Myths, media & busting assumptions

NZ March 2018

A. Prof. Lesley Braun PhD

Group Director Blackmores Institute

A/Prof National Institute of Complementary Medicine (hon)

NICM
THE NATIONAL INSTITUTE OF COMPLEMENTARY MEDICINE

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THE CONVERSATION

Still no good evidence that most complementary medicine works

July 23, 2014 11.25pm AEST

PN Pharmacy News

No good evidence that complementary medicine works: academic 2014

What Is Integrative Medicine?

Experts explore new ways to treat the mind, body, and spirit -- all at the same time.

The Telegraph

Are vitamins and supplements a waste of time? We asked the experts

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The Washington Post

Health & Science

On medication? These supplements can be dangerous, April 2015.

'Dangerous' vitamins and supplements revealed in PBS Frontline, New York Times investigation; Four corners, May 2016

Prevention

15 common supplement ingredients that could make you seriously sick

Published Sept 2, 2016

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Key themes that keep coming up

- Show me the evidence
- People with a good diet won't benefit from supplements
- Risky business – or is it ?
  - Herbs cause drug interactions
  - Herbs cause liver injuries

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Don’t ask, don’t tell, don’t know

PhD Thesis

Surveys at 4 Victorian hospitals with

- Cardiac surgery patients
- General surgical patients
- Hospital surgeons
- Hospital anaesthetists
- Hospital physicians
- Hospital pharmacists

- Major discrepancy between patient and medical doctors views on a range of complementary medicine approaches

- **How did this happen ?**
- **How do opinions form ?**

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How do you form an opinion ?

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Influences

- Opinions of family & friends
- Professional peer-group influence
- Education / training
- Personal experience
- Feedback stories from others
- Media influence

In medicine ..

- Best evidence available
  - Limited by available resources? Ability to use?
  - Limited because there are always gaps & changes
- Less obvious influences
  - Publication bias/censorship
  - Personal *heuristics and biases*

Scott Plous

THE PSYCHOLOGY OF JUDGMENT AND DECISION MAKING

WINNER OF THE
William James
Book Award

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Common heuristics

Assumptions –> known or unknown

Recency effect -> greater importance is given to the information most recently read or experienced

Hindsight bias -> *'I knew it all along' or 'it's obvious'*

Pseudo-opinions -> expressing an opinion about something you know nothing about instead of saying *'I have no opinion'* or *'its not my area of expertise'*

Information neglected –> knowingly or unknowingly

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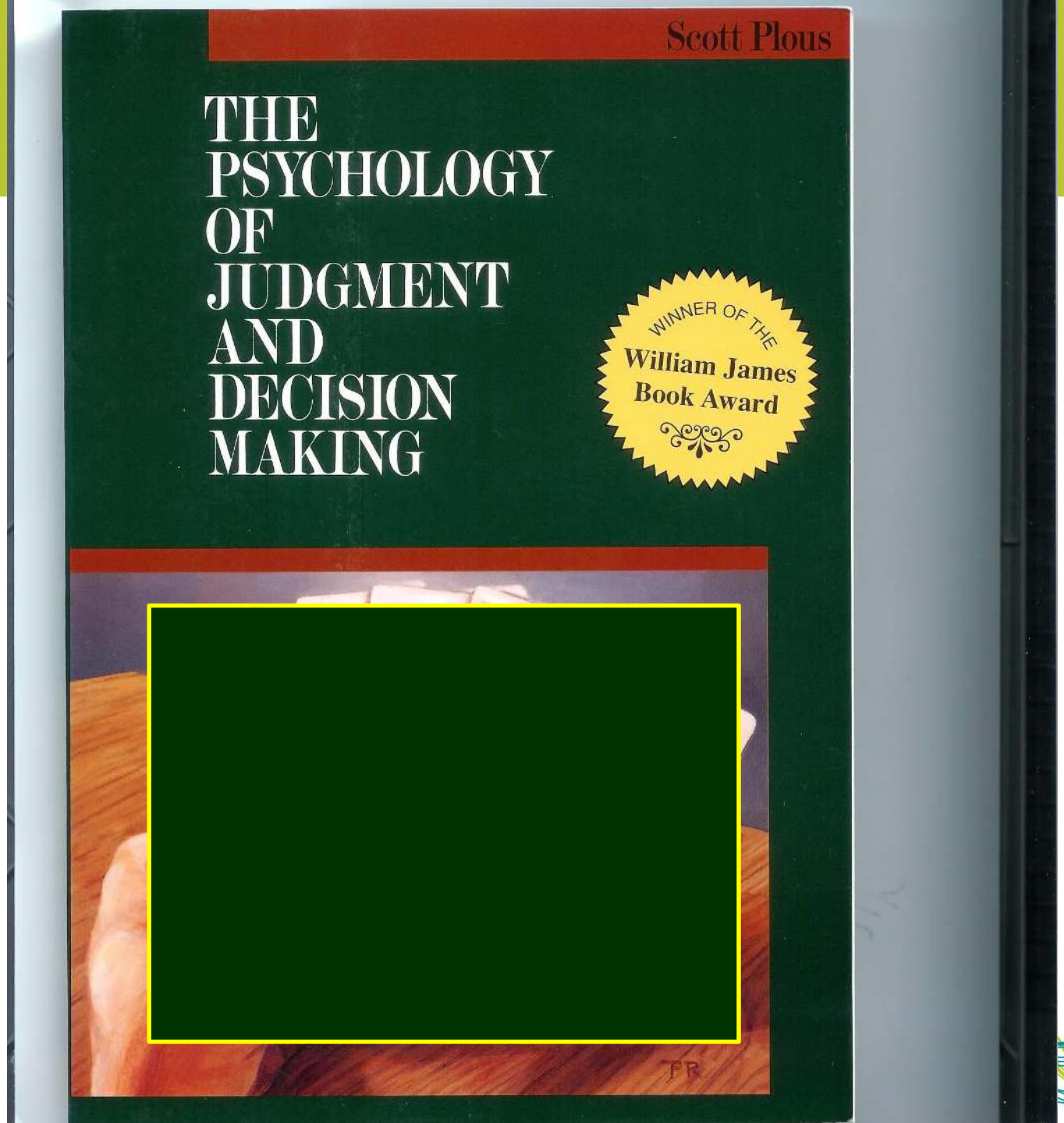
Perceptual denial
Or
Seeing what you expect to see



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Assumption 1. There’s little evidence

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Where does the evidence come from?

1. Traditional evidence
   - Longitudinal : based on careful observation and deduction over generations
     - Eg saffron for depression, kava kava for anxiety, garlic for infection
   - Different cultures have own systems of use
     - eg Chinese medicine, Ayurvedic medicine
2. Clinical practice – patient observation
3. Epidemiological studies – population trends
4. Scientific research
   - in vitro – test tube studies
   - in vivo/preclinical – animal models
   - clinical studies - RCTs

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today tonight today tonight today

Vitamins: tested and rated

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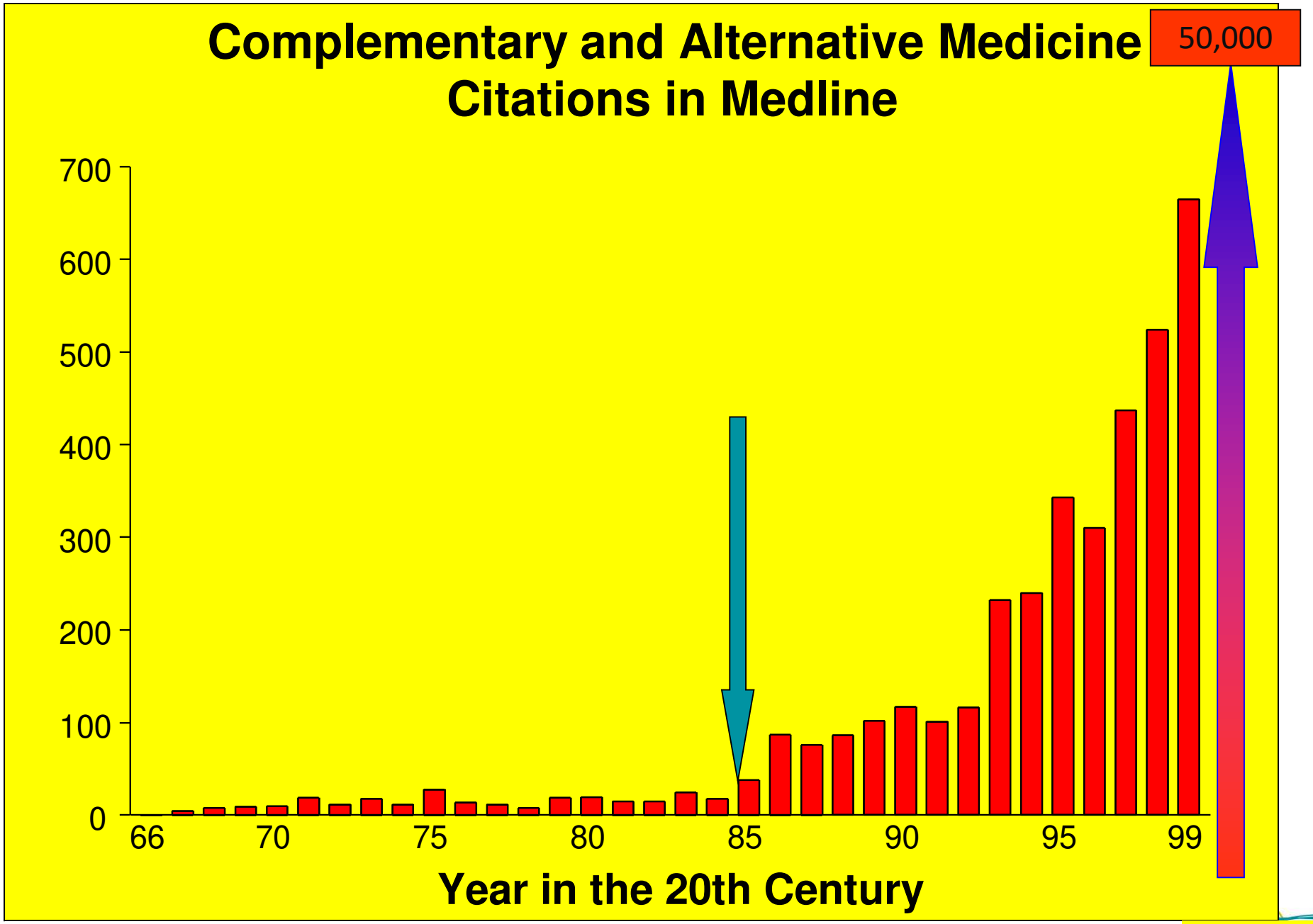

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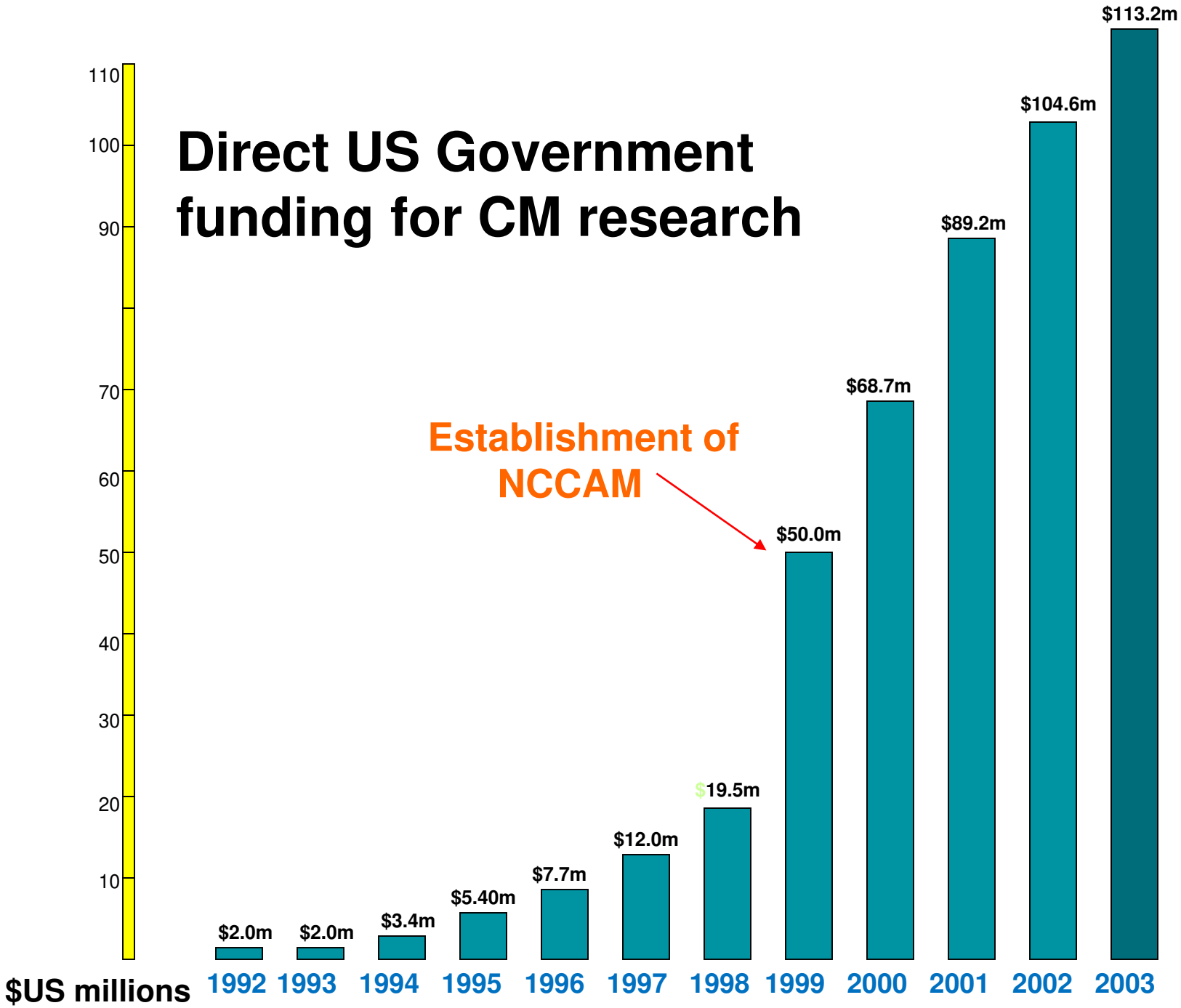
Direct US Government funding for CM research



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Traditional evidence: herbal medicine

- Oldest system of medicine
- Used in every culture
- Currently primary medicine - 60% world
- Eastern tradition - India, China
- Western tradition - traced to Egyptians
- WHO traditional medicine policy encourages continued use, supports agricultural initiatives to increase access

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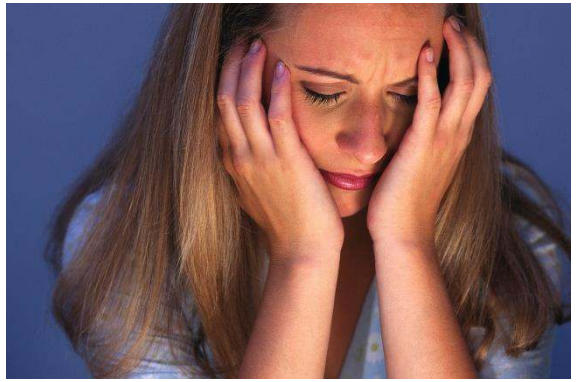
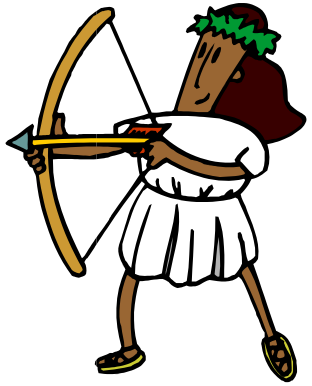


The name ‘hypericum’ was first given by the ancient Greeks to a plant placed above religious figures in order to ‘ward off evil spirits’

St John’s wort used to treat ‘nervous unrest’

The spice saffron used in Persian medicine for improving mood



Kava kava – used in the Pacific islands to welcome people from different tribes, promote co-operation

Valerian used in Europe for last 500+ years to treat ‘nervousness or hysteria’, dyspepsia and flatulence

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Herbs in mental health

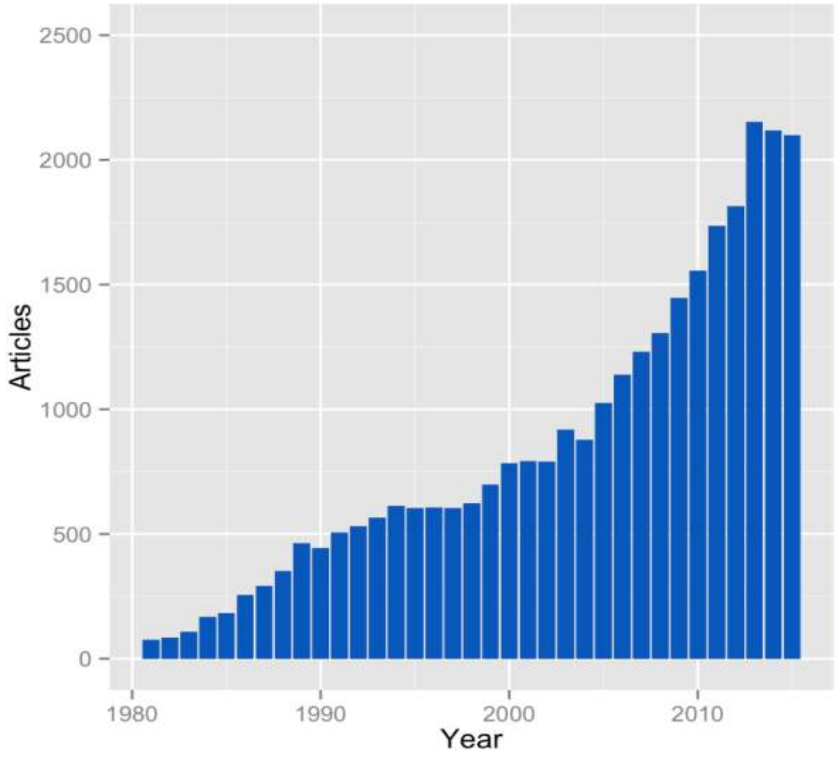
	Suggestive traditional evidence	Mechanisms identified with animal models
Kava kava		Anxiolytic effects & antispasmodic
St John's wort		Anxiolytic, antidepressant , AO
Rose root		Antidepressant
Passiflora		Anxiolytic
Saffron		AO, antidepressant
Black cohosh		AO, anti-inflammatory, selective oestrogen receptor modulator
Lavender		Sedative/hypnotic for methanolic extract
Lemon balm		Antidepressant – GABA increases Anticholinesterase activity
Withania		Reduces chemical and physical response to stress, AO, anti-inflammatory
Valerian		Sedative, hypnotic, anxiolytic, antispasmodic

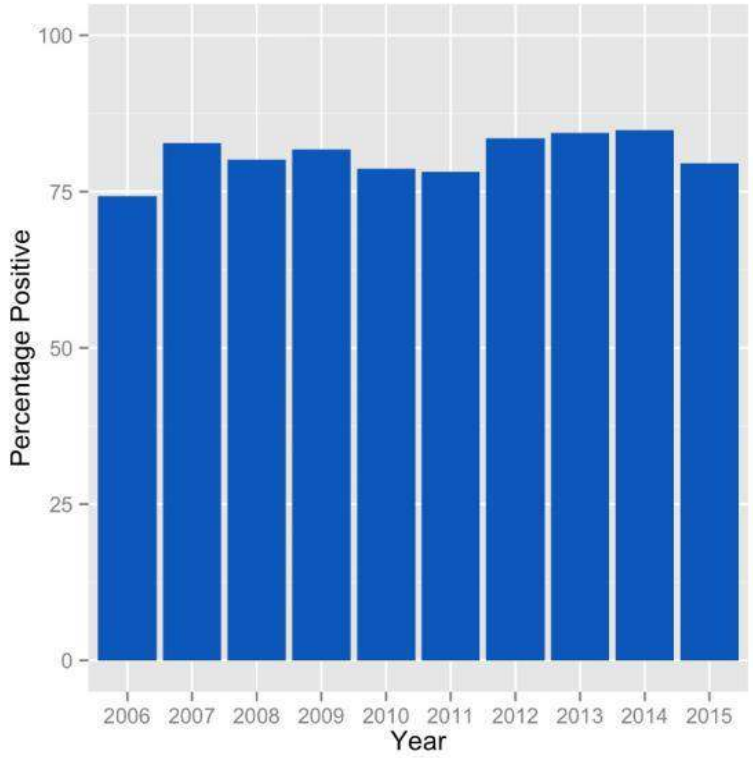
Clinical studies – as per 2015

Herbal medicine	Indication studied	Clinical studies	Summary
Kava kava	Anxiety	Meta-analysis of RCTs	++
St John's wort	Depression	Meta-analysis of RCTs	++
Passiflora*	Anxiety before surgery	2 RCTs	+
Rose root	Depression / insomnia	1 RCT	+
Saffron	Depression	4 RCTs	+
Black cohosh + SJW	Mood in menopausal women	1 RCT	+
Lavender oil – oral (Salexan®)	Mild to moderate anxiety	3 RCTs + 1 open study	+
Lemon balm	Anxiety	1 open study	+
Withania	Anxiety/depression	1 RCT	+
Valerian*	Anxiety	2 RCTs	+

Scientific trials – omega 3's amongst the most studied

- Almost 31,000 scientific articles on EPA and DHA published
- EPA and DHA among most studied compounds in scientific literature
- 1863 articles on interventional trials published 2006 - 2015
- **1516 (81.4%) had positive result for primary outcomes**





http://www.goedomega3.com/index.php/blog/2016/04/putting-the-grey-and-bolland-research-letter-into-perspective Aldo Bernasconi posted: 2016-04-21

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Assumption 1. There's little evidence

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Assumption 2. People who have a good diet won't benefit from supplements

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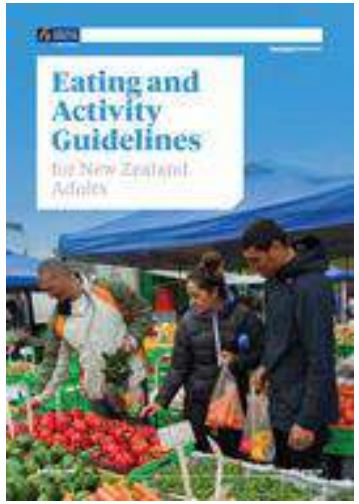
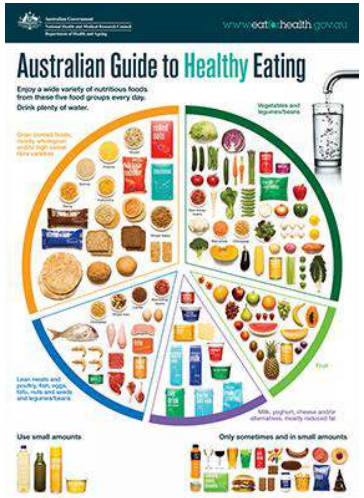
What is a good diet ? Do many people have one ?

Depends who you ask ….

- The American Heart Association
  - 8 or more servings of F & V daily
- Australian gov't guidelines
  - Women - at least 2F and 5V daily
  - Men - at least 2F and 6V daily
  - 2017 CSIRO reports **4 out of 5 people not eating adequate F & V** to meet dietary requirements
- Ministry of health NZ
  - Adults - at least 2 F and 3V daily





Australian diet worse than originally thought, CSIRO study suggests

AUSTRALIANS' diets are worse than first thought, with the nation's largest ever survey showing that 99 per cent of us are hammering the junk food.

Vanessa Brown and AAP

news.com.au SEPTEMBER 26, 2016 1:35PM

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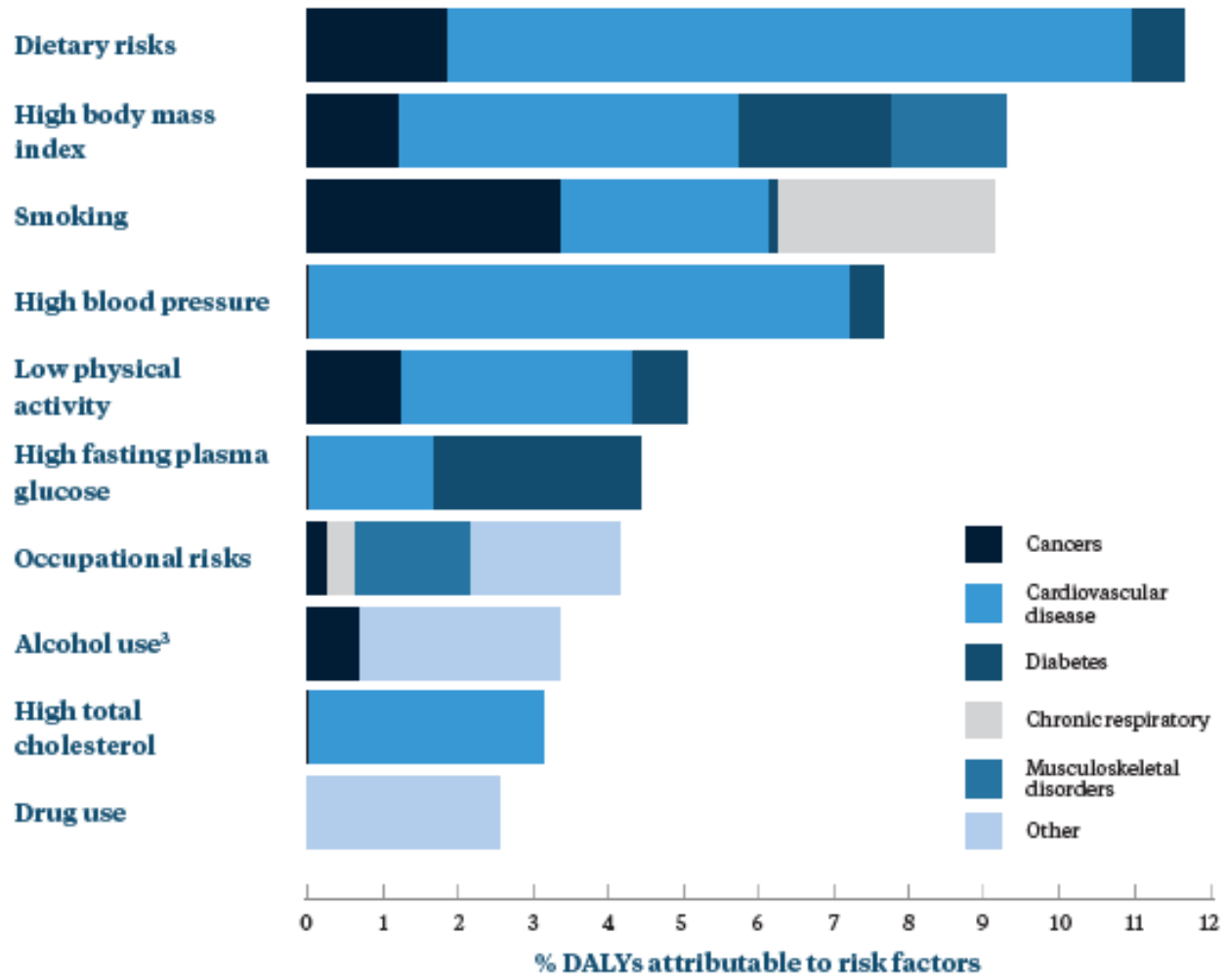
NZ stats

Figure 1: Major causes[2] of health loss in New Zealand 2010 (as % total DALYs)



Source: IHME 2013. DALY = disability adjusted life year
Notes: The percentage of health loss is correct for each cause separately, but the separate percentages cannot be added across causes.

What are New Zealand adults doing?

In 2013/14, more than half of New Zealand adults[6] ate the recommended quantities of either vegetables or fruit, but less than half (41%) ate the recommended amounts of both.

64 %

ate three or more servings of vegetables a day.

57 %

had two or more servings of fruit a day.

Less likely to eat the recommended amounts of vegetables

Younger adults, Pacific and Asian adults and adults living in the most socioeconomically deprived areas.

Less likely to eat the recommended amounts of fruit

Younger adults, Māori and Pacific adults and adults living in the most socioeconomically deprived areas.

6 The 2013/14 New Zealand Health Survey (Ministry of Health 2014a) provides data for adults from 15+ years of age. The Eating and Activity Guidelines define adults as 19–64 years.

Citation: Ministry of Health. 2015.
Eating and Activity Guidelines for New Zealand Adults.
Wellington: Ministry of Health.

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What is a good diet ? Mediterranean diet

Multiple studies shows the closer you adhere to the Mediterranean diet, the greater the risk is reduced of :

- CV disease
- Cancer
- Obesity
- Dementia
- Depression
- All-cause mortality

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Eating a good diet ? What can undermine your nutritional status– medication

- Antihypertensive drugs and zinc status
  - Several BP drug classes reduce zinc absorption via gut and increase excretion via kidneys
- PPIs and magnesium
  - These gastric-acid reducing drugs reduce magnesium absorption via gut
  - Long term use has been shown to induce hypomagnesaemia
    - Case reports of muscle spasms, heart rhythm disturbances and hospitalisation
    - UK government advises not to use > 4 weeks
    - Risk is further increased when taking diuretics
    - B12, calcium, iron status is also at risk
- Statin drugs and coenzyme Q10
  - These common cholesterol lowering drugs reduce the body's own production of CoQ10
    - At least 9 observational studies and 6 RCTs show statins reduce plasma/serum levels of CoQ10 by **16–54%**

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Antibiotics altering nutritional status

(beyond the microbiome)

- Aminoglycosides INC urinary K & Mg excretion
- Chloramphenicol : DEC protein synthesis and INC need for B2,B6 and B12
- Neomycin : DEC absorption of fat soluble vitamins
- Penicillins : INC urinary K excretion
- Sulfonamides : DEC synthesis of folic acid, B cx and Vit K, DEC iron absorption, INC urinary excretion vit C
- Tetracyclines : DEC absorption Ca, iron, zinc, Mg, amino acids, INC urinary excretion vit C

Antibiotics and Drugs: drug-nutrient interactions; Gur A, 2016, pgs 174-191 Encyc food and health, Elsevier

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Other factors affecting nutritional status

Cooking effects

Nutrient affected	Maximal loss through cooking
A	40%
D	40%
E	55%
K	5%
B GROUP VITAMINS	50-80%
Folate	100%
C	100%

Wahlqvist M. Food and Nutrition, Elsevier publishers

Fussy eaters
Gastrointestinal function
Nausea and vomiting
Diarrhoea
Malabsorption
Food storage techniques
Farming techniques
Fad diets
Vegetarian diets
Vegan diets
Cultural factors
Cigarette smoking
Institutionalisation
Access to healthy food
Dental issues
Chewing and swallowing ability

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Nutrient Deficiencies: A global issue?

Most at risk of nutrient deficiencies:[1]

- Pregnant women
- Children under 5 years of age

Most common deficiencies:[1]

- Iron
- Zinc
- Iodine
- Folate
- Vitamin A

Globally, 50 % of all pregnant women are anaemic[2]

Bailey RL, West KP, Jr., Black RE. The epidemiology of global micronutrient deficiencies. Ann Nutr Metab. 2015;66 Suppl 2:22-33.

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Are micronutrient intakes sufficient during pregnancy ?

Meta-analysis and SR 2013

- Micronutrient intakes assessed in multiple countries

Australia, New Zealand , Canada, USA, Japan, UK, continental Europe

Results :

- Pregnant women had <u>less than adequate intakes</u> of :
  - **Folate** RDI=600 µg; median intake=190 µg
  - **Iron** RDI=27 mg; median intake=12.1 mg
  - **Vitamin D** AI=5 µg (200 IU); median intake=1.3 µg

Also low in calcium and magnesium:

- **Calcium** RDI=1000 mg; median intake=806 mg/d
- **Magnesium** RDI=350; median intake=265 mg/d

Blumfield M et al. Nutr Rev 2013;71(2):118–132

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Pregnancy nutrition – healthy mother, healthy baby, healthy society

Micronutrient deficiencies or inadequacies in pregnancy can increase the risk of :

- Neural tube defects (folate *Aust 500mcg*)
- Pre-term births (iron, calcium, vit D)
- Low birth weight (iron, omega 3s)
- Perinatal mortality (iron, folic acid, calcium)
- Reduced IQ and cognitive performance (iron, iodine)
- Learning difficulties (omega 3s)
- Infant allergies and asthma (omega 3s)
- Motor skills and visual skills impaired (iodine)
- Language impairment (vit D)
- Behavioural and emotional problems (folic acid)

For mother :

- Fatigue and lethargy (iron)
- Gestational diabetes (Vit D)
- Pre-eclampsia (vit D, calcium, magnesium)

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Australian kids at risk - Calcium, Magnesium, omega 3

Most recent Australian childhood nutrition survey

- 4,487 children aged 2-16 years
- Data collected via 24 hour recall at 2 interviews

Calcium – NOT meeting ave requirements

- 82-89% of 12-16 year old girls, and
- 44-50% of 12-16 year old boys

Magnesium – NOT meeting ave requirements

- 56% of 14-16 year old girls,
- 34% of 14-16 year old boys

Omega-3 intake:[1]

- Inadequate in **68%** of children aged 1 to 5 years
- Unbalanced by excess saturated fat which provides 50% of daily energy

2007 AUSTRALIAN NATIONAL
Children's Nutrition and Physical Activity Survey

Australian Government
Department of Health and Ageing

AUSTRALIAN FOOD AND GROCERY COUNCIL

Australian Government
Department of Agriculture, Fisheries and Forestry

Jemma Braun 16 years old
(Aust Ballet)
photo by Tanya Zail

Australian Government Department of Health and Ageing. Children's Nutrition and Physical Activity Survey. 2007.

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Preventing or treating disease with supplements

Using nutritional supplements at doses beyond usual dietary intakes to prevent disease

Diet alone won't always get you there !

- Nicotinamide and non-melanoma skin cancer
- Coenzyme Q10 and migraine prevention
- Coenzyme Q10 and heart failure
- Curcumin and memory

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Nicotinamide and NMSC reduction in high risk people

/ Pharma & Healthcare

MAY 13, 2015 @ 05:00 PM 15,568 VIEWS

Vitamin B3 Prevents New Skin Cancers In Study

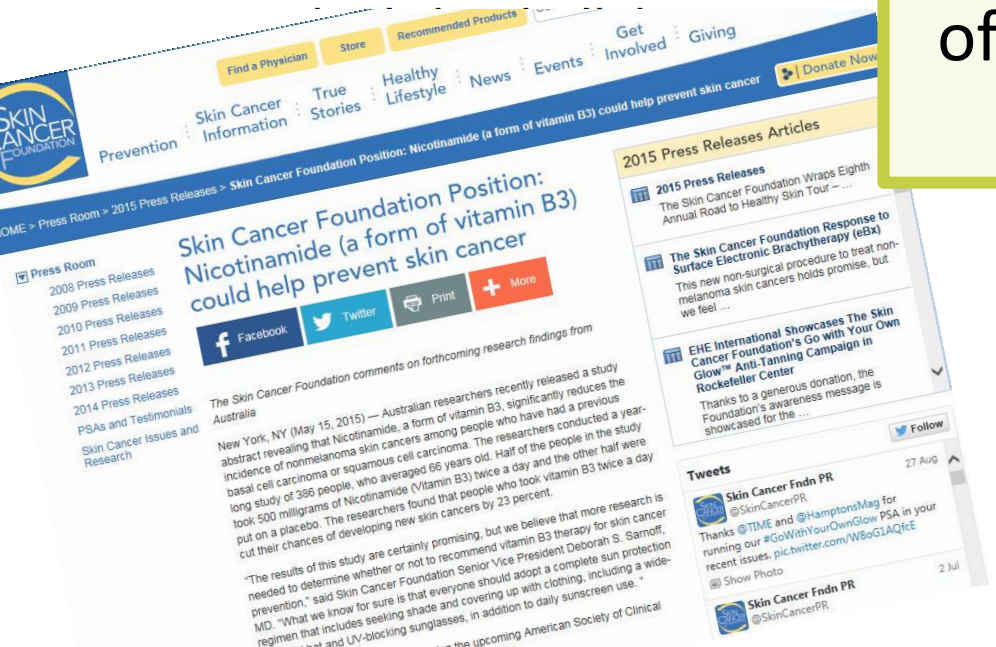
Matthew Herper
FORBES STAFF

I cover science and medicine, and believe this is biology's century.

FOLLOW ON FORBES (2031)

Literally millions of people take vitamins in the hopes that doing so will improve their health – b
scientific evidence has pointed to vitamin supplementation being useless or worse. Beta carotene
supplements may actually increase mortality, as might vitamin E and vitamin A. Other seeming
promising supplements, like fish oil for heart disease, have seen their promise dissipate. The be
advice seems to be to just eat a healthy diet.

But that doesn't mean that vitamins never have health
stunning demonstration that one seems to: a form of
dramatically reduce the risk of non-melanoma skin ca
cancer.



Nicotinamide 500mg twice a day reduces risk of NMSC compared to placebo by 23%

Vitamin B3 could help reduce skin cancer risk

7 Comments / Sh... / 126 Tweets / Stumble / @ Email

...015 8:08 AM EDT More +

...the way doctors treat patients at high risk for skin ...ny high-priced new pharmaceuticals -- the key may be ...n supplement that costs less than $10 a month.

...rm of vitamin B3 called nicotinamide could help ...ncer recurring in patients who've had it before. ...amin B3 called niacin was not used in this study.)

...researchers in Australia looked at nearly 400 people who had had at ...least two non-melanoma skin cancers. They found patients who took vitamin B3 twice a day cut their chances of developing new skin cancers by 23 percent.

"That's a dramatic number," Dr. David Agus, director of USC's Norris Westside Cancer Center, told "CBS This Morning." "It could make a major impact."

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It’s all about dose - Can I get enough from food?

718 beers
every single day

130 serves of vegemite every single day

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CoQ10 preventing migraines – its about dose

- Double-blind, randomised controlled trial
- CoQ10 (3 × 100 mg/day) vs placebo in 42 migraine patients

- Results : CoQ10 was superior to placebo
  - Reduced attack-frequency
  - Reduced number of headache-days
  - Reduced number of days-with-nausea in the third treatment month
  - Well tolerated

Neurology February 22, 2005; 64 (4)

The average western diet contains 3-5mg daily of CoQ10

CoQ10 Food sources (per 100gm)	
Sardines	6.5mg
Pork	3.5mg
Beef	3.5mg
Olive oil	3mg
Poultry	1.8mg
Broccoli	1mg

CoQ10 improving heart failure – Qsymbio RCT

420 patients with severe heart failure (NYHA* Class III or IV) from nine different countries participated.

CoQ10 (ubiquinone100mg 3x day) vs placebo over 2 years

Results :
CoQ10 patients had a 43% decrease in CV death compared to placebo.

CoQ10 also significantly **reduced the risk of death from all causes by 42%** compared to the placebo group.

JACC: Heart Failure; Volume 2, Issue 6, Dec2014, Pages 641-649

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Curcumin – its all about bioavailability

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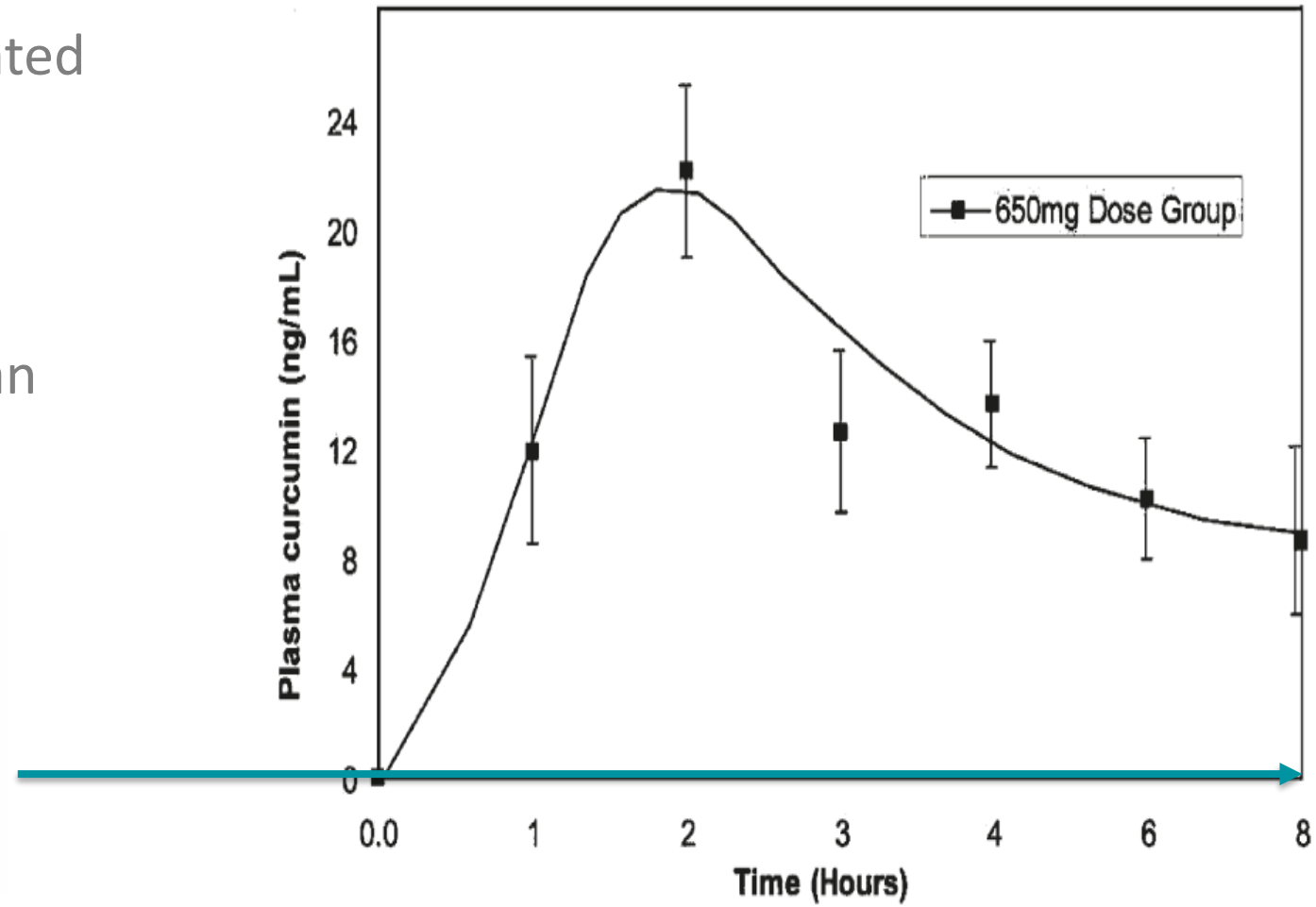
Pharmacokinetics of SLCP

- 650 mg SLCP vs unformulated curcumin
- Free curcumin detected in plasma with SLCP
- 65 x more bioavailable than unformulated curcumin

No detectable curcumin from unformulated extract in healthy volunteers



Gota VS, Maru GB, Soni TG, Gandhi TR, Kochar N, Agarwal MG. Safety and Pharmacokinetics of a Solid Lipid Curcumin Particle Formulation in osteosarcoma Patients and Healthy Volunteers. J Agric Food Chem 2010;58(4):2095-99

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Solid lipid curcumin RCT – Cox 2014

- Cognition and mood in healthy older population (n=61)
  400 mg SLCP Longvida® containing 80 mg curcumin
  Acute (1 and 3 hr) and chronic (4 wks) effects
  - **1 hr:** significant improvement in performance on sustained attention and working memory
  - **4 wks: significant improvement in working memory and mood**. Improved resilience to the detrimental impact of cognitive stress on mood.
  - Decreased fatigue.
  - Decreased total and LDL cholesterol

Cox KH, Pipingas A, Scholey AB. Investigation of the effects of solid lipid curcumin on cognition and mood in healthy older population. J Psychopharm 2014:1-10

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Other benefits

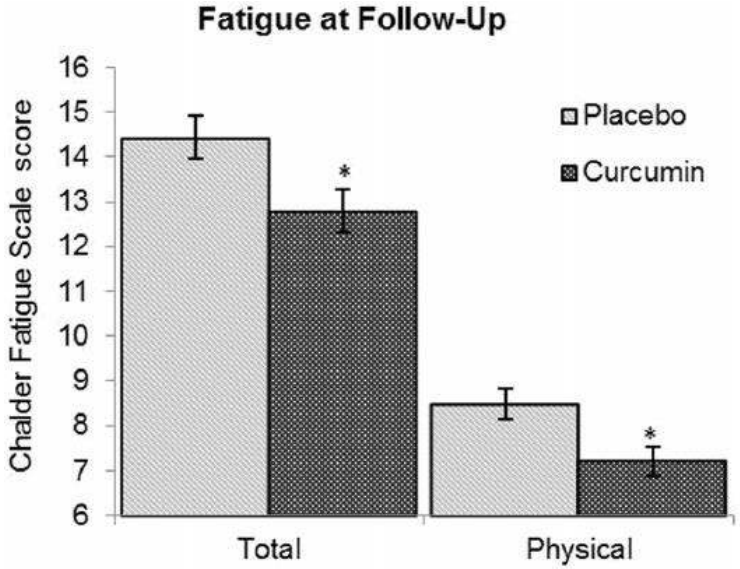

Figure 2. Significant effect of four weeks of chronic curcumin treatment on state-non-specific fatigue. $*p < 0.05$.

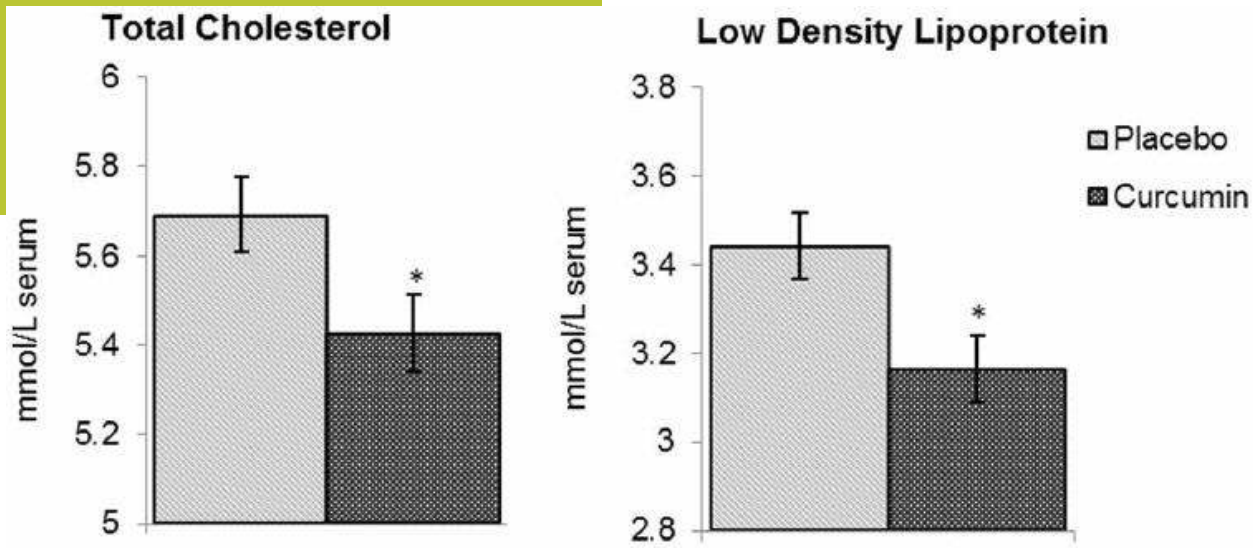

Figure 6. Lipid measures significantly affected by chronic treatment. $*p < 0.05$.

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Assumption 2.
People with a good diet won't benefit from supplements

1. Few people actually have a 'good diet' on a consistent basis

   Definition of a good diet varies between countries, scientists, nutritionists etc

2. Even if people follow the recommended dietary intakes, many other factors affect their nutritional status

   Eg cooking, medications, gut health, food storage, cigarette smoking, pregnancy etc

3. Some natural ingredients exert therapeutic effects in doses higher than found in the diet *eg CoQ10, B3*

4. Some natural ingredients are poorly absorbed from the diet making it difficult to reach therapeutic effects

   eg curcumin from turmeric

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Assumption 2. People who have a good diet won't benefit from supplements

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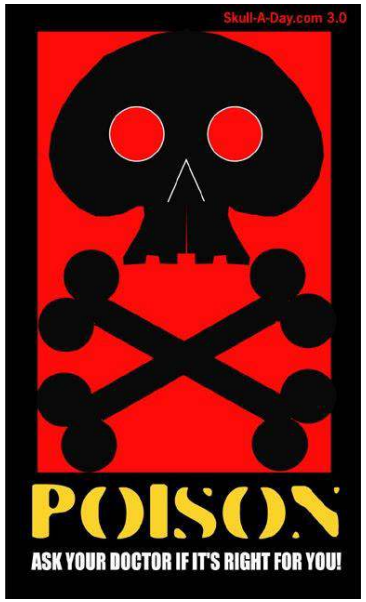
Assumption 3. Supplements are very risky business

Likelihood versus consequence



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Safety

‘ all things are poisons,

nothing is without poisonous qualities,

it is only the dose that makes something

a poison or not’

Paracelsus

grandfather of pharmacology

early 1500’s Switzerland

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Risky business—Or is it? Risk perception and integrative medicine

Lesley Anne Braun [a,b,c,*]

[a] Centre for Medication Use and Safety, Pharmacy Department, The Alfred Hospital, Melbourne, Australia
[b] Centre for Ethics in Medicine and Society, Department of Medicine, Monash University, Australia
[c] National Institute of Complementary Medicine, University of Western Sydney, Australia

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ABSTRACT

We are living with risks all the time; it's just a fact of life. There are some risks we happily accept, others we fear so much that they over-ride our rational decision making and some very large risks that are so mundane that we often ignore them. Identifying, minimising and communicating risk is necessary for improving public safety and a frequent concern for many working in healthcare. However, there is relatively little discussion about risk perception, which ultimately influences how people respond and can explain why some make seemingly irrational decisions, regardless of the evidence. This has obvious implications for clinicians and patients, but also committees and policy makers who consist of individuals with varying levels of experience, knowledge and risk perception. Deciding to restrict or promote a particular behaviour, access to a medicine, practice of a profession or integration of a therapy will be influenced by these factors. This article reviews some of the social science and psychology literature which has identified the key factors which attenuate or amplify risk perception. In particular, Ropeik's perception gap is discussed together with Slovic's work identifying factors which affect risk perception and heuristics. Several examples are given which are relevant to integrative medicine as it relates to safety. Drug–herb interactions and the perceived danger of herbal and nutritional medicines in surgery are key examples. The 'risk as feelings' hypothesis is also discussed as a means of better understanding barriers to the adoption of evidence based integrative medicine, and how it may affect practitioner–patient interactions.

Mind the ‘perception’ gap

1. Choosing more risky alternatives, assuming they are safer than they are.

E.g. lack of immediate danger, creates an impression of safety eg NSAIDS, antibiotics are perceived as safer than they are because adverse events occur with chronic use

2. Assuming something is more dangerous than the evidence indicates.

Eg. Acute and dramatic adverse effects increase perception of risk such as echinacea anaphylaxis

A large perception gap can influence public policy

which may end up reducing public fear

rather than maximising public health, spending and access

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Factors which affect risk perception

7 Amplifiers

- Exotic, new, unfamiliar
  - Eg Herbals
- Memorable, dramatic effect
  - eg airline crash
- High dread/fear
  - Eg cancer
- Rare and striking
  - Eg lightning, shark attacks
- Immediate/acute
  - Eg anaphylaxis, choking hazards, food poisoning
- Manmade
  - Eg toxic waste
- Risks to children

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Factors which affect risk perception

7 Diminishers

- Familiar
  - Eg using household chemical cleaners
- Not memorable
  - eg road accidents
- Voluntary – our choice to do it
  - Eg driving a car, skiing, medical radiation exposure
- Common event
  - Known side effect
- Chronic risk
  - Long term use of NSAIDs
- Delayed effect
  - Cigarette smoking, emphysema
- Affects adults

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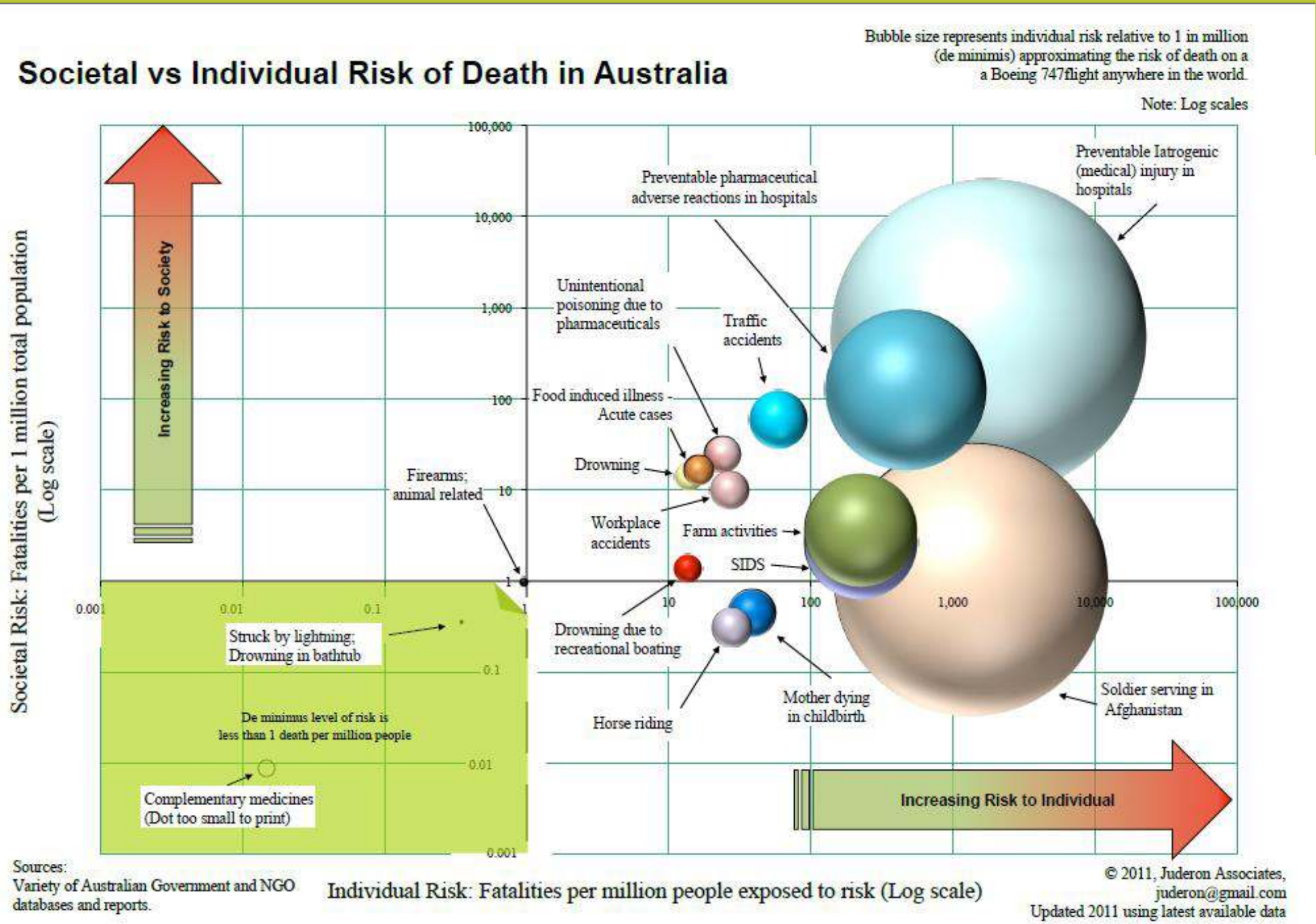
Over 12 mths

An Australian is :

45X more likely to be killed by a lightning strike than dying from using a CM product

63,000 more likely to die from an AE due to a pharma drug than a CM product

243,000 more likely to die due to preventable med injury than a CM product



Drug interactions and CMs – raising the alarm '98

- 1998 Archives Internal Med : first scientific paper makes the mainstream media

" If used beyond 8 weeks, ***Echinacea*** could cause hepatotoxicity and therefore should not be used with other known hepatoxic drugs, such as anabolic steroids, amiodarone, methotrexate, and ketoconazole."

"**Feverfew, garlic, *Ginkgo*, ginger, and ginseng** may alter bleeding time and should not be used concomitantly with warfarin sodium"

"**Valerian** should not be used concomitantly with barbiturates because excessive sedation may occur."

"Immunostimulants (eg, ***Echinacea* and zinc**) should not be given with immunosuppressants (eg, corticosteroids and cyclosporine). "

Miller et al *Arch Intern Med.* 1998;158(20):2200-2211

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Drug interactions and CMs

- 2000 Lancet follows up : review of medline from 1966-1998

> "Many reports of herb-induced interactions lack crucial documentation on temporal relations and concomitant drug use."

> "Perhaps the most serious problem encountered in analysing such reports is the **consistent absence of any effort (beyond that of reading the label) to establish a positive identification of the herb involved, and to exclude the effect of contaminants or adulterants."**

> "Unless noted otherwise, the reports mentioned herein did not include chemical analyses."

Fugh-Berman A; Lancet 2000 (Jan 8); 355 (9198): 134-138

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Is this the tip of the iceberg ?

What's happened since then ?

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Research shows you cant predict interactions with test tube studies

e.g. test tube & animal models show both CYP induction and inhibition for ***Ginkgo biloba***

In contrast, **4 clinical studies** did NOT identify a clinical significant effect on a variety of cytochromes

e.g. in vitro tests show ***saw palmetto*** inhibits CYP3A4 & CYP2D6

In contrast, **2 clinical studies** did NOT identify a significant effect on CYP3A4 or CYP2D6

Milk thistle and P. ginseng showed CYP3A4 inhibition in test tubes.

No significant clinical effects in humans with a range of test drugs

midazolam, irinotecan, docetaxel and imatinib

Braun & Cohen, HNS 4th edt, Elsevier; 2014. Goey et al; Cancer Treatment Reviews 39 (2013) 773–783

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What is clinically relevant ?

Pharmacokinetic Herb-Drug Interactions (Part 2): Drug Interactions Involving Popular Botanical Dietary Supplements and Their Clinical Relevance

Bill J. Gurley[1], Espero Kim Fifer[2], Zoë Gardner[2]

[1] Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, College of Pharmacy, Little Rock, AR, USA
[2] Department of Plant, Soil & Insect Sciences, University of Massachusetts, Amherst, MA, USA

Gurley BJ et al. Pharmacokinetic Herb-Drug Interactions (Part 2)... Planta Med 2012; 78: 1490–1514

Review of in vitro, in vivo and clinical studies

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Review of clinically relevant pharmacokinetic drug interactions

Proven to have significant potential for drug interactions

- Black pepper
  - >10mg piperine, piperamides
  - Bioavailability enhancer via CYP3A & P-gp
- Goldenseal
  - Inhibits CYP 2D6, 3A4
- Schisandra
  - Inhibits CYP 3A4, Pgp
- St Johns wort
  - Induces CYP 3A4, P-gp

Proven to have NO pharmacokinetic drug interactions

✓Black cohosh
✓*Echinacea* spp.
✓Garlic *- Allium sativum*
✓*Ginseng* spp. – Asian ginseng & American ginseng
✓*Ginkgo biloba* <240mg/d
✓Kava kava
✓St Mary's thistle

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Do herbs interact with drugs ?

- Yes, however
- There are only a handful with the potential to create a clinically significant interaction
- The vast majority don't cause clinically significant interactions

- The proverbial 'iceberg' didn't materialise

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Drug induced liver injury (DILI)

Liver injuries are rare clinical events; population data suggests 20 cases per 100,000 persons exposed to a drug

Review of 300 liver injury cases USA
73% single prescription drugs
Most common drugs were amoxicillin-clavulanate, isoniazid & NSAIDS
7% suspected VDS (unconfirmed)

Navarro et al. Hepatology 2014;60:1399–1408; Navarro et al. Clin Liver Dis. 2013 Nov;17(4):715-352

- Predictable responses
  - eg **paracetamol** (responsible for over 50% of cases of acute liver failure in USA)
- Idiosyncratic responses
  Environment, drug and host factors
  eg Genetic variations in drug metabolizing genes & immune responses
- Eg kava kava

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Liver injury & herbal medicines
7 year Mayo clinic study

- **Review of 83,265 in-patient admissions at the Mayo Clinic in Scottsdale, Arizona over 7 years (1998–2006)**
- 0.048% (N = 40) due to drug-induced liver injury i.e 5.7 cases/year
  - 70% (27/40) due to paracetamol (18 intentional overdose)
  - 33% (13/40) due to primarily antibiotics.

  - **No cases of liver injury caused by herb use** reported at this location during this period.

Carey et al., Dig. Dis. Sci., 53 (7) (2008), pp. 1977–1982

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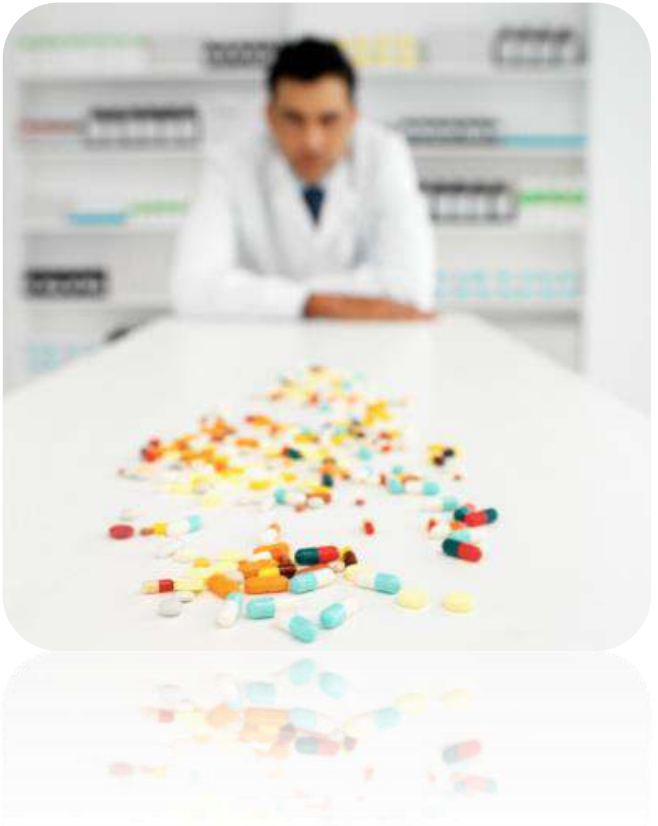
2016 review of drug induced liver injury (DILI)

- More than 800 drugs implicated in DILIs
- Drugs cause 2000 cases /year acute liver failure in USA
  - Herb induced liver reactions **extremely rare** – tend to be reversible, self limiting



"The dangers of dietary supplements have been inflated in the media, and need to be normalized for scientific accuracy."

Liver toxicity related to herbs and dietary supplements: Online table of case reports. Brown A. Part 3 of 6; Food and Chem Toxicol 2016

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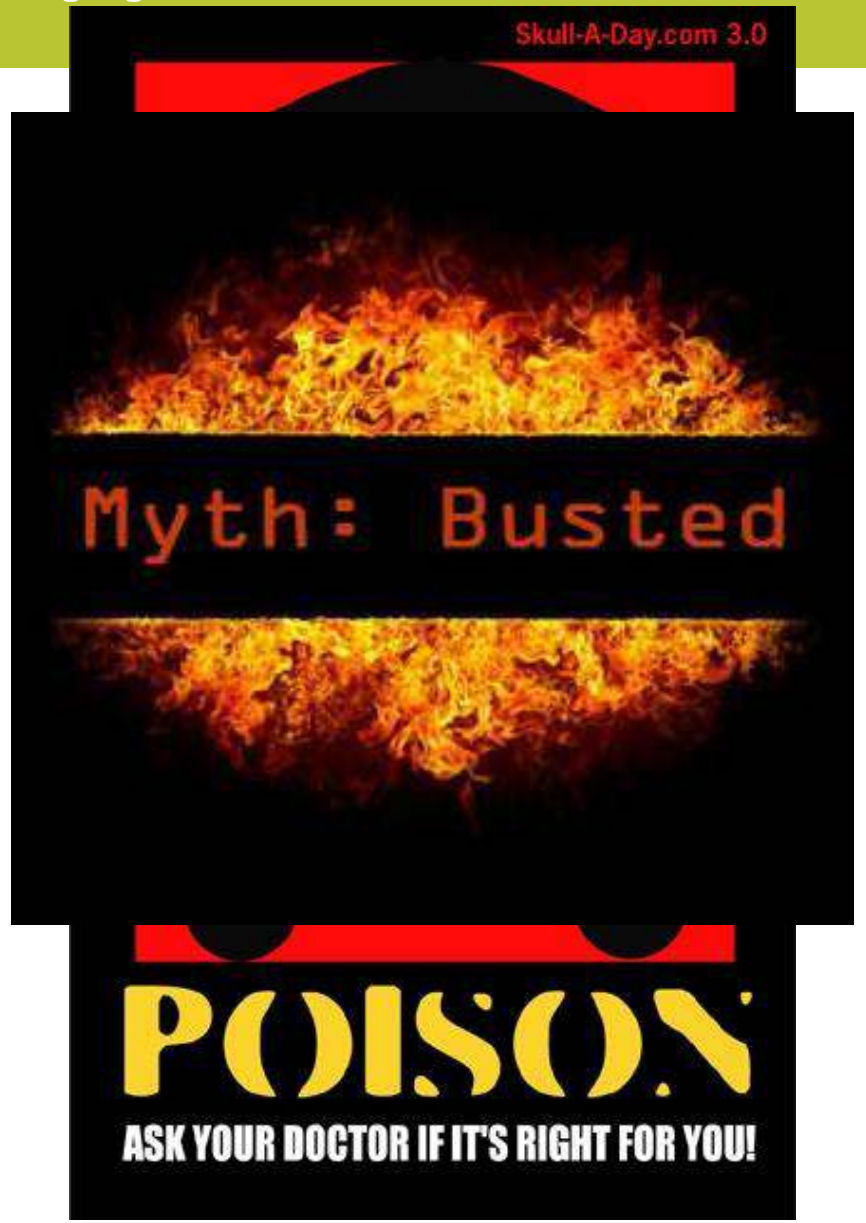
Assumption 3. Supplements are very risky business



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Majority of people don't eat F & V daily

Many early suspected herb-drug interactions have been proven unfounded

Evidence comes from traditional & scientific areas

All medicines have the potential to cause drug interactions and liver injury.
Good regulation, quality control and rational usage reduces risk
Herbs pose an extremely low risk

CM products can fill in nutritional gaps, promote optimal health, act as preventative medicine or therapeutic agents

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First Do No Harm – choose the safest options first – Have prescribers forgotten this basic rule ?
September 28, 2016; The Intelligent Prescriber

10 common medical publications that can make your liver seriously sick (about CMs safety)
October 13, 2017; The Patient Advocate syndicated

Risky business or is it ? Do our quiz to find your perception gap
Dec24, xmas edition of The Regulator

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About Blackmores Institute

Academic & professional arm of Blackmores

- Evidence-based approach to natural health
- Primary focus: research & education
- Improving public health through natural medicine

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Questions ?

lbraun@blackmoresinstitute.org

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