesions (Derakhshandi, Acta Neurol Belg 2013; Soilu-Hanninen, J Neurol Neurosurg Psychiatry 2012)
- Sun exposure and vitamin D supplementation have immunomodulatory effects (Pierrot-Deseilligny, Ther Adv Neurol Disord 2013)
- “Vitamin D supplementation should be standard of care for people with MS” (Pierrot-Deseilligny, Ther Adv Neurol Disord 2012)



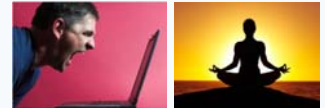
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Modifiable lifestyle factor – physical activity

- People with MS participate less in PA, disability and symptoms are barriers (McCabe 2002)
- Increased PA is associated with healthier BMI, fewer comorbidities, and better physical health overall in MS (Marrie 2010, Gallien 2007)
- PA has a disease-modifying effect (Dalgas, Ther Adv Neurol Disord 2012)
- PA may have beneficial effects through changes in anti-inflammatory and neurotropic factors (Golzari, Int Immunopharmacol 2010; Bansal, Mult Scler 2013; White, Sports Med 2008)
- Meta-analysis shows the effect of PA on QOL superior to medication (Kuspinar, Mult Scler 2012)
- Benefits could be mediated through improvements in social participation, fatigue, mood, self-efficacy, perceived stress and/or body functions (Motl, 2012; 2009; Suh 2012; Stuifbergen 2006)
- Fatigue is positively affected by PA (Andreasen, Mult Scler 2011)



Modifiable lifestyle factor – stress



- 85% of MS exacerbations associated with stressful life events (Ackerman, *Psychosom Med*, 2002)
- Moderate stressors associated with new brain lesions 4-8 weeks after (Mohr, *Neurology*, 2000)
- Meditation is associated with stress reduction, decreased maladaptive coping strategies, and increased resilience in MS (Senders, *J Evid-B Complem and Altern Med*, 2014)
- Mindfulness based RCT results in improved QoL, decreased depression, anxiety, and fatigue up to six months after (Grossman, *Neurology*, 2010).
- No known effects of meditation on disability or relapse rate



HOLISM study - aims

Explore associations between MS outcome measures and modifiable lifestyle factors

- | | |
|--------------------|----------------------------|
| 1. Disability | 1. Smoking |
| 2. Relapse rate | 2. Alcohol |
| 3. Quality of life | 3. Diet |
| 4. Depression | 4. Omega 3 supplementation |
| 5. Fatigue | 5. Vitamin D and sunlight |
| | 6. Exercise |
| | 7. Meditation |

- In a large sample of people with MS internationally



HOLISM study - methods

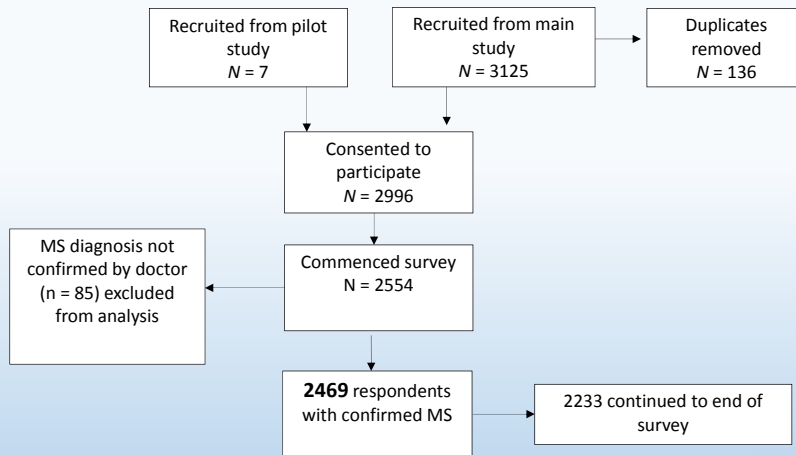
Recruitment through the internet



Variable	Instrument	Nr items	Authors
Disability	Patient Determined Disease Steps (PDDS)	1	Hohol et al. 1995
Comorbidities	Self-Administered Comorbidity Questionnaire (SCQ)	13	Sangha et al. 2003
Health-related quality of life	Multiple Sclerosis Quality of Life-54 (MSQOL-54)	54	Vickrey et al. 1995
Fatigue	Fatigue Severity Scale (FSS)	9	Krupp et al. 1999
Depression	Patient Health Questionnaire Short Version (PHQ-2)	2	Kroenke et al. 2003
Dietary habits	Diet Habits Questionnaire (DHQ), modified	20	McKellar et al. 2008
Physical activity	International Physical Activity Questionnaire (IPAQ)	7	Craig et al. 2003
Social support	Single Item Measure of Social Support (SIMSS)	1	Blake & McKay 1986
Demographics, relapse rate, vitamin D, sunlight, medication use, smoking, alcohol, omega-3, stress management	Researcher devised	56	



HOLISM study - methods



HOLISM study - demographics

		HOLISM	NARCOMS*	MSBase*
Country of residence	N			
United States	807			
Australia	628			
United Kingdom	417			
New Zealand	210			
Canada	105			
52 other countries	301			
		Female (%)	74.9	71.5
		Age at diagnosis (years)	36.9 (mean)	32.2 (mean)
		Age at symptom onset (years)	32.4 (mean)	Data not provided
		Age at enrolment (years)	42.8 (mean)	42.7 (mean)
		Disease duration at enrolment (years)	Data not provided	10.4 (mean)

* Substantially drug company-funded

Type of MS	%
Relapsing-remitting	61.0
Primary progressive	7.5
Secondary progressive	11.7
Progressive relapsing	1.9
Benign	4.1
Unsure/ other	13.9

32.1% working full time, 23.4% retired due to medical reasons/disability

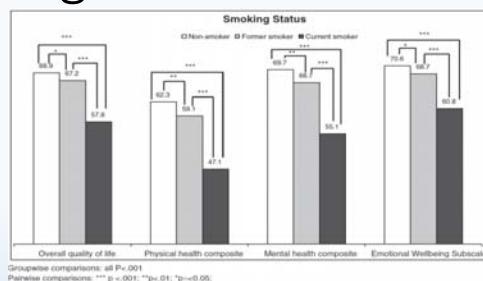
61.1% married, 66.7% one or more biological children

58.7% holds Bachelor's degree or higher

Mean self-reported relapse rate 1.09 (last 12 months)



HOLISM study results - smoking



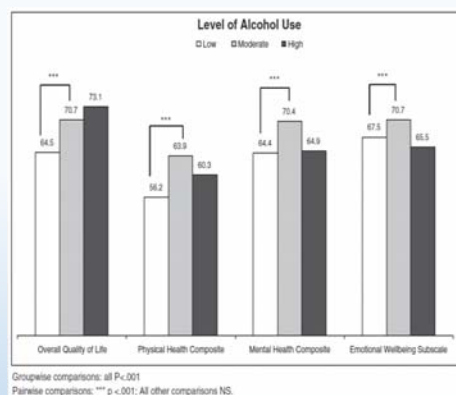
- Consistent with findings for general population (Heikkinen Nicotine Tob Res 2008)
- Never smokers had the lowest odds for depression, with increasing odds for former smokers, and greatest odds for current smokers
- Smoking was associated with higher likelihood of gait or cane disability
- Smoking status did not affect relapse rate

Weiland TJ, Hadgkiss EJ, et al *J Neurol Sci* 2014



HOLISM study results - alcohol

- Moderate alcohol consumption associated with better quality of life
- Low alcohol use was associated higher disability while moderate alcohol use was associated with lower disability
- Moderate alcohol intake had significantly lower odds of screening positive for depression
- Very few with high alcohol use
- No association with relapse rate



Taylor KL, Hadgkiss EJ, et al. *BMC Psychiatry* 2014



HOLISM study results - diet



- Healthy fruit and vegetable subscore, and moderate or healthy fat subscore significantly predicted quality of life scores
- Low/no disability was associated with healthy fruit and vegetable subscore and healthy fat subscore, and not consuming meat or dairy.
- Moderate and high disability was associated with poor fruit and vegetable score, poor or moderate fat score, and meat and dairy consumption (fish excluded)
- There was a clear dose-response effect for increasingly poor diet being associated with greater odds of having a higher disability, of screening positive for depression, and clinical fatigue.
- Better diet was associated with a small improvement in relapse rate

Jelinek GA, Hadgkiss EJ. *Int J Neurosci* 2013



HOLISM study results – omega 3 supplements and fish consumption



- Consuming fish 3 or more times weekly and taking flaxseed oil or fish oil increased the odds of a lower level of disability (controlled for gender and age)
- All QOL domains were significantly better for those taking omega 3 supplements consuming fish more frequently
- Consuming fish was associated with reduction in relapse rate in a dose response manner
- No effect of taking fish oil, whereas flaxseed oil supplementation was associated with a relapse rate reduction and decreased odds of clinical fatigue
- Omega 3s supplementation was associated with reduced odds for depression (more so with flaxseed oil)
- There was a dose-response effect for frequency of fish consumption on the odds of depression

Jelinek GA, Hadgkiss EJ. *Int J Neurosci* 2013



HOLISM study results – sunlight and vitamin



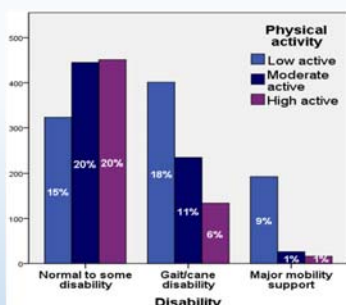
- Increase of latitude by one degree (further away from the equator) associated with increased odds of being in a moderate or high disability category
- Vitamin D supplementation associated with better quality of life outcomes, but latitude or intentional sun exposure was not
- Vitamin D supplements associated with a third lower annualised relapse rate, but latitude or intentional sun exposure was not
- Data suggest a complex relationship between latitude, sun exposure and vitamin D supplementation, and the variables controlled for; exercise and frequency of fish consumption which are likely to affect both serum vitamin D levels and the outcome variables
- Vitamin D supplement was associated with lower odds of screening positive for depression and clinical fatigue, taking >5,000 IU daily was associated with the greatest odds.

Jelinek G, Marck CH, et al. *Submitted*



HOLISM study results – exercise

- Regression analyses controlling for level of disability, age and gender showed that increased exercise predicted better quality of life



Estimated marginal means for health related quality of life scores

Domain	Low active	Moderate active	High active	Change from low-high
Energy	35.9	44.5	49.8	38.7%
Physical health	47.7	56.0	59.9	25.6%
Social function	57.8	66.1	68.4	18.3%
Overall QOL	58.5	64.5	67.7	15.7%
Mental health	60.6	67.0	68.8	13.5%

*Controlled for age, gender and level of disability

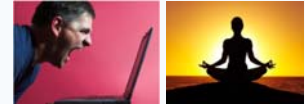
Cross-sectional data cannot disentangle strong association with disability

- A dose-response effect with increasing levels of exercise associated with lower odds of screening positive for depression, and of being clinically fatigued
- No association with relapse rate

Marck CH, Hadgkiss EJ, et al. *BMC Neurology* 2014
Weiland TJ, Jelinek GA, et al. *PLoS ONE* 2015



HOLISM study results - meditation



- Frequency of meditation associated with disability, with those who were more disabled meditating more frequently!
- Logistic regression controlling for gender, age, and education showed those who meditated once or more per week had half the odds for depression
- Higher QoL for those meditating
- No association with relapse rate or fatigue
- Those who meditated once or more per week had lower odds of screening positive for depression

Levin A, Hadgkiss EJ, et al. Behavioural Neurology 2014



HOLISM study – integrative overview

Variable	Not smoking	Moderate alcohol use	Healthy diet	Omega 3 supplementation	Sun exposure and vit D supplementation	Moderate to high physical activity levels	Frequent meditation
Disability	↓	↓	↓	↓		↓	↑
Quality of life	↑	↑	↑	↑		↑	↑
Relapse rate				↓	↓		
Fatigue			↓	↓	↓	↓	
Depression	↓	↓	↓	↓	↓	↓	↓

Regression models included demographics and all modifiable lifestyle factors, medication use and number of comorbidities



HOLISM study - conclusion

Limitations:

- Self-reported
- Cross-sectional (can't infer causality)
- Younger, more female and high educated

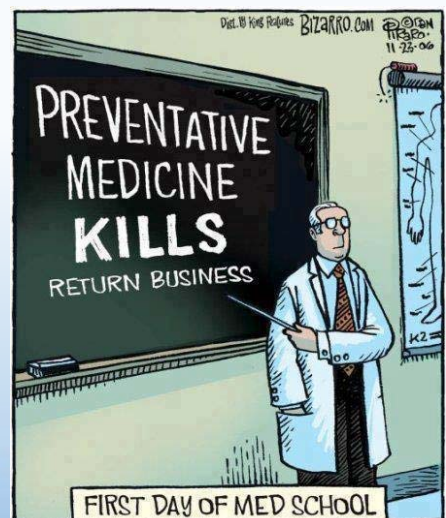
Strengths:

- Many with ultra healthy lifestyle
- Large sample
- International sample



HOLISM study - future directions

- Longitudinal data collection will show how changes in lifestyle factors will correlate to changes in health outcomes
- More clinical trials are needed to elucidate the effects of some modifiable lifestyle factors and medications on outcomes such as relapse rate, long term disability, change in type of MS, depression, fatigue, QoL and comorbidities.
- Lifestyle change is becoming mainstream in diabetes and cardiovascular disease care, why not in MS?!



STOPMS retreat study - background

“As both RRMS and PPMS are inflammatory diseases, they can be influenced by proinflammatory or anti-inflammatory dietary habits and lifestyle through their action on cell metabolism and gut microbiota.” (Ricio 2015)

Lifestyle intervention program providing evidence based lifestyle advice

- One week live-in retreat including all meals
- Fee covers expenses, not-for-profit
- Follow up at 1, 3, 5 and 10 years



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STOPMS retreat study - program

Smoking cessation

Diet and supplements:

- A plant-based wholefood diet plus seafood, with no saturated fat, as far as is practical
- Omega-3 fatty acid supplements: 20+mls a day of flaxseed oil

Exercise:

- 30 minutes around five times a week, preferably outdoors

Vitamin D:

- Sunlight 15 minutes daily three to five times a week, as close to all over as is practical
- Vitamin D3 supplement of 5000-10,000 IU daily
- Aim to keep blood level of vitamin D between 150-225nmol/l

Meditation:

- 30 minutes daily

Alcohol:

- Moderate use is ok
- Avoid heavy use



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STOPMS retreat study - methods

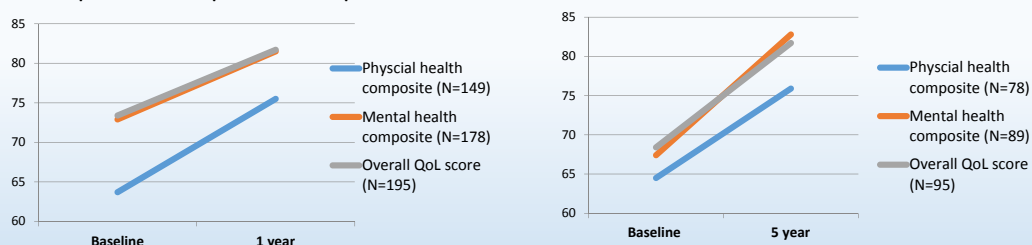
- Participants completed baseline surveys before retreat
- Online or paper survey is sent out at 1, 5 and 10 years
- Until 2012 only quality of life was assessed
- Since 2012 comprehensive survey assessing QoL, disability, relapse rate and engagement with the program
- Ongoing data collection and analyses



STOPMS retreat study - results

- Quality of life improvements at 1 and 5 years

Comparisons all $p < .001$ compared to baseline



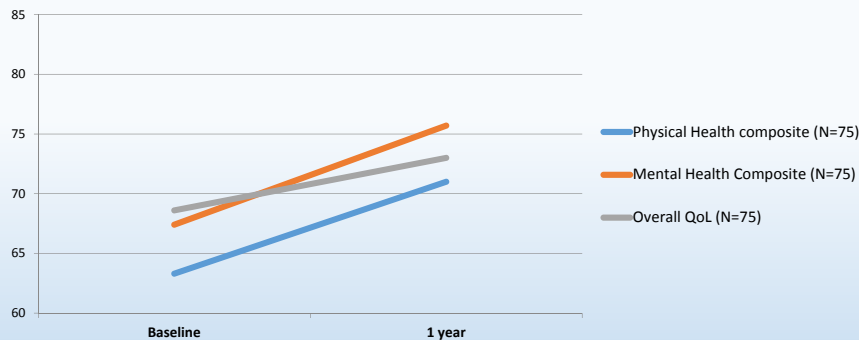
Approx 10% of people in the HOLISM study also participated in the STOPMS study

- Retreat attendees had higher QoL scores, were significantly less likely to have fatigue and depression (while having a longer MS duration)



STOPMS retreat study – preliminary 1 yr results

- 82% had better physical health scores, 74% had better mental health scores



- Stable disability as measured by PDDS (2.14 to 2.16, $p=.741$, $N=71$)
- MSIS-20 showed a trend towards a decrease in disability (33.3 to 31.7 ($p=.06$, $N=68$))
- Reduction in 12 month relapse rate (2.1 to 1.3 ($p<.001$, $N=58$))



STOPMS retreat study – conclusion

- Lifestyle intervention shows clinically significant improvements in QoL over time
- Marrie (2013) found no change in mental health score and a statistically (but not clinically) significant decline in physical health score over 5 years
- Solari found that health status declined over a 5-year period, with worsening in both general health and physical function. In contrast, social function, mental health, and health distress improved.
- McCabe (2009) found improvement in global HRQOL but no change in physical or psychological HRQOL over a 2-year period
- Usually disability declines in MS over time
- Preliminary results show there may be improvements in relapse rate and a trend towards improving disability, but further data collection will be required



Future directions

- 3, 5 and 10 year follow up of STOPMS study
- Longitudinal follow up
- Associations between outcome measures and adherence to healthy lifestyle
- Refine the lifestyle intervention so that it can be delivered as adjunct to current MS management
- Randomized controlled trials
- Clinician measured and patient reported outcomes



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- All HOLISM and STOPMS participants



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