Journey to Optimised Health: Longevity and the future of personalisation of complementary medicine

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Dr Brad McEwen PhD
Head of Products, Trends, and Innovation
Complementary Medicines Group

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#2022CMAConference

OUR 50 YEAR JOURNEY TO HEALTH

CMA 23RD ANNUAL CONFERENCE

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We would like to acknowledge the Gadigal of the Eora Nation, the traditional custodians of the land and waters upon which we stand.
We pay respect to the Elders both past, present, and emerging.

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- The future of optimised health through personalised complementary medicine
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- Trending categories
- Trending ingredients
- Review and final comments

Topic Outline

- The last 50 years have seen significant advances in complementary medicine. Australia has been leading the way with the education and research of complementary medicines, along with the highest standards of complementary medicine products worldwide.
- The next exciting stage of advancement is personalised complementary medicine.
- Life expectancy has substantially increased over the last century from age 55 for people born in the early 1900s to age 80 or more for people born after 2010.
- Although living a longer fuller life, a drawback of increased lifespan is the increased years of living in ill health with chronic diseases, such as cardiovascular disease, metabolic conditions (e.g., diabetes), musculoskeletal conditions, cognitive decline and dementia, cerebrovascular disease, respiratory diseases, and increases in mental health conditions.
- There is significant evidence of herbal medicines, vitamins, minerals, diet, and lifestyle medicine in the prevention and management of chronic diseases.

Topic Outline

- Personalised complementary medicine customises health care to an individual and their needs.
- It tailors and adapts medicines to achieve the best outcome for individuals, rather than treating people with a ‘one size fits all’ approach.
- The customised application of personalised complementary medicine is expected to result in better overall health outcomes.
- Diagnostic testing methods have also enhanced the way personalised complementary medicine benefits individualised health care outcomes.

- This presentation highlights the journey and future of optimised health through personalised complementary medicine technology, diagnostic tests, innovative products, dosage forms, and trending ingredients.

Complementary Medicines Group (CMG)

- Complementary Medicines Group (CMG) was born out of the desire to service the complementary medicines industry with the necessary products and services needed all in the one place.
- We are the conduit for innovation, by bringing new concepts and technology to sponsors of complementary medicines in Australia and take the hassle out of the management and sourcing of products and services.
- At CMG, we are committed to making your life easier by offering a single point of contact for a wide range of products and services designed to help you to successfully get your products to your customers.
- CMG has the expertise to make you continue to stand out from the crowd.
- 12 years of excellence

About Dr Brad McEwen

Dr Brad McEwen PhD is a leader in preventive and personalised health, particularly in the area of cardiometabolic health and mental and cognitive health. He is an award-winning naturopath, nutritionist, herbalist, educator, researcher, and mentor. Dr Brad has over 23 years of clinical experience and over 18 years' experience in education and presenting on health. He has a PhD from University of Sydney, Master of Health Science (Human Nutrition) and Master of Public Health from Deakin University, along with qualifications in Naturopathy, Nutrition, Herbal Medicine, and Sports Medicine. He is Head of Products, Trends, and Innovation at CMG.

Dr Brad has a passion for education and research of complementary medicine. He has numerous articles published in peer-reviewed journals. He is an advocate for optimum health. His research interests include the effects of diet, nutrition, and lifestyle medicine on cardiovascular disease, cardiometabolic syndrome, depression, anxiety, polycystic ovary syndrome, endometriosis, cognition, stress, type 2 diabetes, chronic disease, and public health.

Dr Brad McEwen has a special interest in increasing public health, increasing and improving access to health services, overall chronic disease prevention, increasing access to nutritional foods and information for all schools and universities, and enhancing the environment for future generations.

During his career, Dr Brad has received numerous national and international awards, including the Eberhard F. Mammen Young Investigator Award (an international award in thrombosis and haemostasis), Excellence in Practice Lecturer Researcher of the Year award, and the Dorothy Hall Memorial Award for Practitioner Excellence (an award for the advancement of natural medicine in Australia). Dr Brad has been a multiple finalist for Practitioner of the Year, Researcher of the Year, and Educator/Lecturer of the Year.

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The journey of health

Very, very, very briefly…

Along time ago in 1972…

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Australian population
1972: 13,177,000
2022: 25,890,773
World population
1972: 3.837 billion
2022: 8.001 billion

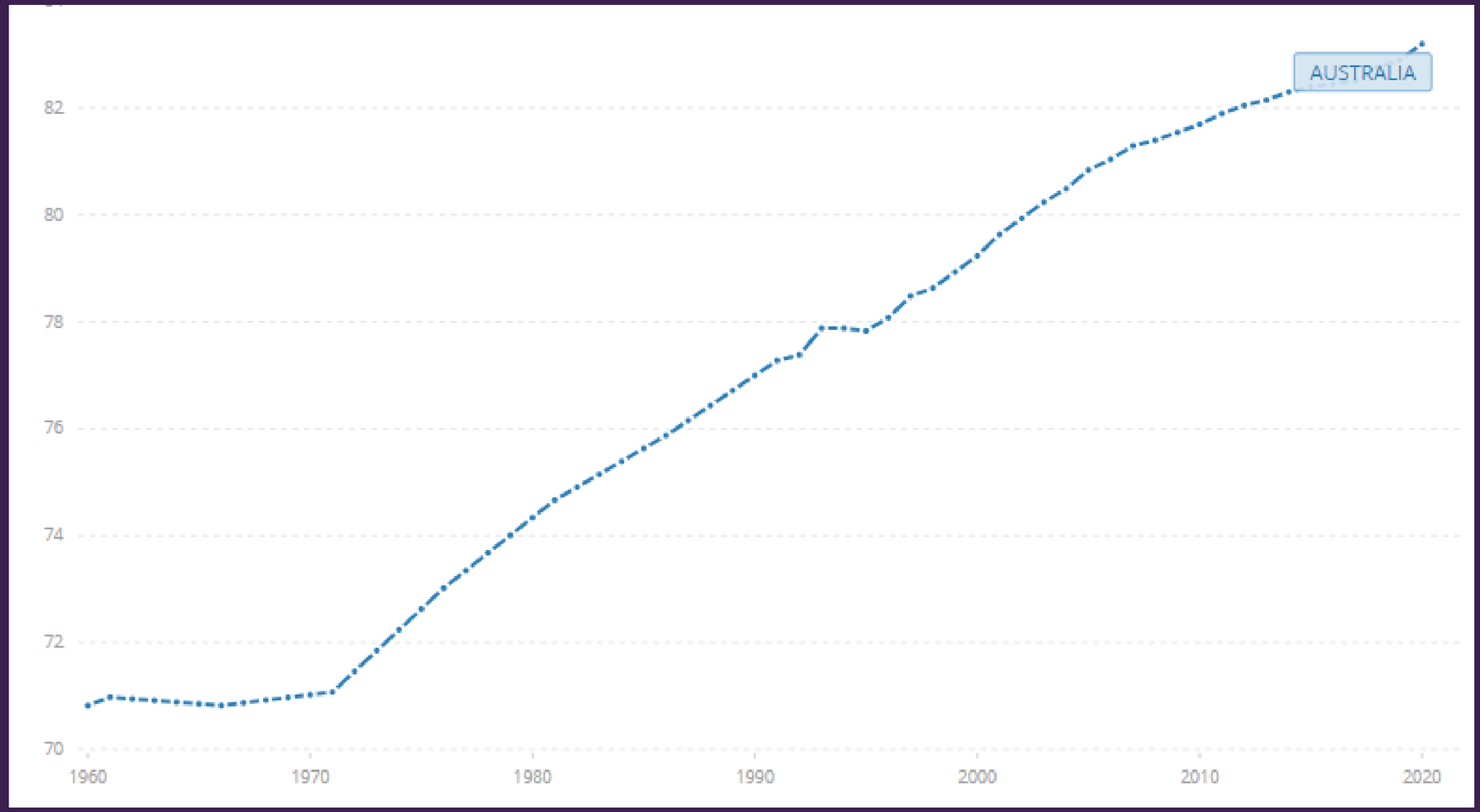
1972 World

- From early March, a widespread influenza epidemic developed throughout Republic of Korea
- Outbreak of smallpox in Yugoslavia and Serbia
- Plague in Khmer Republic close to the border of the Republic of Vietnam. First case since 1957 (WHO 1972)

- In the US, the top 10 causes of death in 1972 were:
    - Diseases of heart
    - Cancers
    - Cerebrovascular disease
    - Accidents
    - Influenza and pneumonia
    - Type 2 Diabetes
    - Mortality in early infancy
    - Cirrhosis of the liver
    - Arteriosclerosis
    - Bronchitis, emphysema

CDC 1976

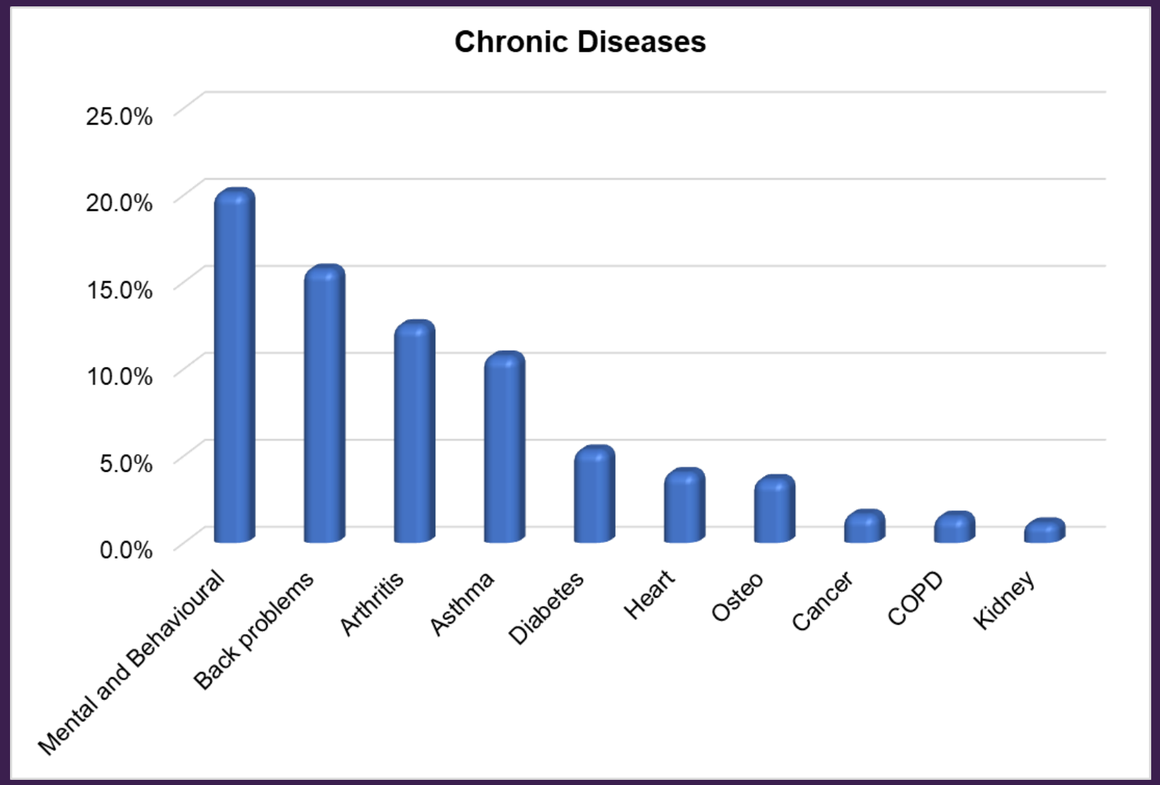
Life expectancy 1960 - 2020



2020s Australia's Health

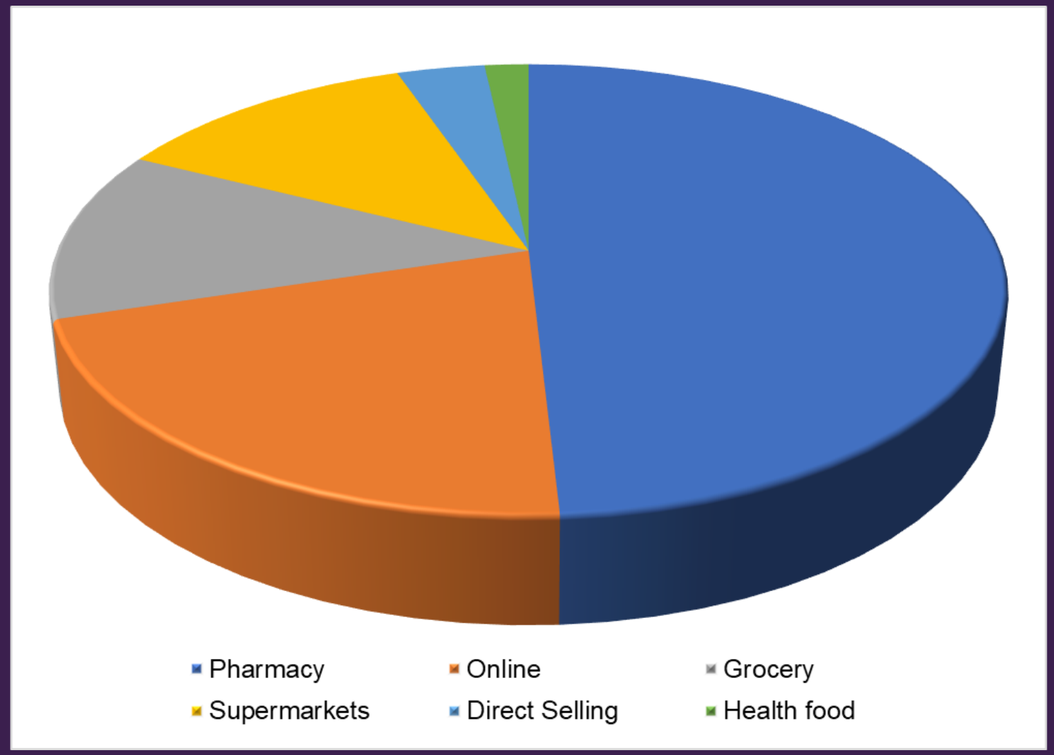
- Australia has one of the highest life expectancies in the world.
- Chronic diseases such as cancer, coronary heart disease and diabetes are the leading cause of ill health and death in Australia.
- Two-thirds of the burden of disease is due to 5 disease groups:
  - cancer
  - cardiovascular diseases
  - mental and substance use disorders
  - musculoskeletal conditions
  - injuries
- Overall, males experienced more burden of disease (53% of total burden) than females (47%).

Sources: Australian Institute of Health and Welfare, ABS



Consumer purchasing

- The complementary medicines industry is a $5.5 billion market nationally.
- 3 out of 4 Australians regularly use a complementary medicine.
- Even during the pandemic period there has been growth in the industry.
- Increase in online sales.
- 7.5% swing away from Pharmacy to Grocery channel.
- Women are more likely to have purchased complementary medicine in the last 12 months (women 83% vs. men 73%).



CMA 2022

The future of optimised health through personalised complementary medicine

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Personalised medicine

Personalised medicine represents an exciting opportunity to improve the future of individualised healthcare for all people.

Vicente AM et al. *J Transl Med*. 2020;18(1):180.

Personalised medicine aims to integrate genomic with biological, physiological, and physical parameters together with environmental information, such as lifestyle, to depict a more comprehensive picture of each individual and improve dedicated preventive and therapeutic interventions.

Bollati V et al. *Med Lav*. 2020;111(6):425-444.

Personalised medicine

One of the benefits of personalised medicine is that it will have a positive impact on disease screening and prevention, by enabling more person-specific estimates of risk, and hence more personalised strategies for screening and risk reduction.

Gaitskell K. *New Bioeth*. 2017;23(1):21-29.

The 4 Ps of personalised medicine:

- Personalised
- Predictive
- Preventive
- Participatory Medicine

Cesuroglu T, et al. *BMJ Open*. 2016;6(7):e010243.

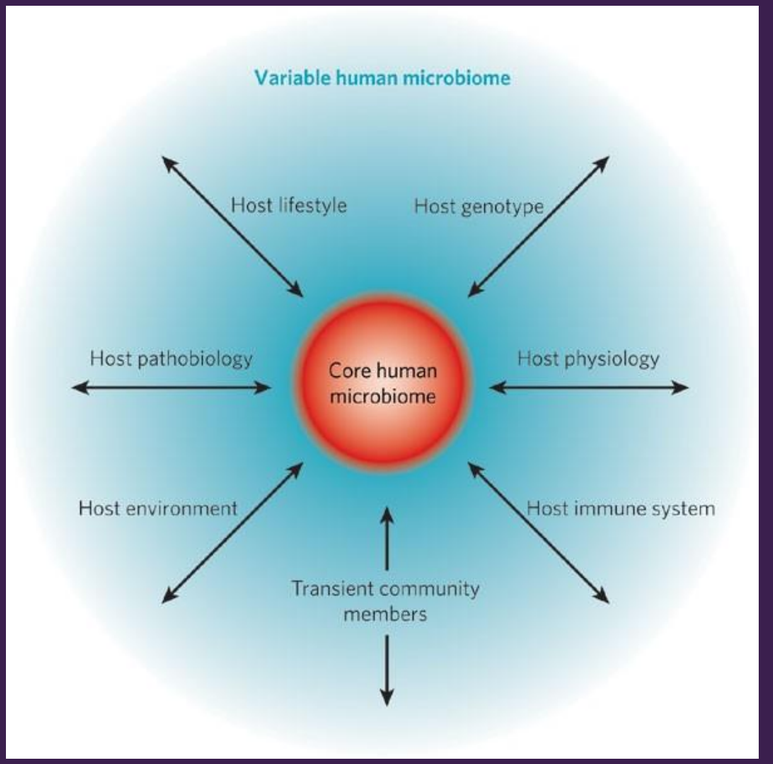
Some Pillars of personalised medicine

- Treat the whole person
- Identify and treat the cause
- Prevention and health promotion in all areas
- Regular hydration
- Nourish with wholefoods
- Support with herbal medicines
- Daily physical activity and regular movement
- Mindfulness
- Sleep and rest

McEwen B. *JATMS*. 2021; 27(4): 200-207.

The Microbiome

- The gastrointestinal (GI) tract is the residence of trillions of microorganisms that include bacteria, archaea, fungi and viruses.
- The collective genomes of whole microbial communities (microbiota) integrate the gut microbiome.
- Up to 100 genera and 1000 distinct bacterial species were identified.
- Gut microbiomes exert permanent pivotal functions by promoting food digestion, xenobiotic metabolism and regulation of innate and adaptive immunological processes.



Belizário JE, Faintuch J. *Exp Suppl*. 2018;109:459-476.

The Microbiome

- Proteins, peptides and metabolites released locally and at distant sites trigger many cell signalling and pathways.
- This intense crosstalk maintains the host-microbial homeostasis.
- Diet, age, stress, and diseases, among other factors, cause increases or decreases in relative abundance and diversity bacterial specie of the gastrointestinal system and other body sites.

Belizário JE, Faintuch J. *Exp Suppl*. 2018;109:459-476.

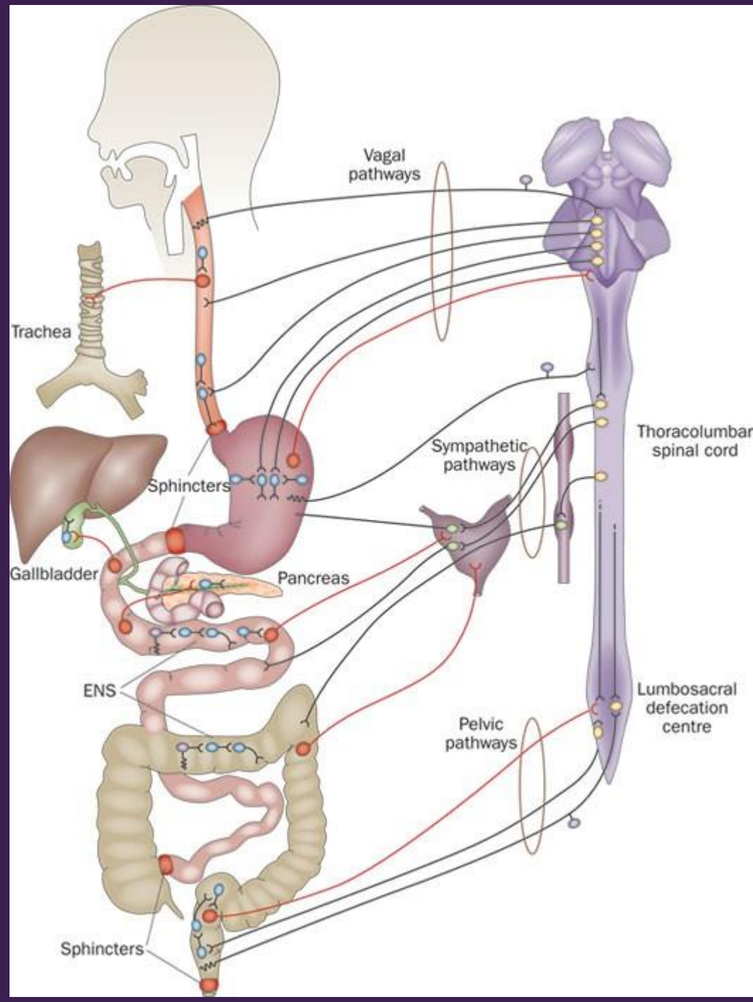
The Human Microbiome Project

- The Human Microbiome Project has been defining criteria for high-quality and comprehensive metagenomic analysis of genetic material recovered directly from distinct sites on the human body to determine the microbial relative abundance of multiple strains and species of different phyla at physiological conditions.

Belizário JE et al. *Mediators Inflamm*. 2018;2018:2037838.

The enteric nervous system

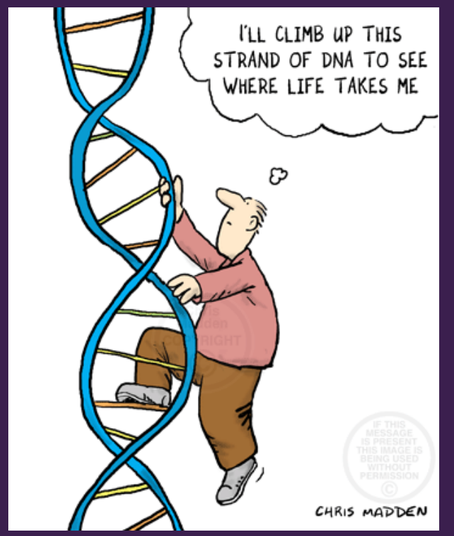
- The gastrointestinal tract possesses its own nervous system known as the enteric nervous system.
- This system communicates with the central nervous system through nerves, such as the vagus, neuromodulators, and neurotransmitters of sympathetic and parasympathetic branches of the autonomic nervous system.
- Bacterial richness and diversity in the gastrointestinal microbiota occupy a central role in normal metabolic and immunological functions of tissues and organs.



Furness JB. *Nature Rev Gastroent & Hepat*. 2012; 9:286-294

Belizário JE et al. *Mediators Inflamm*. 2018;2018:2037838.

The Genome



- The human reference genome has provided the foundation for years of genetic discovery and research.
- The Human Genome Project published its first draft in 2001.
- To better reflect the structure of the genome, focus has shifted to the concept of a pan-genome to capture the complete set of variations present in a species.

Kaye AM, Wasserman WW. *Trends Genet*. 2021 Sep;37(9):807-818.

- The science of the genomes, or “genomics”, initially dedicated to the determination of DNA sequences (the nucleotide order on a given fragment of DNA), has promptly expanded toward a more functional level
  - studying the expression profiles and the roles of both genes and proteins.

Del Giacco L, Cattaneo C. *Methods Mol Biol*. 2012;823:79-88.

Diagnostic tests

The Omega-3 Index

- The Omega-3 Index is the most reliable surrogate marker of Omega-3 status.
- It is the red blood cell (RBC) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) content expressed as a percentage of the total weight of RBC membrane fatty acids.

Harris WS. *Pharmacol Res*. 2007;55(3):217-23.
Harris WS. *Curr Atheroscler Rep*. 2009;11(6):411-7.

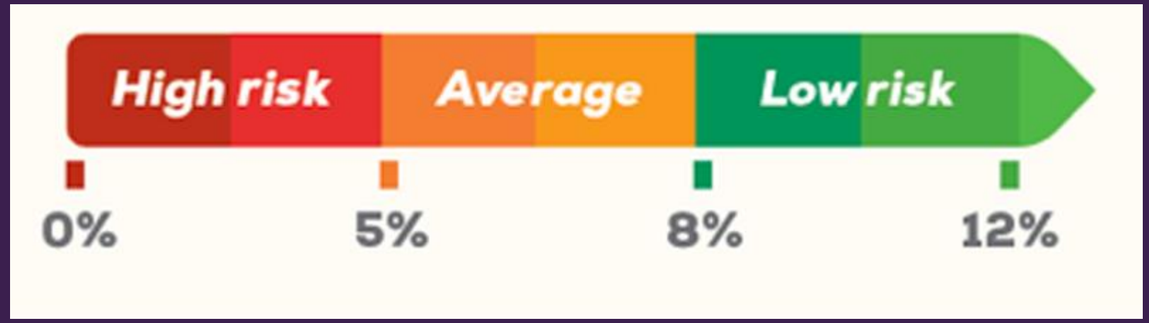
The Omega-3 Index

- Proposed omega-3 index risk zones are (in percentages of erythrocyte FAs):
  - high risk <4%
  - intermediate risk 4-8%
  - low risk >8%

Harris WS. *Am J Clin Nutr*. 2008;87(6):1997S-2002S.

- Optimal levels appear to be 8% or greater.

Harris WS. *Curr Cardiol Rep*. 2010;12(6):503-8.



The Omega-3 Index

- A low Omega-3 Index can be considered a risk factor for sudden cardiac death and for non-fatal cardiovascular events, whereas a high Omega-3 Index can be used as a therapeutic target.

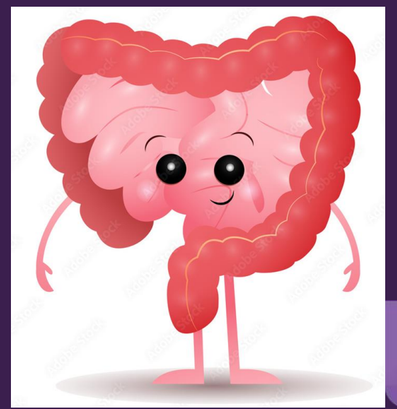
  von Schacky C. *Cell Mol Biol*. 2010;56(1):93-101.

- Low Omega-3 Index has been correlated with:
  - Total mortality
  - Cardiovascular mortality
  - Cardiovascular disease
  - Coronary heart disease
  - Congestive heart failure
  - Myocardial infarction
  - Stroke
  - Blood pressure
  - Post-partum depression
  - Chronic fatigue syndrome

von Schacky C. *Proc Nutr Soc*. 2020; 79(4):381-7.

Gastrointestinal Microbial Assay Plus (GI-MAP)

- The Gastrointestinal Microbial Assay Plus (GI-MAP) is unique in the field of comprehensive stool testing.
- The GI-MAP was designed to assess a patient's microbiome from a single stool sample, with particular attention to microbes that may be disturbing normal microbial balance and may contribute to perturbations in the gastrointestinal flora or illness.



Gastrointestinal Microbial Assay Plus (GI-MAP)

- The panel is a comprehensive collection of microbial targets as well as immune and digestive markers, secretory IgA (sIgA), anti-gliadin sIgA, pancreatic elastase 1, lactoferrin, and occult blood.
- It relies exclusively on quantitative polymerase chain reaction (qPCR) technology to screen for and detect:
  - pathogenic bacteria
  - commensal bacteria
  - opportunistic pathogens
  - fungi
  - viruses
  - parasites
- By targeting the specific DNA of the organisms tested.

MTHFR

- 5,10-Methylenetetrahydrofolate reductase (MTHFR) catalyses the irreversible reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (5-MTHF), the primary form of folate.

McEwen BJ. *Adv Integ Med*. 2016; 3(3): 79-81.

MTHFR

- Altered MTHFR activity is the most common inherited disorder of folate metabolism, where there is an impairment in the ability to process folate effectively.
- C677T and A1298C are the most commonly occurring MTHFR polymorphisms.
  - In patients with C677T polymorphism, homozygotes have 30% enzyme activity, while heterozygotes have 65% of MTHFR enzyme activity.
  - In patients with the MTHFR 1298 CC genotype, there is approximately 60% MTHFR activity.

Advances in Integrative Medicine 3 (2016) 79–81

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Guest Editorial

Methylenetetrahydrofolate reductase (MTHFR): Mythology or polymorphism(ology)?

In recent years MTHFR has been popularised in social media and blogs with various levels of information and potential misinformation. A search on google.com.au using the term "MTHFR" provided 1,330,000 results in 0.40 s [1] With all of this different information being available 24 h per day, all year round, it can be confusing for practitioners and patients to sift through to determine what is scientific, clinical or "hearsay".

5,10-Methylenetetrahydrofolate reductase (MTHFR) catalyses the irreversible reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (5-MTHF) [2,3], the primary form of folate [4]. This conversion produces a methyl donor for the conversion of homocysteine to methionine [5] and S-adenosyl-methionine (SAMe) [6]. This conversion is catalysed by methionine synthase, where Vitamin B12 is a cofactor [5], in the presence of either reduced flavin adenine dinucleotide (FAD) (derived from vitamin B2) or reduced nicotinamide adenine dinucleotide (NAD) (derived from vitamin B3) [2]. Furthermore, homocysteine can be converted to cysteine via the vitamin B6 dependent trans-sulphuration pathway [5]. MTHFR is essential for the metabolism of single-carbon fragments (transmethylation reactions) such as the methylation of DNA and synthesis of purine and pyrimidine, the process of covalent addition of a methyl group to cytosine [7]. SAMe is a universal methyl donor for DNA, RNA, proteins, hormones, neurotransmitters, and membrane lipids [6] Methylation reactions are compromised people with altered MTHFR activity.

Altered MTHFR activity is the most common inherited disorder of folate metabolism, where there is an impairment in the ability to process folate effectively [8,9]. All people have 2 MTHFR genes, one inherited from each parent. Some individuals have a genetic mutation in one or both of their MTHFR genes. Individuals with mutations in one MTHFR gene are called "heterozygous" for the MTHFR mutation. Whereas, a person is "homozygous" for the mutation when mutations are present in both genes [9]. There is also compound heterozygous, where there is one mutated allele on both the 677 and 1298 base position. C677T and A1298C are the most commonly occurring MTHFR polymorphisms. The C677T polymorphism results in a substitution of cytosine (C) to thymine (T) at nucleotide position 677, consequently leading to a substitution of alanine for valine in the N-terminal catalytic domain of the protein [10]. In patients with C677T polymorphism, homozygotes have 30% enzyme activity, while heterozygotes have 65% of MTHFR enzyme activity [11]. The prevalence of C677T homozygote varies between populations, ethnicity and geographic location with the highest prevalence (>20%) found among US Hispanics, Colombians, and Amerindians in Brazil. The prevalence ranges from 8 to 20% in Europe, North America, United Kingdom, Canada, Japan, and Australia [5]. In Black populations, there is less than 2% prevalence of MTHFR C677T. [11]. Furthermore, a Japanese study found a lower frequency of homozygote MTHFR C677T among those over 80 years of age (7%) compared with those aged between 55 and 79 years (14%) and 14–55 years (19%) [5].

The MTHFR A1298C polymorphism results in a substitution of adenosine (A) to cytosine (C) at nucleotide position 1298 (A1298C) leading to a substitution of glutamate to alanine within C-terminal, SAMe regulatory domain of the protein [12]. In patients with the MTHFR 1298 CC genotype, there is approximately 60% MTHFR activity [13]. The prevalence of the homozygote A1298C ranges from 7 to 12% in populations from North America and Europe with a lower prevalence reported in Hispanics (4–5%), Chinese and Asian populations (1–4%) [11]. Studies report an impact of A1298C on plasma homocysteine, with CC homozygotes exhibiting higher plasma concentration of homocysteine [14]. Research suggests that both MTHFR C677T and A1298C polymorphisms influence lower MTHFR enzyme activity [12,13]. Further research is suggested in investigating the prevalence of both MTHFR C677T and A1298C polymorphisms globally.

Research into MTHFR enzyme activity has been conducted since the 1960s [2,3]. An MTHFR polymorphism represents a potential risk factor for numerous diseases, including, but not limited to, non-alcoholic fatty liver disease (synopsis this issue) [15], cardiovascular disease [10,16], coronary artery disease [10], peripheral arterial disease [10,17], hypertension [18], ischaemic or haemorrhagic stroke [5], hyperhomocysteinaemia [8,10], polycystic ovary syndrome [19], neural tube defects, pregnancy complications [20], hypertension in pregnancy [21], birth defects [16], inflammatory bowel disease [22], pain, fatigue, sleeplessness [23], depression, schizophrenia, bipolar disorder [5,11], neurological symptoms [24], osteoporosis, osteopaenia [25], fracture risk [26], migraine [5,23], psoriasis [27], colorectal cancer [28,29], gastric cancer [5,30], and cervical dysplasia [31].

Testing for MTHFR C677T and A1298C polymorphisms is suggested in patients with chronic disease to assist in formulating an optimal dietary and nutritional plan. Methylation is genetically predetermined by genes which influence methylation, such as MTHFR. Methyl groups required for methylation are synthesised within the body or are supplied in the diet, primarily from folate

http://dx.doi.org/10.1016/j.aimed.2017.02.005

McEwen BJ. *Adv Integ Med*. 2016; 3(3): 79-81.

Trending health categories
Trending health ingredients

Trending health categories

- Immune
- Mood/Stress and Anxiety
- Beauty, Hair, Skin, Nails
- Energy
- Sleep
- Cognition, Nootropics, Memory
- Liver and Digestive health
- Men’s health
- Eye health
- Vegan Omega-3 EPA/DHA
- Metabolism
- Blood glucose
- Muscular aches and pains

Trending Ingredients

- Ashwagandha
- Bluenesse Lemon Balm
- Collagen
- Echinacea
- Magnesium
- MenaQ7 (Vitamin K2)
- Nicotinamide riboside
- Passionflower
- Probiotics
- Quatrefolic®
- Rhodiola
- Saffron
- Tocotrienols
- Vegan Omega-3 EPA/DHA
- Vitamin D

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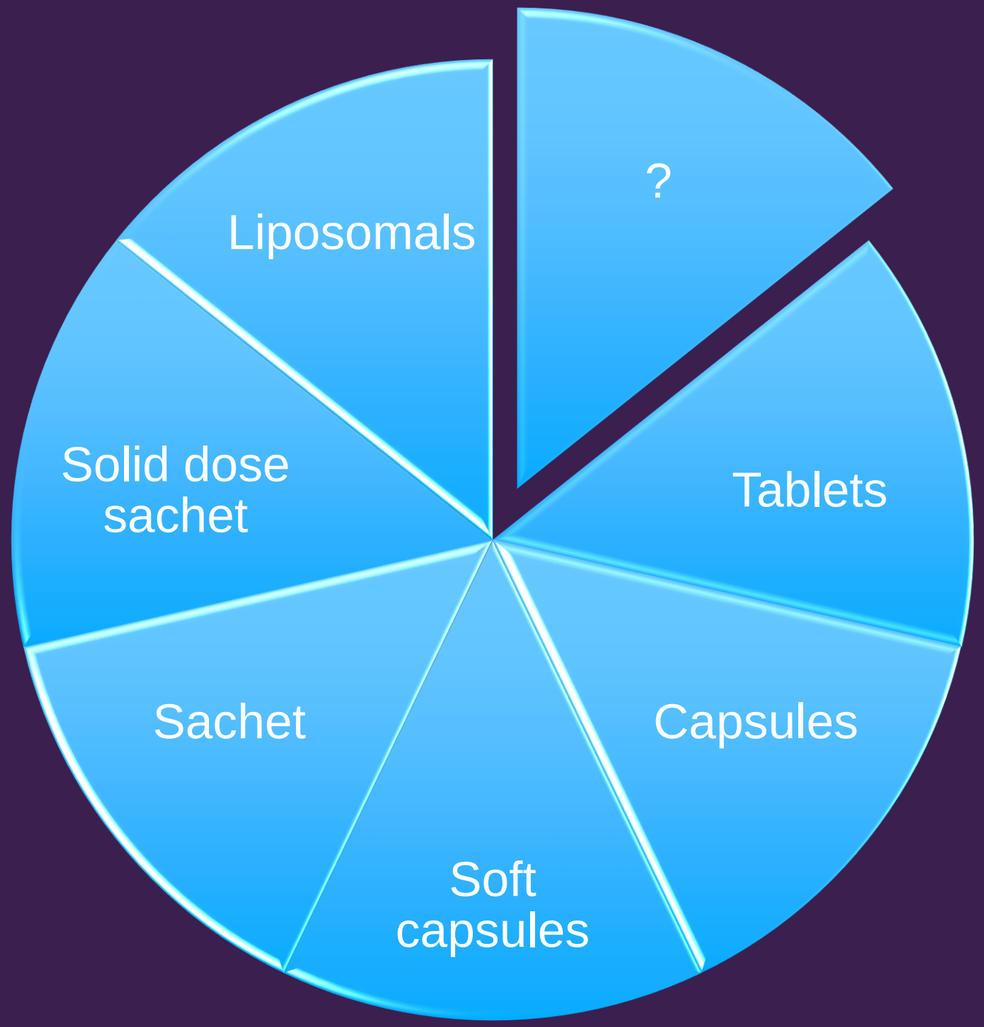
CMG Dosage forms



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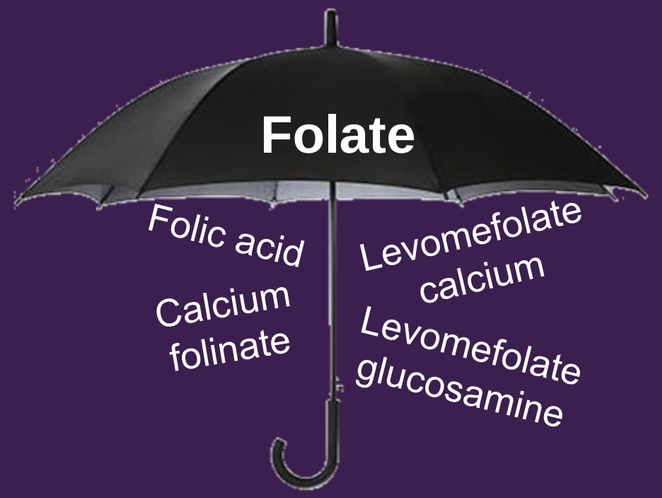
Folate



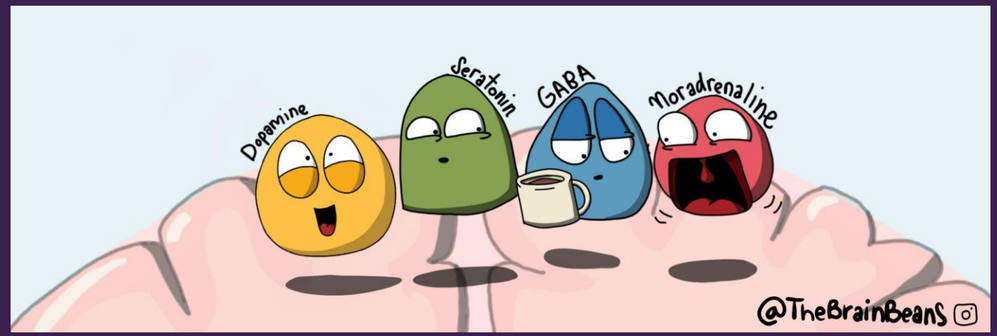
- Folate is an umbrella term for:
  - Folic acid
  - Folinic acid (from calcium folinate)
  - Levomefolic acid (from levomefolate calcium)
  - Quatrefolic®, the fourth-generation folate as Levomefolate glucosamine
- Humans cannot synthesise folate. So, it must be obtained from the diet or in supplemental form

5-MTHF (5-methyltetrahydrofolate)

- 5-MTHF has important advantages over synthetic folic acid:
  - well absorbed even when gastrointestinal pH is altered
  - bioavailability is not affected by metabolic defects
- An essential micronutrient
- A critical cofactor in one-carbon metabolism
- Functions as a methyl donor in many metabolic reactions, including:
  - conversion of homocysteine into methionine
  - biosynthesis of glycine from serine
  - methylation of DNA
  - biosynthesis of DNA precursor molecules

5-MTHF

- Plays a role as cofactors in essential one-carbon pathways donating methyl-groups to:
  - choline phospholipids
  - neurotransmitters
  - proteins
  - amino acids
  - glutathione
  - adrenaline
- Re-methylation of creatine

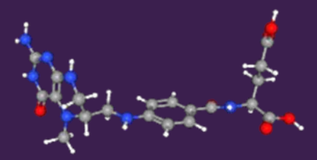


5-MTHF

- Low folate status may be caused by low dietary intake, poor absorption of ingested folate and alteration of folate metabolism due to genetic defects or drug interactions
- Folate deficiency has been linked with an increased risk of:
  - neural tube defects
  - cardiovascular disease
  - anaemia
  - cognitive dysfunction

What is Quatrefolic® (Levomefolate glucosamine)

- Quatrefolic® the innovACTIVE folate
  - The methyltetrahydrofolate (MTHF) glucosamine salt
- Quatrefolic® is the active form of folate
- Readily available for transport and use in human body and tissues



Quatrefolic®

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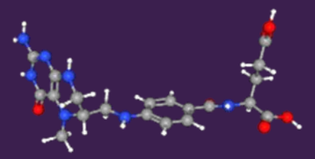
What is Quatrefolic® (Levomefolate glucosamine)

- Keypoints for Quatrefolic®:
  - high water solubility
  - improved bioavailability
  - absorbed mainly in the small intestine by a carrier mediated mechanism (unsaturated carrier)
  - well-established safety
  - not from animal sources, suitable for vegan/vegetarian



Why Quatrefolic® (Levomefolate glucosamine)

- Humans cannot synthesise folate
- Folic acid is inactive and needs to be metabolised to 5-methyltetrahydrofolate (5-MTHF) to become metabolically effective via the enzyme methylenetetrahydrofolate reductase (MTHFR)
- Some people do not metabolise folic acid efficiently
  - This includes people with a MTHFR polymorphism (a difference in DNA sequence)

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In recent years MTHFR has been popularised in social media and blogs with various levels of information and potential misinformation. A search on google.com.au using the term "MTHFR" provided 1,330,000 results in 0.40 s [1] With all of this different information being available 24 h per day, all year round, it can be confusing for practitioners and patients to sift through to determine what is scientific, clinical or "hearsay".

5,10-Methylenetetrahydrofolate reductase (MTHFR) catalyses the irreversible reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (5-MTHF) [2,3], the primary form of folate [4]. This conversion produces a methyl donor for the conversion of homocysteine to methionine [5] and S-adenosyl-methionine (SAMe) [6]. This conversion is catalysed by methionine synthase, where Vitamin B12 is a cofactor [5], in the presence of either reduced flavin adenine dinucleotide (FAD) (derived from vitamin B2) or reduced nicotinamide adenine dinucleotide (NAD) (derived from vitamin B3) [2]. Furthermore, homocysteine can be converted to cysteine via the vitamin B6 dependent trans-sulphuration pathway [5]. MTHFR is essential for the metabolism of single-carbon fragments (transmethylation reactions) such as the methylation of DNA and synthesis of purine and pyrimidine, the process of covalent addition of a methyl group to cytosine [7]. SAMe is a universal methyl donor for DNA, RNA, proteins, hormones, neurotransmitters, and membrane lipids [6] Methylation reactions are compromised people with altered MTHFR activity.

Altered MTHFR activity is the most common inherited disorder of folate metabolism, where there is an impairment in the ability to process folate effectively [8,9]. All people have 2 MTHFR genes, one inherited from each parent. Some individuals have a genetic mutation in one or both of their MTHFR genes. Individuals with mutations in one MTHFR gene are called "heterozygous" for the MTHFR mutation. Whereas, a person is "homozygous" for the mutation when mutations are present in both genes [9]. There is also compound heterozygous, where there is one mutated allele on both the 677 and 1298 base position. C677T and A1298C are the most commonly occurring MTHFR polymorphisms. The C677T polymorphism results in a substitution of cytosine (C) to thymine (T) at nucleotide position 677, consequently leading to a substitution of alanine for valine in the N-terminal catalytic domain of the protein [10]. In patients with C677T polymorphism, homozygotes have 30% enzyme activity, while heterozygotes have 65% of MTHFR enzyme activity [11]. The prevalence of C677T homozygote varies between populations, ethnicity and geographic location with the highest prevalence (>20%) found among US Hispanics, Colombians, and Amerindians in Brazil. The prevalence ranges from 8 to 20% in Europe, North America, United Kingdom, Canada, Japan, and Australia [5]. In Black populations, there is less than 2% prevalence of MTHFR C677T. [11]. Furthermore, a Japanese study found a lower frequency of homozygote MTHFR C677T among those over 80 years of age (7%) compared with those aged between 55 and 79 years (14%) and 14–55 years (19%) [5].

The MTHFR A1298C polymorphism results in a substitution of adenosine (A) to cytosine (C) at nucleotide position 1298 (A1298C) leading to a substitution of glutamate to alanine within C-terminal, SAMe regulatory domain of the protein [12]. In patients with the MTHFR 1298 CC genotype, there is approximately 60% MTHFR activity [13]. The prevalence of the homozygote A1298C ranges from 7 to 12% in populations from North America and Europe with a lower prevalence reported in Hispanics (4–5%), Chinese and Asian populations (1–4%) [11]. Studies report an impact of A1298C on plasma homocysteine, with CC homozygotes exhibiting higher plasma concentration of homocysteine [14]. Research suggests that both MTHFR C677T and A1298C polymorphisms influence lower MTHFR enzyme activity [12,13]. Further research is suggested in investigating the prevalence of both MTHFR C677T and A1298C polymorphisms globally.

Research into MTHFR enzyme activity has been conducted since the 1960s [23]. An MTHFR polymorphism represents a potential risk factor for numerous diseases, including, but not limited to, non-alcoholic fatty liver disease (synopsis this issue) [15], cardiovascular disease [10,16], coronary artery disease [10], peripheral arterial disease [10,17], hypertension [18], ischaemic or haemorrhagic stroke [5], hyperhomocysteinaemia [8,10], polycystic ovary syndrome [19], neural tube defects, pregnancy complications [20], hypertension in pregnancy [21], birth defects [16], inflammatory bowel disease [22], pain, fatigue, sleeplessness [23], depression, schizophrenia, bipolar disorder [5,11], neurological symptoms [24], osteoporosis, osteopaenia [25], fracture risk [26], migraine [5,23], psoriasis [27], colorectal cancer [28,29], gastric cancer [5,30], and cervical dysplasia [31].

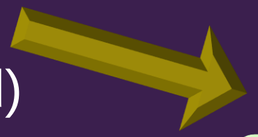
Testing for MTHFR C677T and A1298C polymorphisms is suggested in patients with chronic disease to assist in formulating an optimal dietary and nutritional plan. Methylation is genetically predetermined by genes which influence methylation, such as MTHFR. Methyl groups required for methylation are synthesised within the body or are supplied in the diet, primarily from folate

http://dx.doi.org/10.1016/j.aimed.2017.02.005

McEwen BJ. *Adv Integ Med*. 2016; 3(3): 79-81.

Folate metabolism (flow chart)

Folic acid
(Supplements/Fortified food)



DHF
Dihydrofolate

THF
Tetrahydrofolate

5,10 Methylene
Tetrahydrofolate (THF)

MTHFR

MTHFR polymorphism reduces the metabolism and utilisation at this step

Quatrefolic®

5-Methylene
Tetrahydrofolate (L-Methylfolate [active form])

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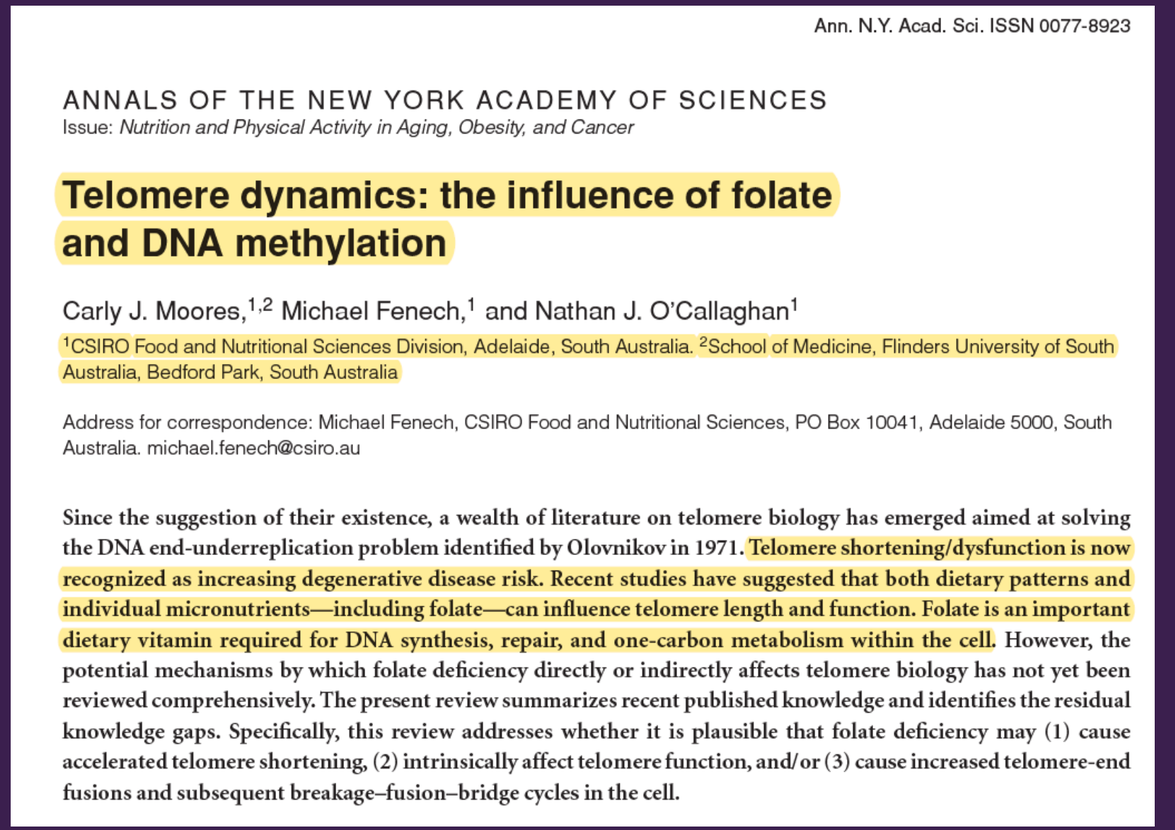
Telomere dynamics: the influence of folate and DNA methylation

- Telomeres are the specific DNA–protein structures found at both ends of each chromosome
- They protect genome from nucleolytic degradation, unnecessary recombination, repair, and interchromosomal fusion.
- Telomeres therefore play a vital role in preserving the information in our genome.
- Telomere length shortens with age.

  Shammas MA. *Curr Opin Clin Nutr Metab Care*. 2011 Jan; 14(1): 28–34.
- Dietary deficiency of micronutrients, including folate, may have an effect on the telomere length and function in humans.
- Both global (genome-wide) and local (gene-specific) DNA methylation patterns are modified by micronutrients such as folate.

  Moores CJ et al. *Ann. N.Y. Acad. Sci*. 2011;1229: 76-88.



Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *Nutrition and Physical Activity in Aging, Obesity, and Cancer*

Telomere dynamics: the influence of folate and DNA methylation

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Since the suggestion of their existence, a wealth of literature on telomere biology has emerged aimed at solving the DNA end-underreplication problem identified by Olovnikov in 1971. Telomere shortening/dysfunction is now recognized as increasing degenerative disease risk. Recent studies have suggested that both dietary patterns and individual micronutrients—including folate—can influence telomere length and function. Folate is an important dietary vitamin required for DNA synthesis, repair, and one-carbon metabolism within the cell. However, the potential mechanisms by which folate deficiency directly or indirectly affects telomere biology has not yet been reviewed comprehensively. The present review summarizes recent published knowledge and identifies the residual knowledge gaps. Specifically, this review addresses whether it is plausible that folate deficiency may (1) cause accelerated telomere shortening, (2) intrinsically affect telomere function, and/or (3) cause increased telomere-end fusions and subsequent breakage–fusion–bridge cycles in the cell.

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Nicotinamide riboside chloride

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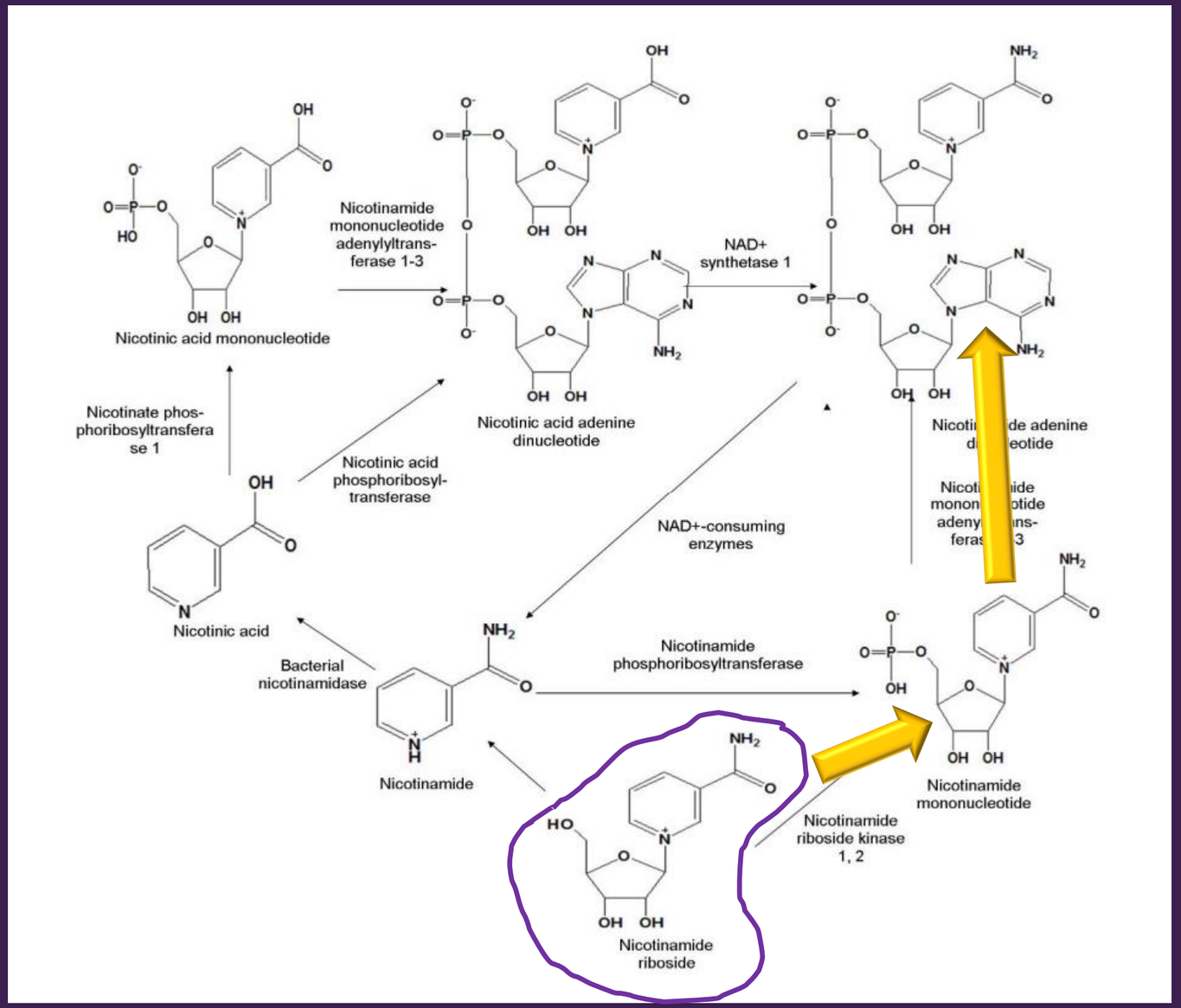
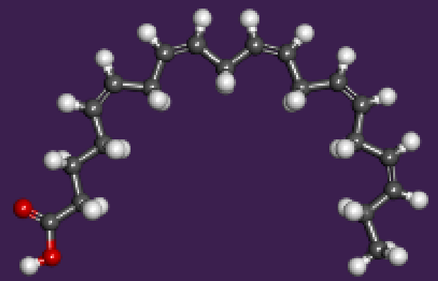
Nicotinamide riboside chloride

- Nicotinamide riboside (NR) is a newly discovered nicotinamide adenine dinucleotide (NAD^+) precursor vitamin
- NAD^+ is a central regulator of metabolism
- Required for fuel oxidation, ATP generation, gluconeogenesis, ketogenesis, haem, lipids, steroid hormones, and detoxification of free radical species
- All tissues produce NAD^+ from nicotinamide or the recently identified NAD^+ precursor, nicotinamide riboside.

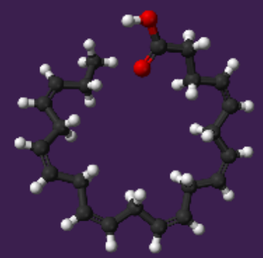
Nicotinamide riboside chloride



Vegan Omega-3 EPA/DHA



EPA (Eicosapentaenoic Acid)



DHA (Docosahexaenoic Acid)

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Vegan Omega-3 EPA/DHA

- 100% Plant-based Microalgae
- Vegan Omega-3 EPA/DHA rather than DHA only
- 100% Vegan Omega-3 ingredient
- Higher concentration = smaller capsule size per dose
- Shift from animal supplement to plant-based
- Concerned about climate action, ocean sustainability, environmental impact, carbon footprint, etc.

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Conclusion

Our industry is amazing
Many opportunities
We are formulating for a brighter future
Onwards and upwards

Thank you

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