A heart healthy diet is good for the brain too

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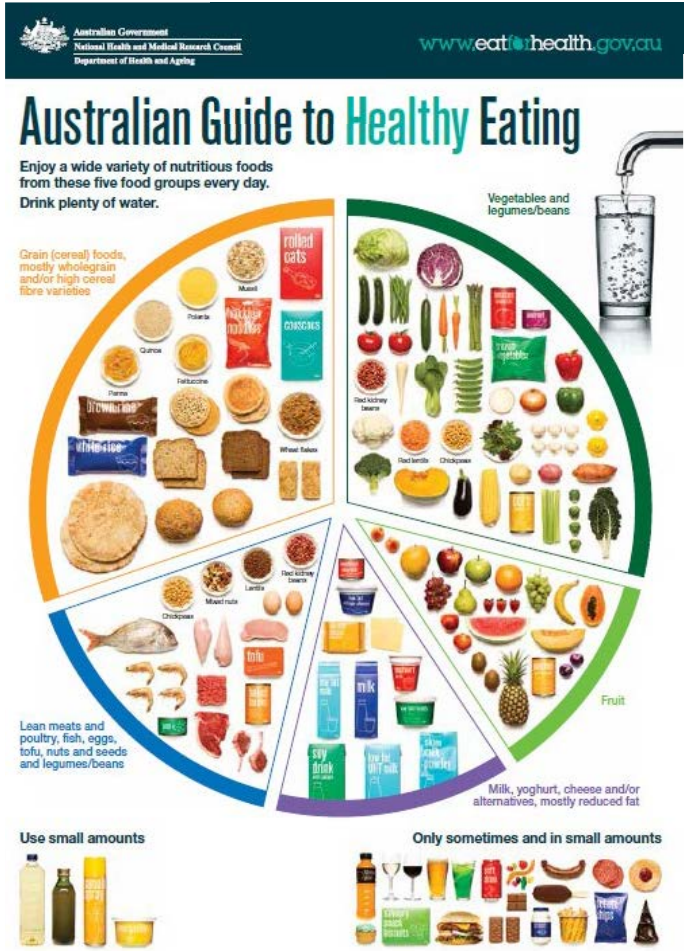
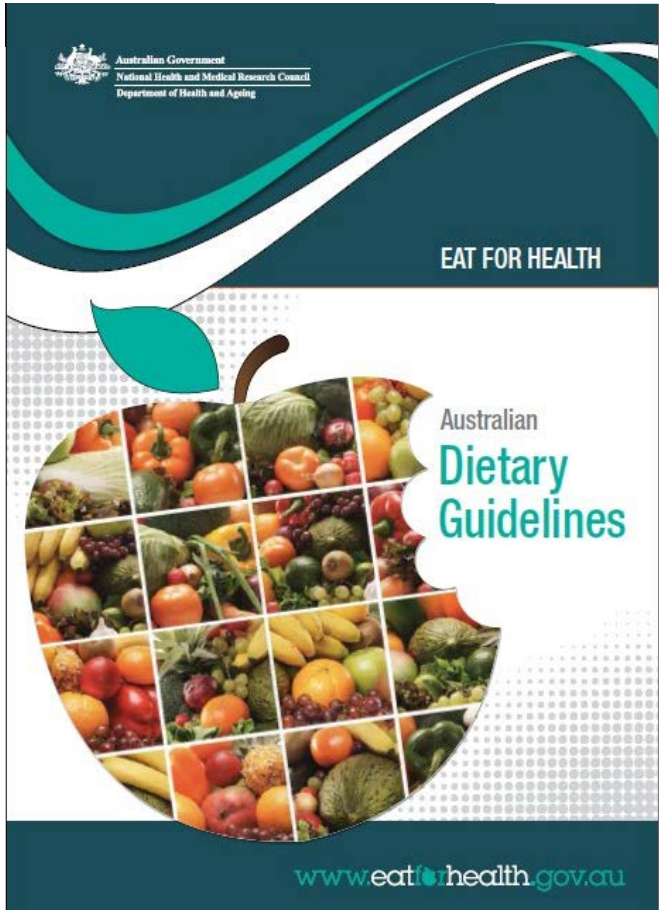
UNIVERSITY OF WOLLONGONG AUSTRALIA

Outline of presentation

Foods for better brain and heart health

- Dementia – prevalence
- Flavonoids – review of evidence and impact on cognition
- Anthocyanins - sources, metabolism, health effects
- Clinical trials – chronic and acute (dementia, MCI, healthy)
    - Effect on cognition
    - Effect on BP, vascular function and inflammation
- Epidemiology: flavonoids and BP
- Dietary intake of Australians: sources and amounts of flavonoids
- Overall effect of diet on brain health in older adults
- Conclusions and Where to Next?





http://www.eatforhealth.gov.au

Heart Foundation Recommendations

Fruits and vegetables (flavonoids and antioxidants)

- Go for Two (fruit) and Five (veg)
- Drink black or green tea or cocoa from raw cocoa powder

All Australians adults

The Heart Foundation encourages all Australian adults to do the following.

1. Consume at least two serves of fruit and five serves of vegetables every day.
2. As part of a healthy balanced diet, drink*:
   - black or green tea†
   - cocoa made from raw cocoa powder.‡

The Heart Foundation **does not** recommend the following.

1. Consuming milk chocolate or dark chocolate for the prevention or treatment of CVD. Due to processing to remove the bitter taste, most chocolate is a poor source of antioxidants and contains saturated and trans fats.
2. Drinking coffee for the prevention or treatment of CVD. If consuming coffee, drink only paper-filtered, percolated, café-style (espresso) or instant (regular and decaffeinated), in preference to boiled (such as Turkish-style) or plunger coffee. Consume less than five cups per day.§
3. Drinking red wine or other types of alcoholic drinks for the prevention or treatment of CVD. The Heart Foundation supports the National Health and Medical Research Council (NHMRC) recommendation for healthy Australians who already drink alcohol to have no more than two standard alcoholic drinks per day for men and women.[3]
4. Using antioxidant supplements, such as vitamins E and C, carotenoids and other antioxidants or combinations, for the prevention or treatment of CVD. There is some concern that high doses (> 800 IU/day) of vitamin E supplements may increase the risk of CVD.

   The Heart Foundation supports the *Nutrient Reference Values for Australia and New Zealand*,[4] which recommends that people consume a diet that would provide these nutrients at levels currently equating to the 90th centile of intake in the population.

Flavonoids

Six sub-classes found in plant foods

Polyphenols

Flavonoids

- Flavan-3-ols
- Flavones
- Flavanones
- Flavonols
- Anthocyanins
- Isoflavones

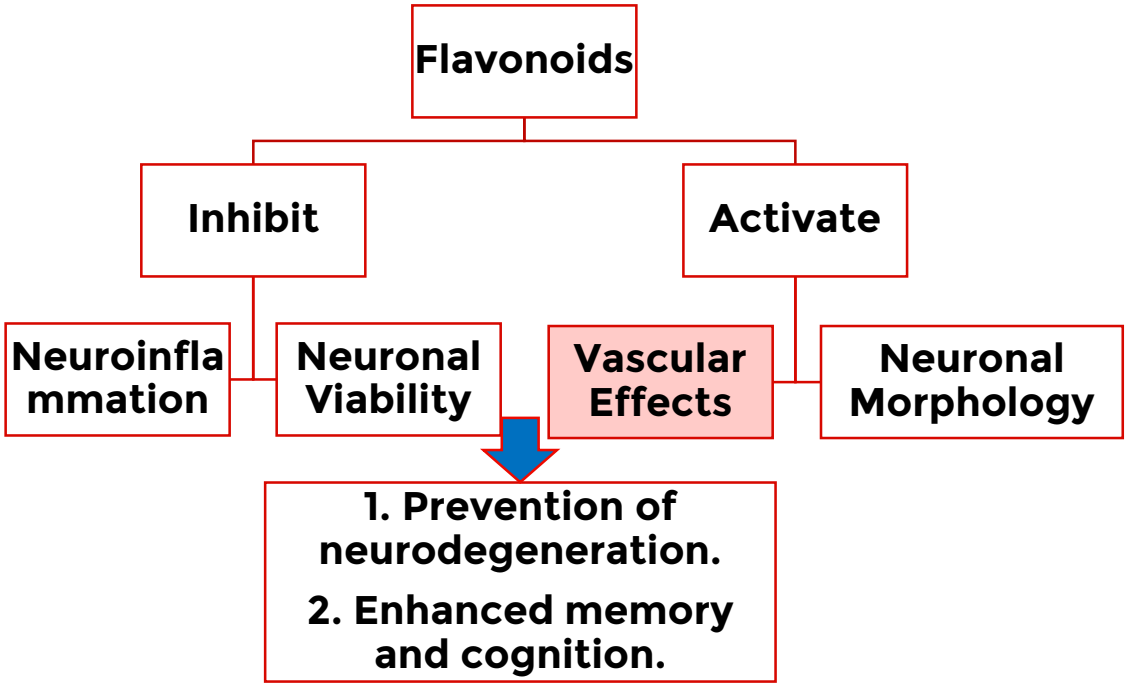
Flavonoid-rich foods influence cognition & dementia

- **Pre-clinical evidence** has shown flavonoid supplementation may improve:
  - Memory acquisition (Wang et al., 2006; Joseph et al., 1998, Hartman et al., 2006)
  - Short-term working memory (Williams et al., 2008; Ramirez et al., 2005)
  - Long-term reference memory (Casadesus et al., 2004)
  - Reversal learning (Wang et al., 2006)
  - Memory retention/retrieval (van Praag et al., 2007)
  - Spatial working memory (Shukitt-Hale, Chen and Joseph 2009)

- **Epidemiological data** has shown flavonoid-rich food consumption may improve:
  - Cognitive performance (Macready et al., 2009; Nurk et al., 2009)
  - Cognitive 'evolution' (Lettenuer et al., 2007)
  - Dementia risk and delay dementia onset (Commenges et al., 2000; Dai et al., 2006; Barberger et al., 2007)

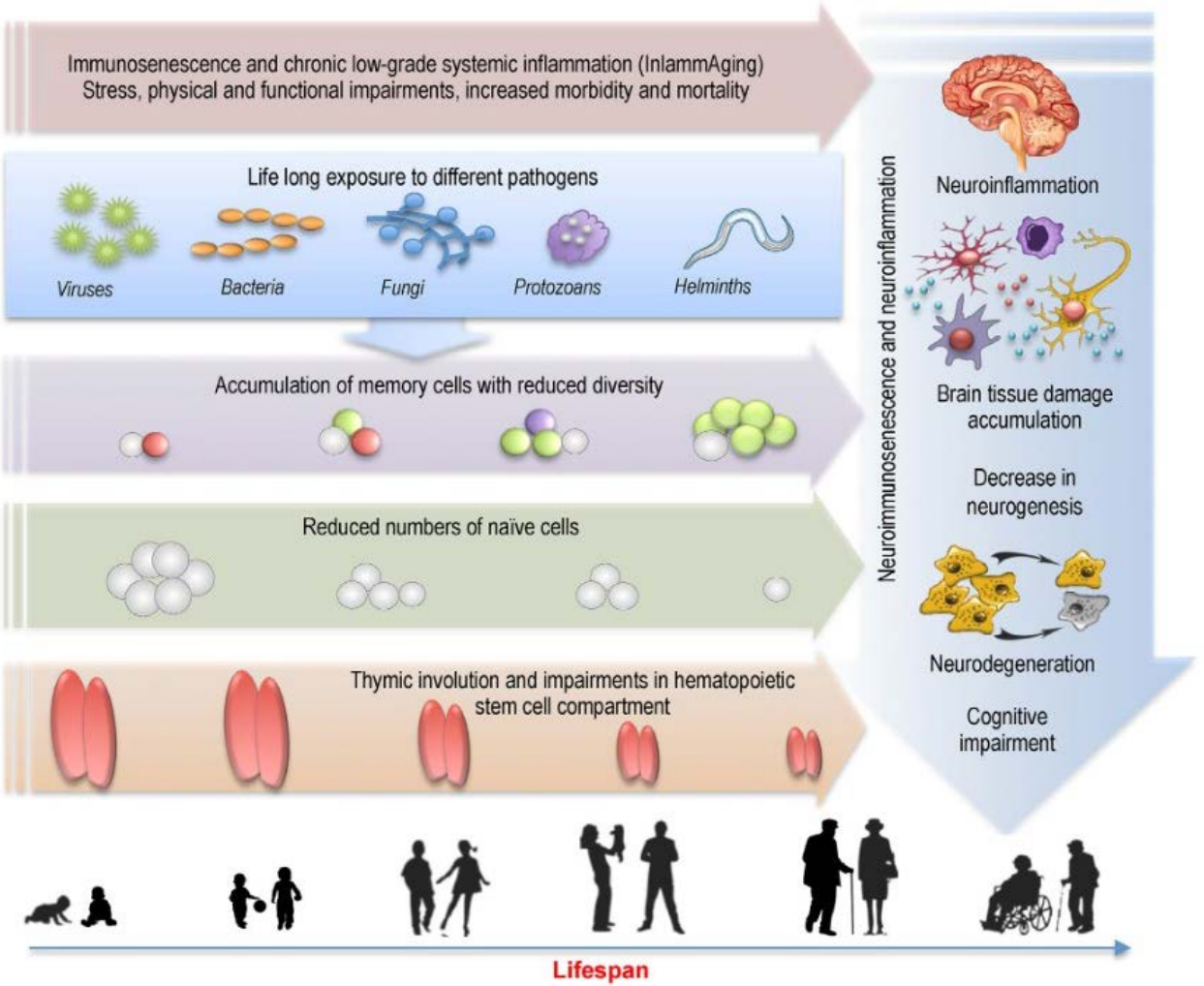
- **Experimental data** is limited but has shown flavonoid-rich foods improve:
  - Verbal learning and memory in older adults (Krikorian et al., 2010)
  - Verbal learning and memory in MCI (Krikorian et al., 2010)

Biological action of flavonoids



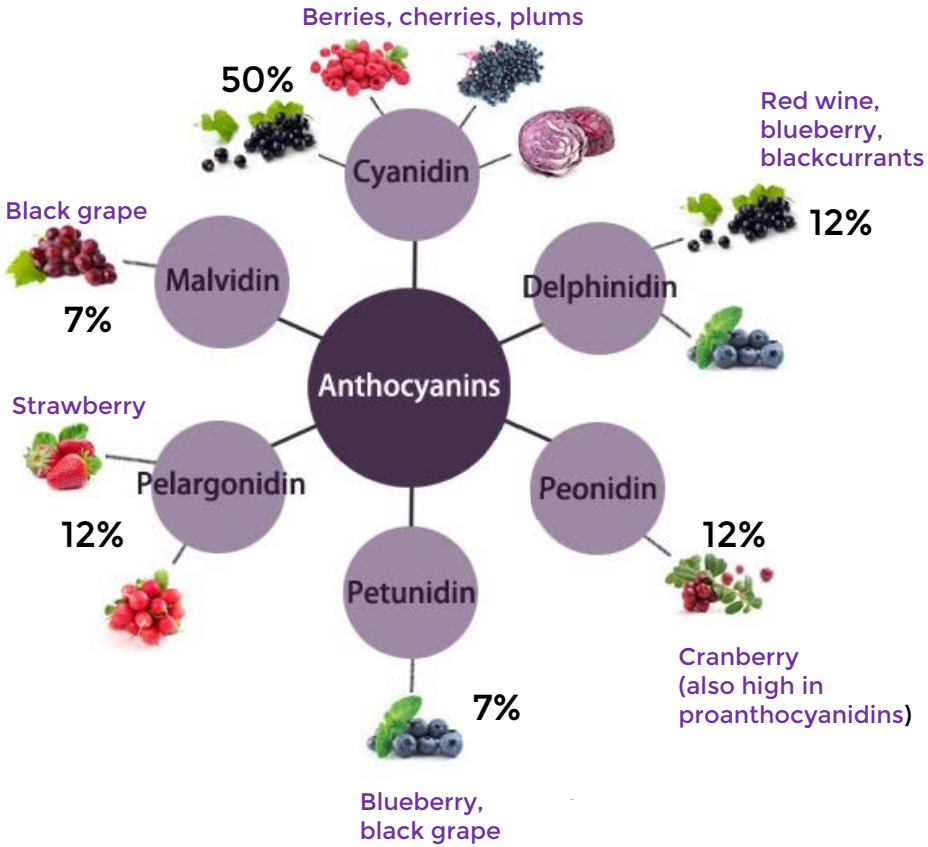
- Antioxidant activity (Spencer, 2008a).
- Extensively metabolised to phenolic acids (Spencer, 2008a).
- Concentration in brain tissue is low (Spencer, 2008a).
- A multiplicity of neuronal and vascular effects are theorised (Spencer 2008b).

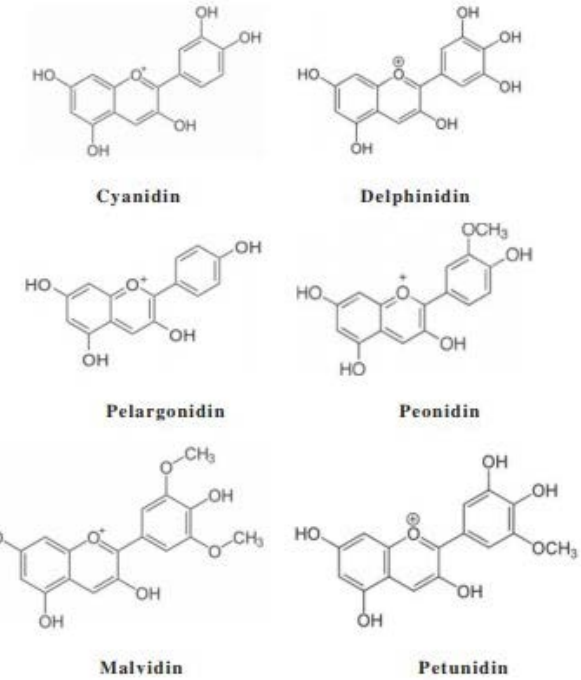
“Inflammaging”: Chronic low grade systemic inflammation



Di Benedetto *et al*. *Neurosci & Biobehav Rev* **2017; 75: 114–128**

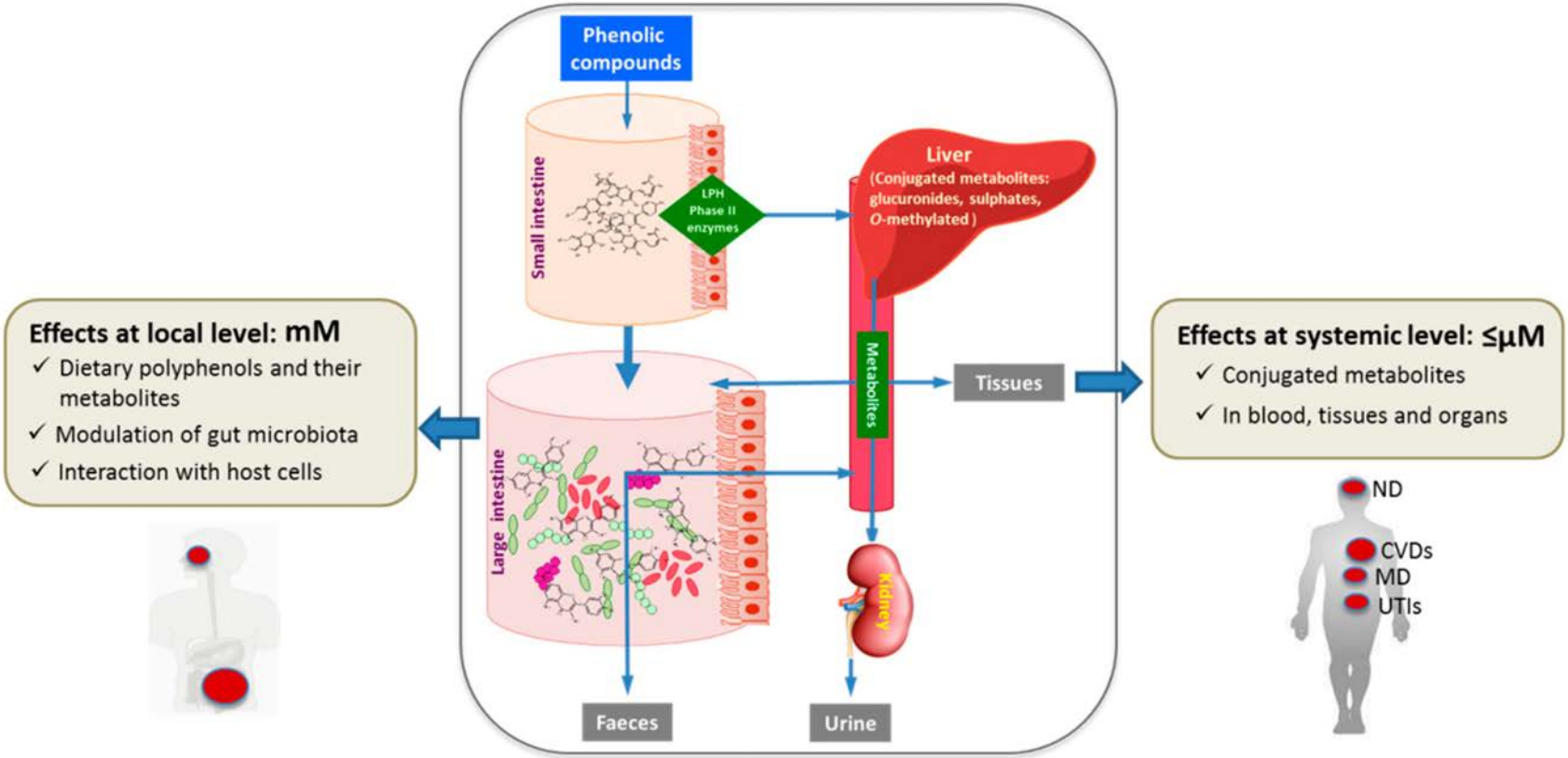
Anthocyanins in foods





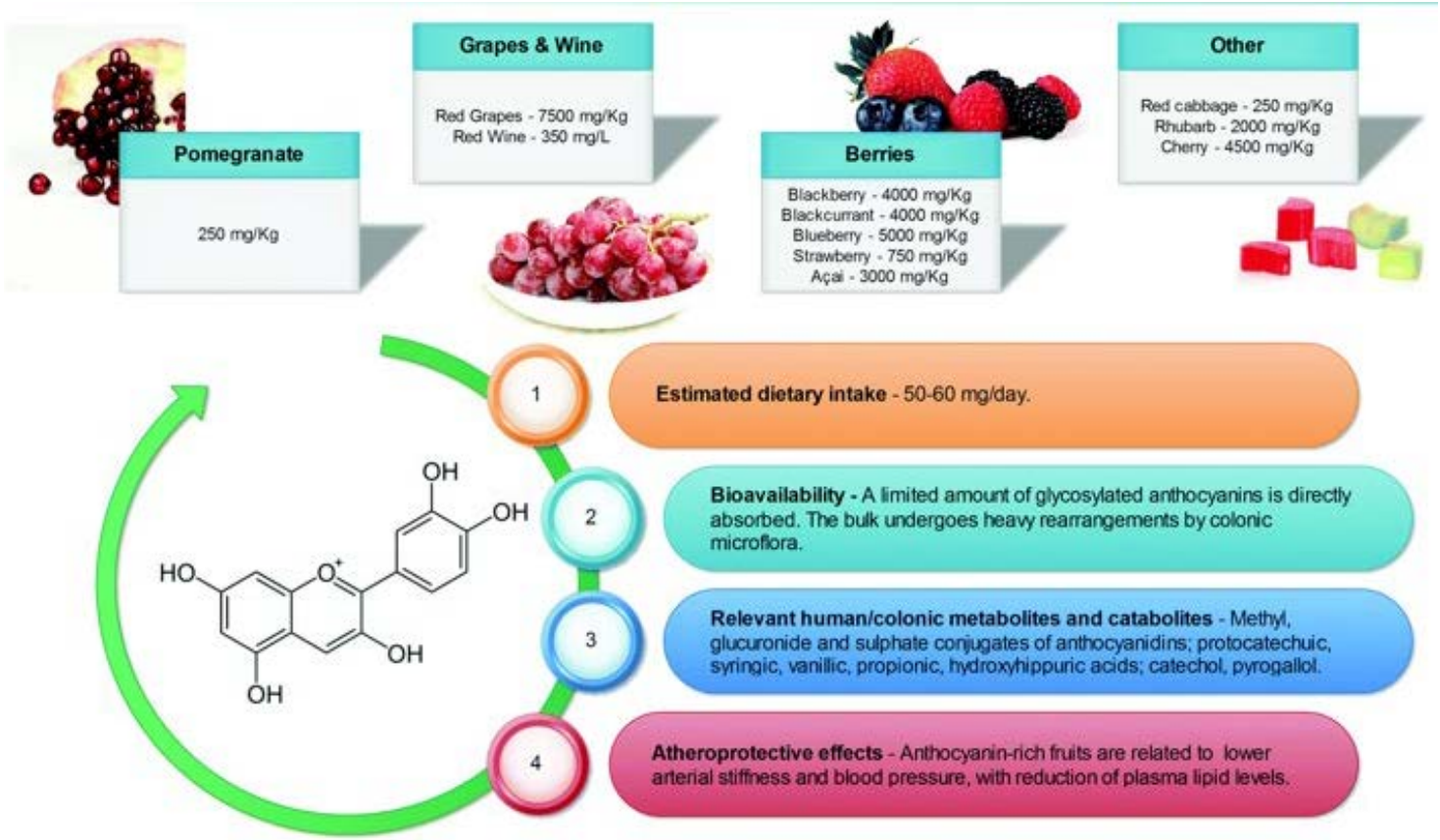
http://www.jtbpd.com/information.php?information_id=41&xcSID=c4d5bcamie8luafofrgq28oqj3

Anthocyanins: Metabolism



Cueva C et al., *Molecules* 2017; 2017, 22, 99.

Anthocyanins: Low bioavailability



Zanotti *et al. Food Funct.*, 2015, 6,13

Effect of anthocyanins from cherries on cognitive function in older adults with dementia: A Randomised Controlled Trial

Kent K, Charlton KE, Roodenrys S, Batterham M, Potter J, Traynor V. Consumption of anthocyanin-rich cherry juice for 12 weeks improves memory and cognition in older adults with mild-to-moderate dementia. *Eur J Nutrition* 2017; 56(1): 333-341.

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Industry partners:
Agritechnology Ltd.

Study Design

Recruitment

Geriatric outpatient dementia clinic | Residential aged care facilities

Randomization (n = 49 dementia patients aged 70+y)

Computer-block aided by independent statistician

CONTROL
Low-flavonoid
Low-anthocyanin

200ml/day either

INTERVENTION
Flavonoid-rich
Anthocyanin-rich

Baseline

Blood sample | Cognitive & physical assessment

6 week follow up

Structured 3-day food diary | Cognitive & physical assessment

12 week follow Up

Blood sample | Cognitive & physical assessment

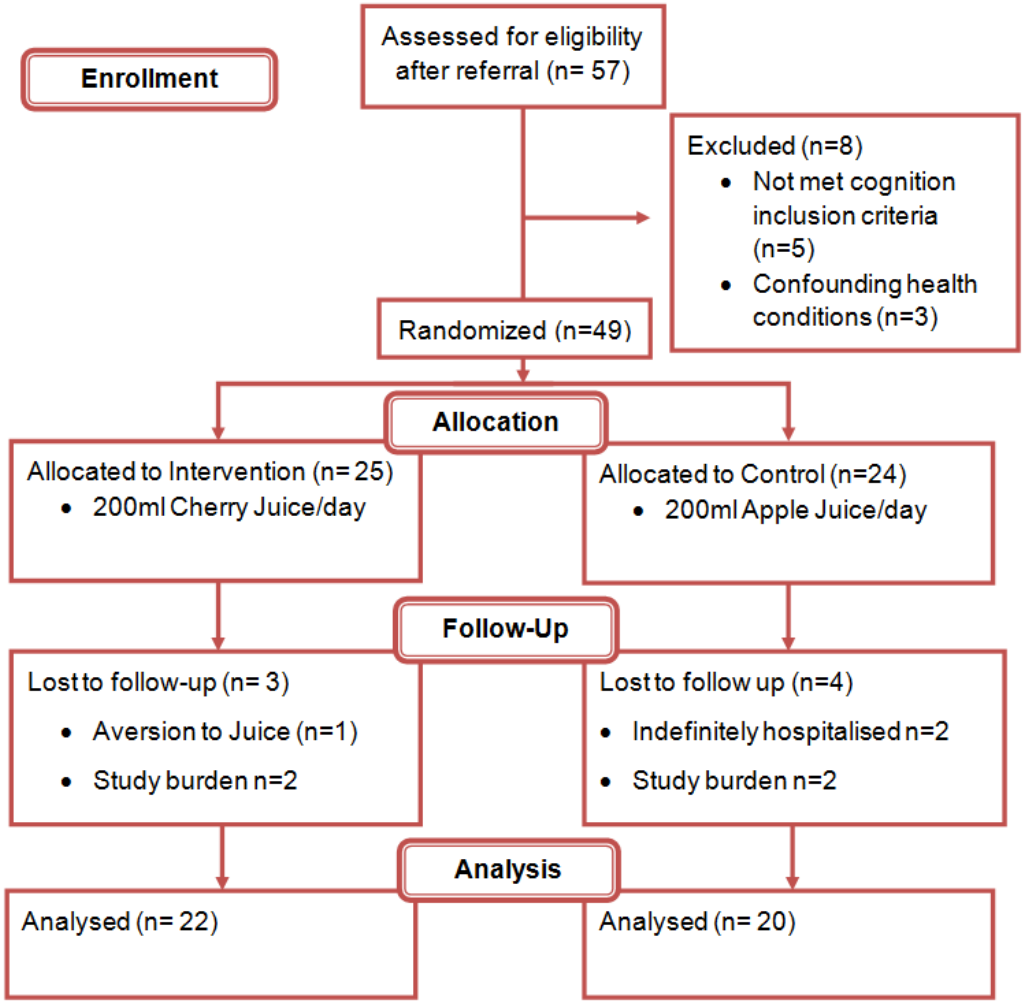
Cognitive tests

Instrument	Domain
The Geriatric Depression scale	Mood
The Rey Auditory Verbal Learning test	Verbal learning and memory
The Serial ordered pointing task	Working memory
Visual paired associates task	Visual memory
The Boston naming task	Semantic memory
The verbal fluency task	Executive function and control processes
Trail-making task	Executive function
Digit-span backwards task	Short-term memory storage and executive control

Rey Auditory Verbal Learning Test (RAVLT)

- Hear a list of 15 words and then recall as many as possible
- This is repeated 5 times with the same list (so should improve over the repetitions)
- Memory for the words tested after hearing another list (which interferes with memory for the first list) and after 20 minutes delay
- This memory task is sensitive to brain damage, age-related decline and pathological decline (e.g. Alzheimer's dementia)

Sample recruitment



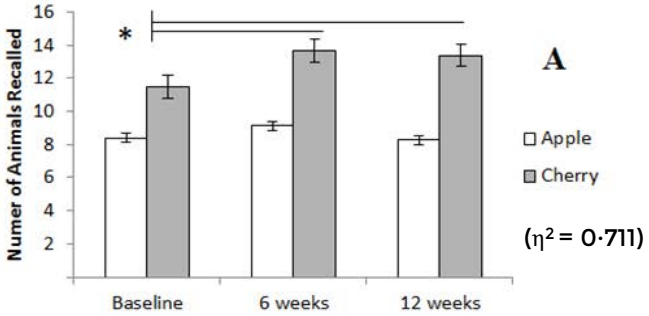
Participant characteristics at baseline

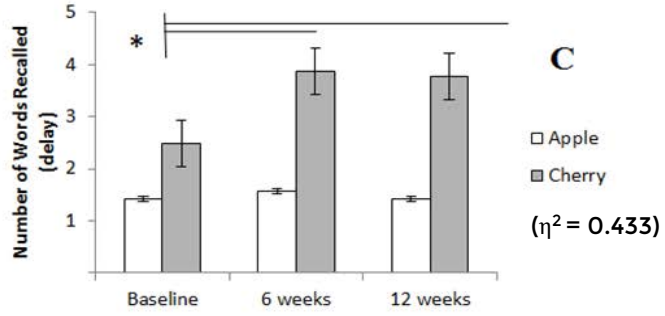
	Control group n=25, mean ± SD	Intervention group n=24, mean ± SD
Age (years)	80.6 ± 6.6	78.9 ± 5.2
BMI (kg/m^2)	26.6 ± 3.5	25.7 ± 3.4
Hand grip strength (kg)	52.1 ± 16.4	62.5 ± 16.1*
Mid-arm circumference	26.9 ± 4.5	27.2 ± 4.1
Calf circumference	33.4 ± 3.7	34.9 ± 3.4
Education (years)	17.5 ± 3.2	18.2 ± 2.4
Mini Nutritional Assessment (MNA)	23.4 ± 3.5	25.6 ± 2.8*
Independent Activities of Daily Living (IADL)	5.7 ± 2.4	7.5 ± 0.8*

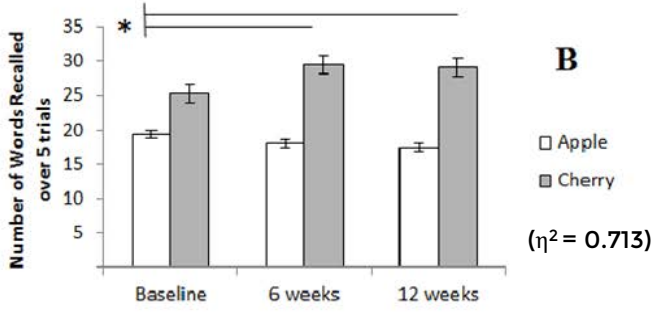
*P<0.05, for differences between groups.

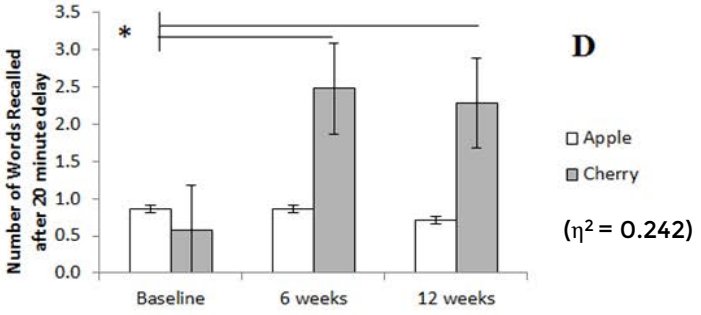
Results: Improvements in cognition

Significant changes in **category fluency (A), RAVLT total (B), RAVLT delayed recall (C) & RAVLT – 20minute delayed recall (D)** at 6 and 12 weeks for intervention group (n = 42).





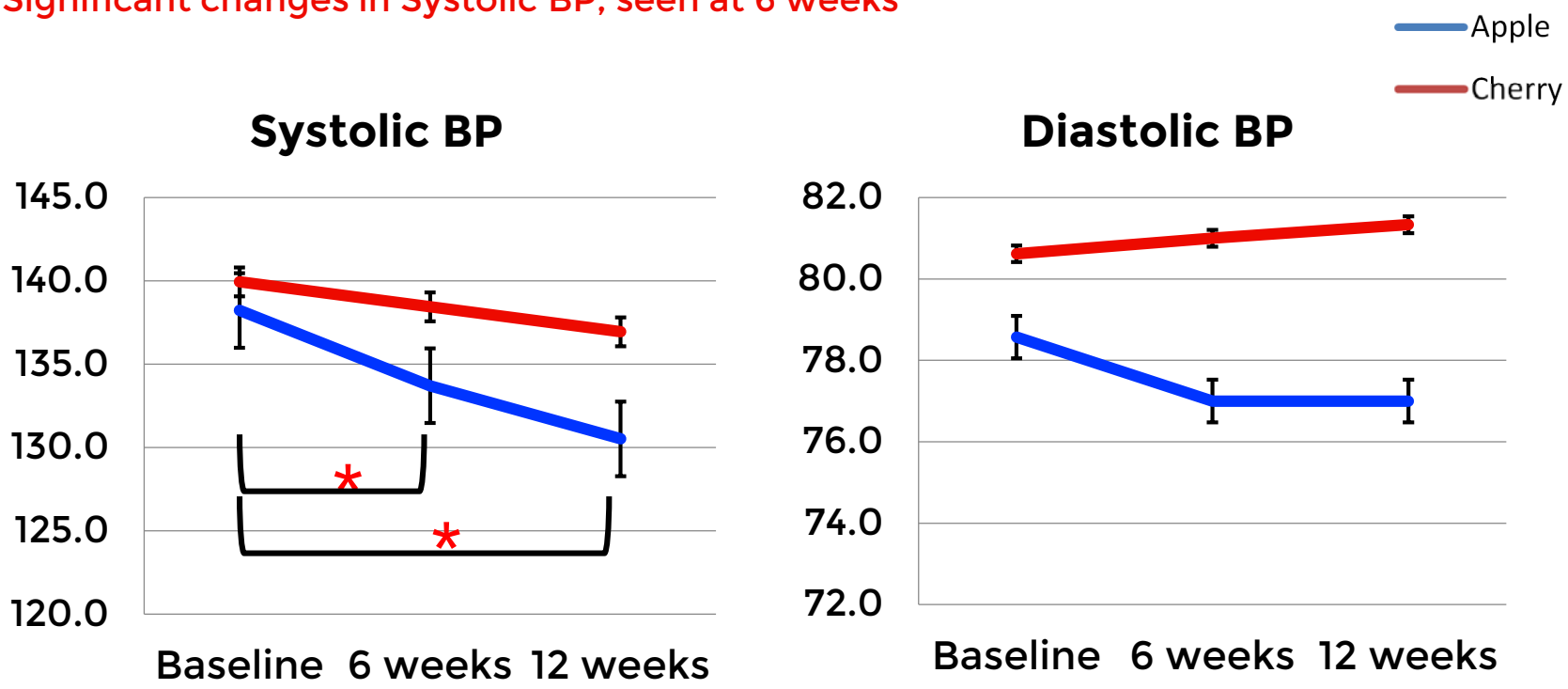




*p=<0.05**p=<0.001

Results: Improvements in Blood Pressure

Significant changes in Systolic BP, seen at 6 weeks



Data are given as mean (mmHg) ± SD; ANCOVA performed (baseline as covariate)

State of the evidence for anthocyanins and cognition: Systematic Literature Review

- Despite a large body of preclinical evidence, there remains a lack of experimental studies conducted in humans.
- Six of the seven studies (4 acute; 3 longer) reported positive benefits of anthocyanin consumption on some aspect of cognition.
- Generalisability of the findings to other clinical or healthy populations is limited by small study samples and inconsistent methodologies.

Kent K., Charlton K.E., Netzel M. & Fanning K. Food-based anthocyanin intake and cognitive outcomes in human intervention trials: a systematic review. *J Hum Nutr Diet* 2016;doi:10.1111/jhn.12431

Unanswered questions… and enter Queen Garnet plum

- Does it matter if anthocyanin-rich foods are consumed in small amounts or is there a physiological dose required to see effects?
- Why do we see such a dramatic BP reduction?
- How do we measure compliance?
- What about biomarkers?
- What is a high versus low intake of anthoycanins?
- What are major dietary sources in Australia?
- How much is consumed daily?
- What is a beneficial doseage?

- Hybrid of the Japanese plum
- Developed by DAF, Queensland, Australia
- High levels of anthocyanins estimated to be ~2x content regular plums (Fanning et al., 2014, Miletic et al., 2012)
- Good vehicle for clinical studies

Effect of anthocyanin-rich plum juice on acute ambulatory BP and cognitive function in younger and older adults: a pilot crossover dose-timing study

Ezinne Igwe (PhD student)

Karen Charlton (UOW)

Steven Roodenrys (UOW)

Katherine Kent (UTas)

Kent Fanning (DAF)

Industry partners: Nutrafruit Pty Ltd.

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Igwe EO, Charlton KE, Roodenrys S, Kent K, Fanning K, Netzel ME. *Nutrition Research* 2017. doi: 10.1016/j.nutres.2017.08.006

Study design

Aims: To determine the ***acute*** dose-interval effect of Queen Garnet plum juice (QGPJ) in young and older adults on:

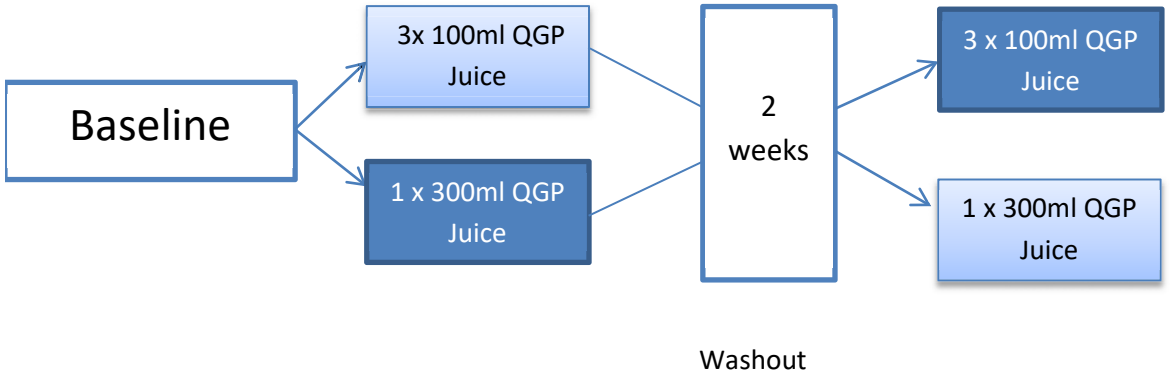
- 24hr Ambulatory blood pressure
- Cognitive functioning.
- Urinary excretion of anthocyanins and anthocyanin metabolites

n = 12 younger adults, 18-45y
(mean age = 30.8 (8.0)y; BMI = 22.5 (2.4))

n = 12 older adults, 65y+
(mean age = 77.4 (6.1)y; BMI = 26.4 (3.3).

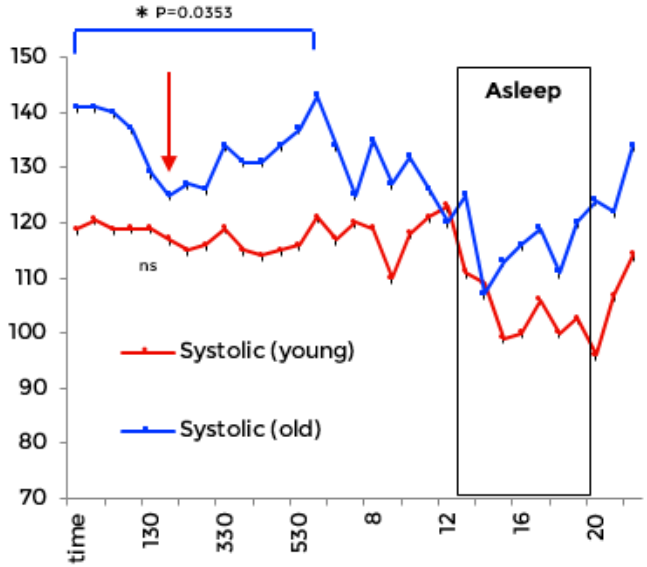
Exclusion criteria

- Uncontrolled HBP
- Type 2 DM
- Dementia

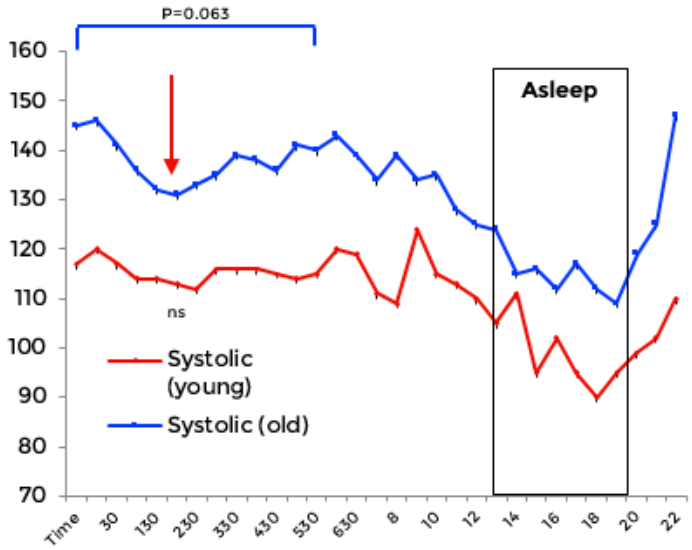


- Juice = 123 mg anthocyanins/100 ml
- Two 6 hour interviews over a two week (washout) period
- Standardised breakfast provided and snacks after 4 hours per visit

Results: 24hr Ambulatory Systolic Blood Pressure



Single dose (300ml)

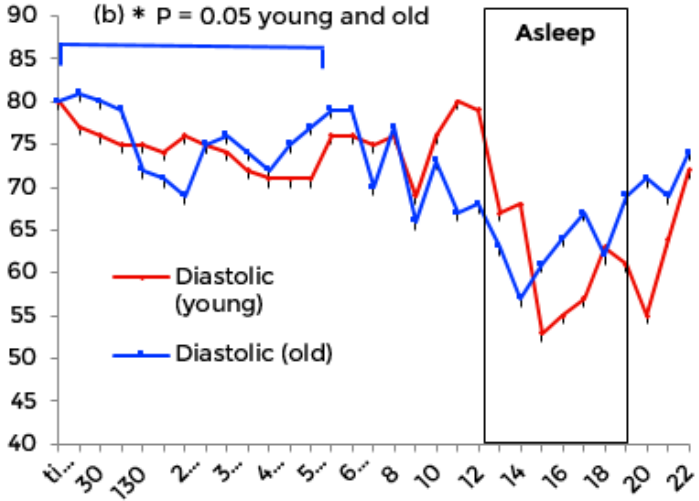


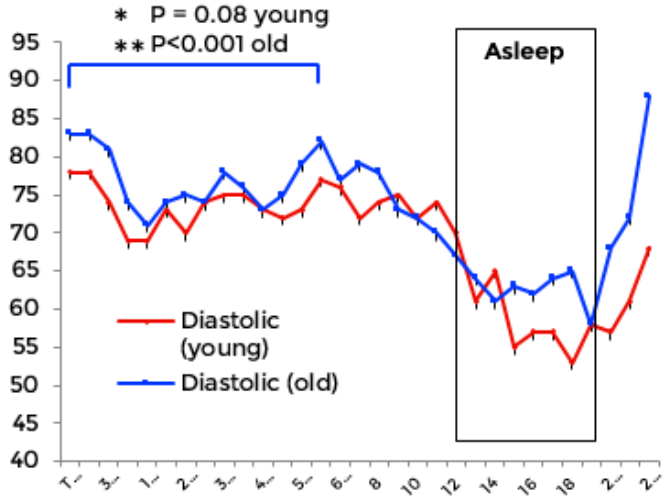
Triple dose (3 x 100ml) over 3 hrs

n = 12 (young) and n = 12 (old)

There was an observed dose timing and group effect, no longer significant after inclusion of an interaction term (age group × dose timing).

Results: 24hr Ambulatory Diastolic Blood Pressure



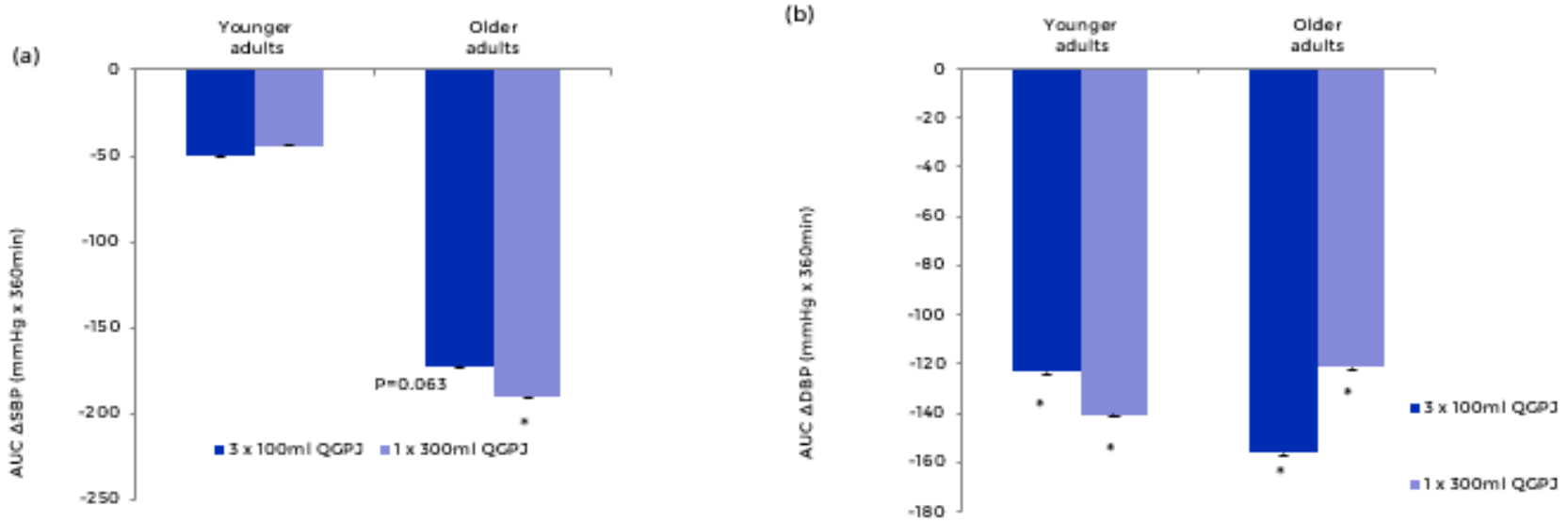


Single dose (300ml) **Triple dose (3 x 100ml) over 3 hrs**

n = 12 (young) and n = 12 (old)

There was an observed dose timing and group effect, no longer significant after inclusion of an interaction term (age group × dose timing).

Results: AUC for Sys and Dias BP



Mean change in area under the curve for (a) Systolic Blood Pressure (SBP) curve and (b) Diastolic Blood Pressure (DBP) from 0 to 6h, following consumption of the single dose (1x300ml)or triple dose (3x100ml) of the QGPJ.

Values are means with standard error of the mean as error bars.

Conclusions

Acute study

- 300ml of Queen Garnet Plum juice does not appear to affect acute cognition but reduces acute blood pressure
- Dose-interval does not appear to be important at this level of supplementation (contradictory to previous acute study with cherry juice, Kent *et al*. 2015)
- Future studies should focus on older adults who are at risk for both elevated blood pressure and cognitive deficit.

Effect of anthocyanins from QGP juice on cognitive function in older, healthy adults: An 8 week crossover RCT

Ezinne Igwe (PhD candidate)

Karen Charlton (UOW)

Steven Roodenrys (UOW)

Katherine Kent (Utas)

Michael Netzel (UQ)

Juice provided in kind by Nutrafruit Pty Ltd.

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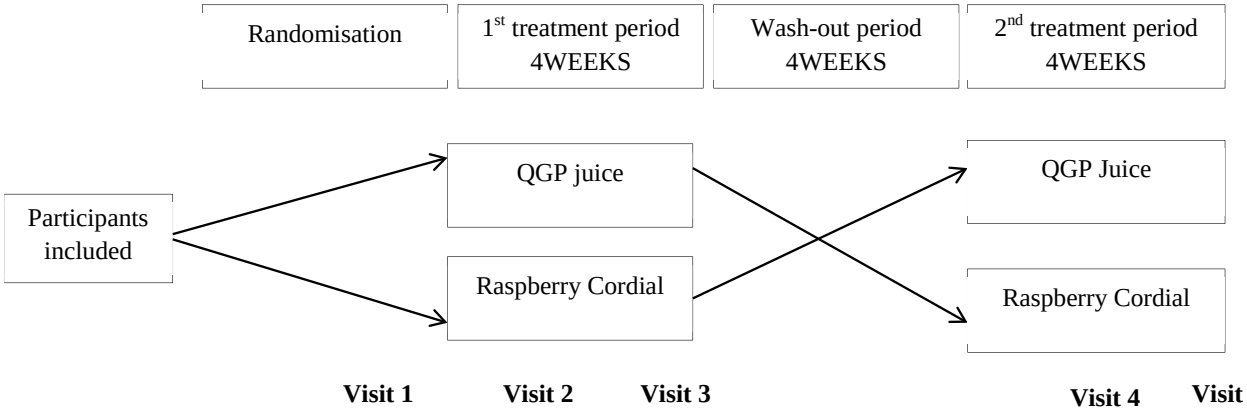
Igwe EO et al. *Nutr Res.* In review.

Study design: Randomised cross-over trial



Expected anthocyanins = 142mg/d

200ml/day
EITHER

Methods and Results

Baseline	4 weeks	8 weeks
- Cognitive Assessment - Blood pressure - Blood sample (BDNF, CRP) - Socio-demo lifestyle data - Anthropometrics - Urine samples - Gut microbiota (*uBiome*™ (San Francisco, CA, USA) 16S-sequencing on Illumina Next Generation Sequencing - 3-day food diary and 24h DR	- Cognitive Assessment - Blood pressure - 24h DR	- Cognitive Assessment - Blood pressure - Urine samples - Gut microbiota - 24h DR

Mean anthocyanin intake was 5 mg/100ml (~10mg/d rather than expected 142mg/d)

N = 28 of 31 completers (14 men; 17 women).
Mean age = 70 ± 10 y,
Mean BMI = 26 ± 4.

Repeated measures ANOVA:
Cognition: No significant difference between arms (p>0.05).
Blood pressure: No significant difference between arms (p>0.05).
Inflammatory biomarkers: No significant difference between arms (p>0.05).

Effect of anthocyanins on cognitive rehabilitation in people with Mild Cognitive Impairment: A Randomised Controlled Trial

Vinicius do Rosario (PhD candidate)

Karen Charlton

Steven Roodenrys

Vida Bliokas

Sue Thomas

Ian Wright

Karen Walton

ISLHD

Dr Zoe Fitzgerald

Dr Samantha Broyd

Dr Amelia Paterson

Prof Jan Potter

Partners:

Dr David Williams, DAF

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Memory Cognitive Rehabilitation Group (CRG)

“Making The Most Of Your Memory” (Radford et al., 2010)

- 2 hour, weekly sessions for 6 weeks
  - Plus one session for carers ~2 hours
- 3-10 people recommended per group
- Run by clinical neuropsychologists and/or clinical psychologists

Content

- **Psychoeducation:** information regarding memory function, the impact of neurological conditions and lifestyle strategies
- **Internal Mental Strategies:** e.g. mental imagery, association, method of loci, face name association, spaced retrieval
- **External Aids:** e.g. notebooks, diaries, alarms, environmental modifications, routines
- **Homework:** Allows the opportunity to practice and generalise learned strategies to other environments

Challenges with blinding of intervention

Participants consumed 250 mL fruit juice daily for 8 weeks, randomized into three groups:

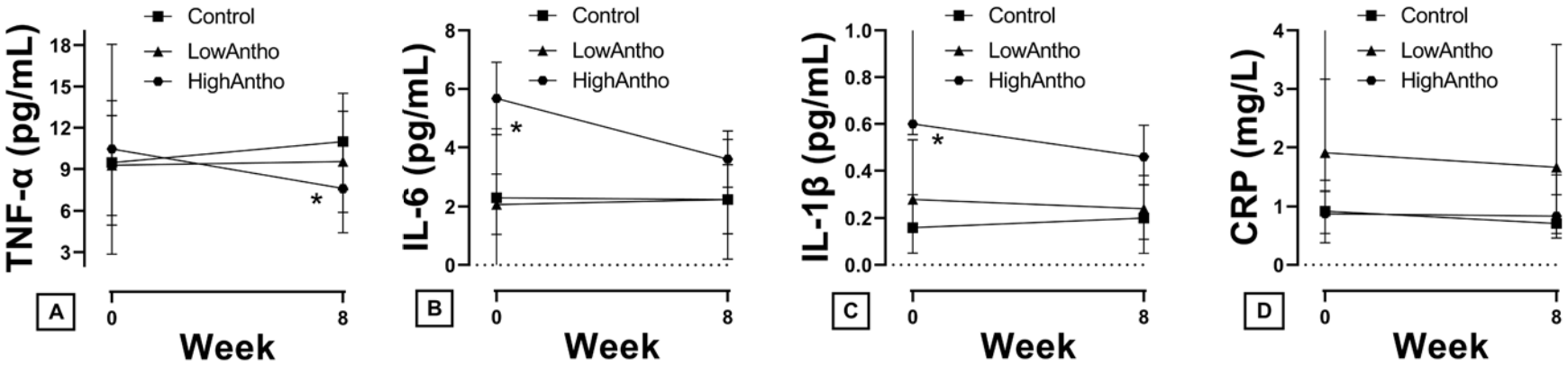
a) high dose anthocyanins (201 mg);

b) low dose anthocyanins (47 mg);

c) control (anthocyanin-free).

N = 31 adults with MCI (19 female, 12 male, mean age 75.3 (SD 6.9) y; BMI = 26.1 (SD 3.3) kg/m^2)

Results: Inflammatory biomarkers



Control: n =14; Low Anthocyanin: n = 10; High Anthocyanin: n = 7

Two-way mixed ANOVA with Time (Pre, Post) as the within subject variable and Treatment Group (High anthocyanins, Low anthocyanins, Control): *P<0.05

Results: Cognitive tests (by diet group)

	Group	n	Pre	Post	Time (P value)	Group (P value)	Time * Group
TEA teleph RS	Control	14	6.21 (SD 2.60)	6.09 (SD 2.96)	0.141	0.688	P=0.057, ηp^2=0.185
	LowAnth	10	5.15 (SD 1.51)	5.51 (SD 1.82)			
	HighAnth	7	6.43 (SD 3.57)	4.77 (SD 1.57)			

Two-way mixed ANOVA

Postprandial effects of Queen Garnet Plum on vascular function and inflammation: An acute feeding study

UOW: Vinicius do Rosario (PhD candidate), Karen Charlton, Katrina Green, Steven Roodenrys, Ian Wright, Monique Francois, Courtney Chang, Jaclyn Spencer

DAF: David Williams

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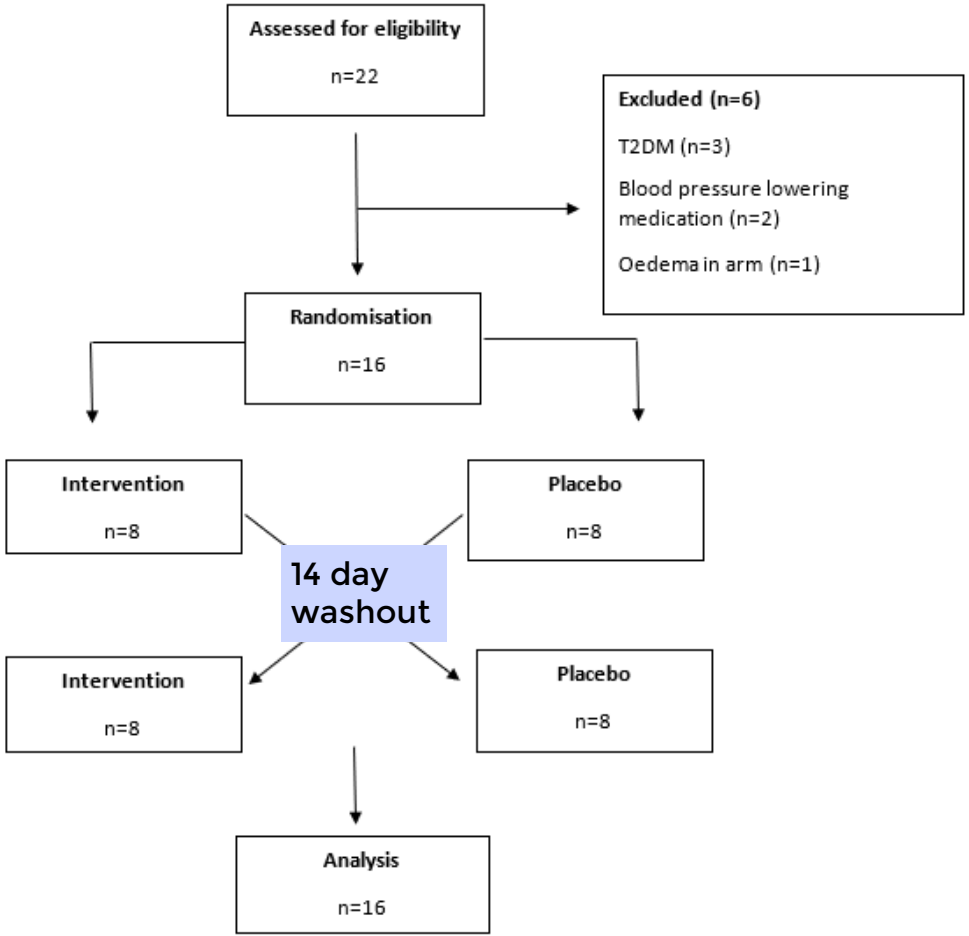
Study design

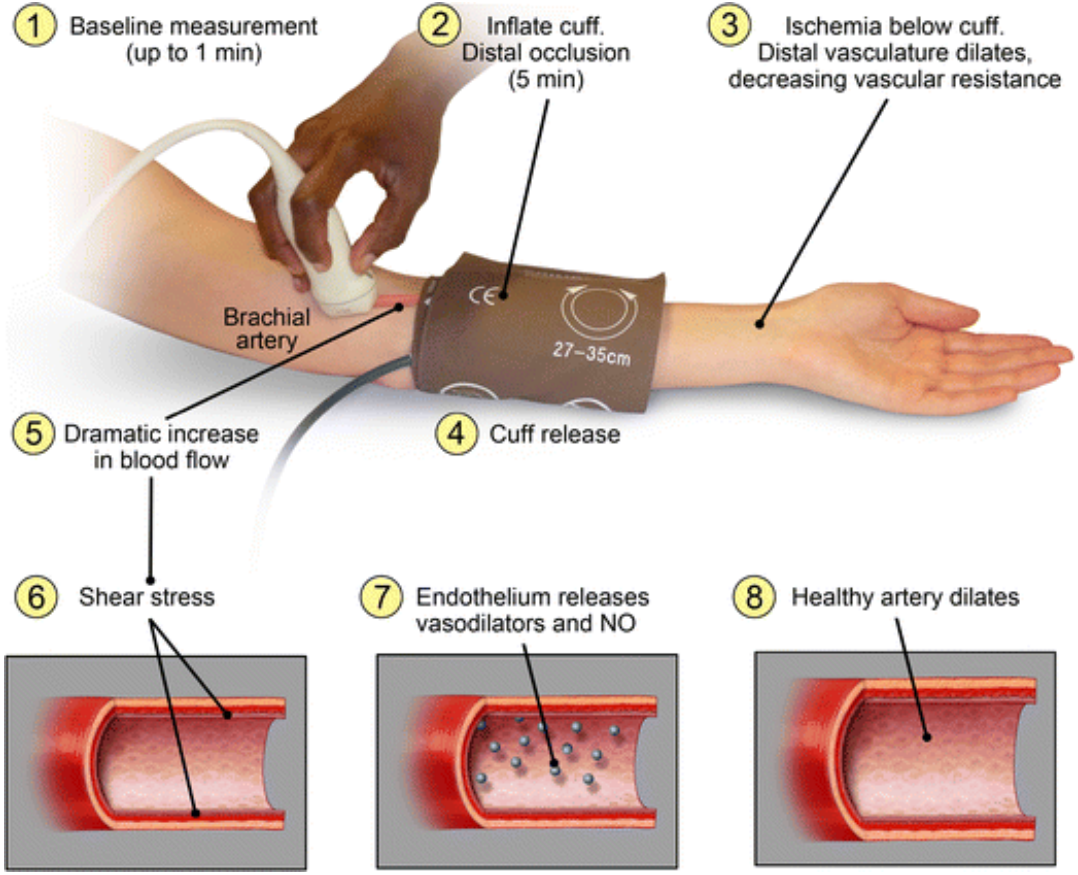
Aim: To investigate the acute postprandial effects of anthocyanins on vascular function, inflammation and cognition in adults, following a high fat meal.

Outcomes:

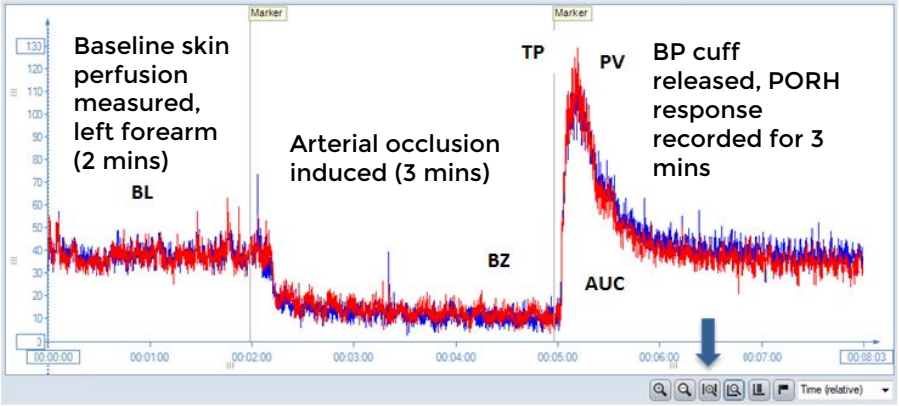
- Endothelial dysfunction (Flow Mediated Dilatation and Laser Speckle Contrast Imaging)
- Inflammatory & oxidative stress biomarkers
- Lipid levels
- Blood pressure
- Cognitive tests



Methods: Flow Mediated Dilatation



Measuring microvascular blood flow



BL: baseline; **BZ**: biologic zero; **TP**: time to peak; PV peak value; **AUC**: area under the curve

Parameters of microvascular blood flow:

(1) Perfusion Units (APU);

(2) Cutaneous Vascular Conductance (CVC): APU/Mean Arterial Pressure (mmHg).

- Laser Speckle Contrast Imaging (LSCI) technology
- Post-occlusive reactive hypermia (PORH)
- Temperature controlled room (22.5°C).

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Methods: Recruitment

- Internet
  - IHMRI
  - UOW
  - Facebook
- Flyers and Posters
  - Community Centres
  - Libraries
- Snowballing

FRUIT AND BLOOD PRESSURE STUDY

Are you 55+ years old, overweight and unaware of your blood pressure?

Come see us to check your blood pressure and see if you are eligible to join our study!

The School of Medicine at the University of Wollongong (UOW), along with the Illawarra Health and Medical Research Institute (IHMRI), will conduct a study to investigate the impact of fruit components on blood pressure and vessel health.

We are looking for overweight and obese individuals who have never been diagnosed or treated for hypertension (high blood pressure). The study will take place at IHMRI/UOW, where participants will come in two days with a two-week interval between them.

The study is focussed on nutrition and dietetics, so participants will be provided a full English breakfast along with the fruit juice/puree that is being studied. Participants will also undergo a series of health tests, and will need to provide blood and urine samples.

If you are interested in joining our study, please contact us at vadr998@uowmail.edu.au or leave a message on Ph: 4221 4072.

Eligibility criteria: ≥55 years; BMI ≥ 25kg/m^2; non-treated hypertension; no diabetes; $100 voucher provided; 3 day food record

Methods: High fat breakfast meal

- Baseline tests
- Breakfast + juice
- ~200mg anthocyanin per serve of intervention juice
- Postprandial tests

	Energy (kJ)	Total fat (g)	Saturated fat (g)
Hash Brown	540	6.8	0.5
Chipolatas	871	16.0	7.2
Croissant with butter & jam	995	13.4	9.3
Scrambled eggs	1310	29.1	15.9
Total	**3716kJ**	**65.3g**	**32.9g**

Methods: Measurements

0hr tests
- BP
- FMD
- LSCI
- Iontophoresis
- Bloods
- Subjective alertness

75min tests
- Digit Span test

2hr tests
- BP
- FMD
- LSCI
- Iontophoresis
- Bloods
- Subjective alertness

3hr tests
- Trail making test A & B
- Test of Everyday Attention
- ANT

4hr tests
- BP
- Bloods
- Subjective alertness

Urine tests- pooled
- 0hr-6hr
- 6-12hr
- 12-24hr

Blood tests

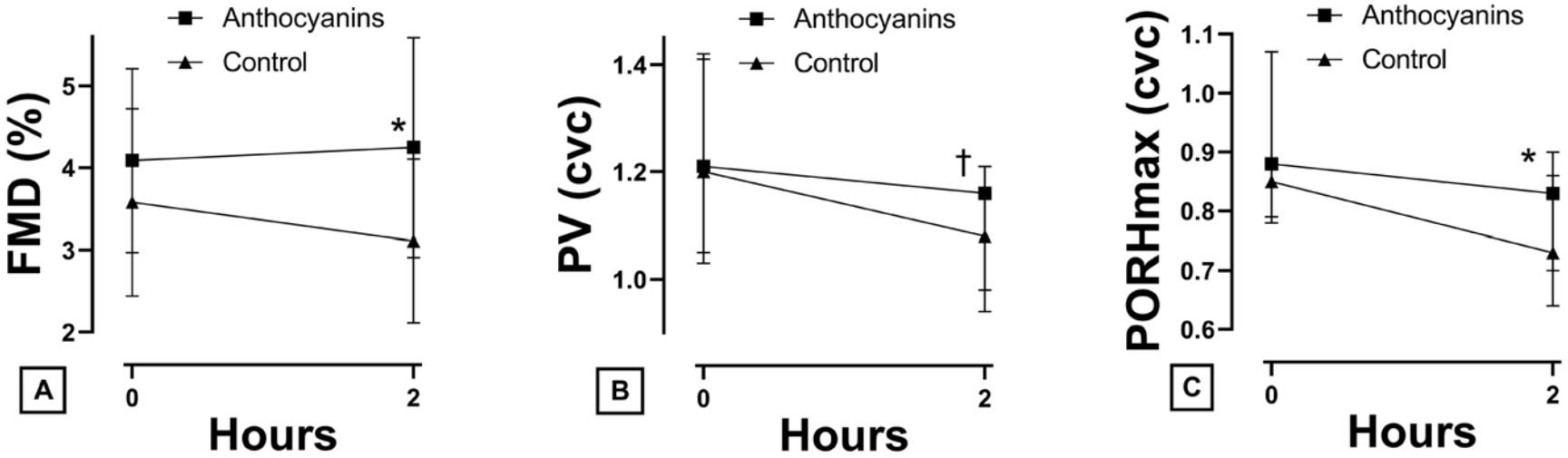
- Inflammatory markers (CRP; IL-6; IL-1β; TNF-α)
- Lipids (Triglycerides; Total cholesterol)
- Oxidative stress markers (Diacron reactive oxygen metabolite: d-ROM)

Results: BP and lipids

Blood pressure, triacylglycerol, total cholesterol before and after a high fat high energy meal challenge in control and intervention groups.

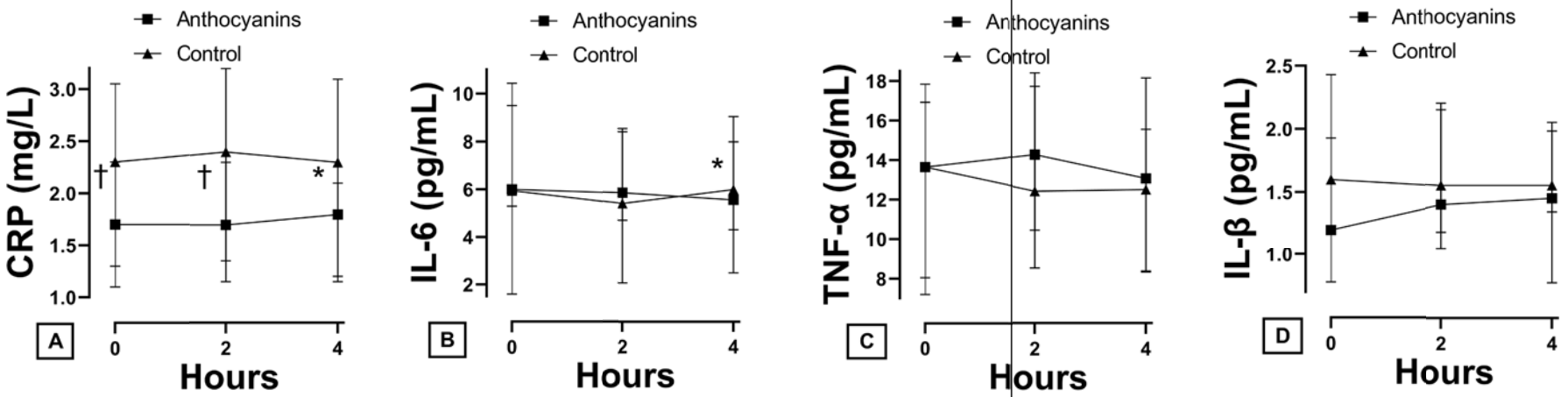
Measures	Group	Baseline	2h	4h	Time[a]	Treat-ment[a]	Time x treatment
SPB (mm Hg)	Control	118.9 (SD 11.1)	116.3 (SD 12.6)	123.2 (SD 12.8)	0.001*	0.692	P=0.759
	Anthocyanins	118.8 (SD 12.9)	117.7 (SD 10.6)	123.4 (SD 12.4)			
DBP (mm Hg)	Control	70.1 (SD 6.9)	67.4 (SD 7.3)	70.5 (SD 7.6)	0.002*	0.148	P=0.203
	Anthocyanins	68.0 (SD 6.7)	66.6 (SD 5.5)	70.8 (SD 6.6)			
Triglyceride (mmol/L)	Control	0.95 (IQR 0.79)	1.30 (IQR 0.96)	2.12 (IQR 1.45)	>0.001*	0.357	P=0.921
	Anthocyanins	0.89 (IQR 0.89)	1.29 (IQR 1.35)	2.22 (IQR 2.35)			
Total cholesterol (mmol/L)	Control	6.16 (IQR 1.39)	6.02 (IQR 1.65)	6.09 (IQR 1.26)	>0.001*	0.756	P=0.530
	Anthocyanins	6.28 (IQR 1.27)	6.40 (IQR 1.16)	6.27 (IQR 1.14)			
DROM (cu)	Control	487.3 (SD 77.6)	497.1 (SD 81.1)	502.6 (SD 68.3)	0.002*	0.298	P=0.480
	Anthocyanins	473.1 (SD 75.5)	496.4 (SD 77.0)	496.5 (SD 78.6)			

Results: Blood flow effects



*P<0.05; †P=0.088; Wilcoxon signed rank test

Results: Inflammatory Biomarkers

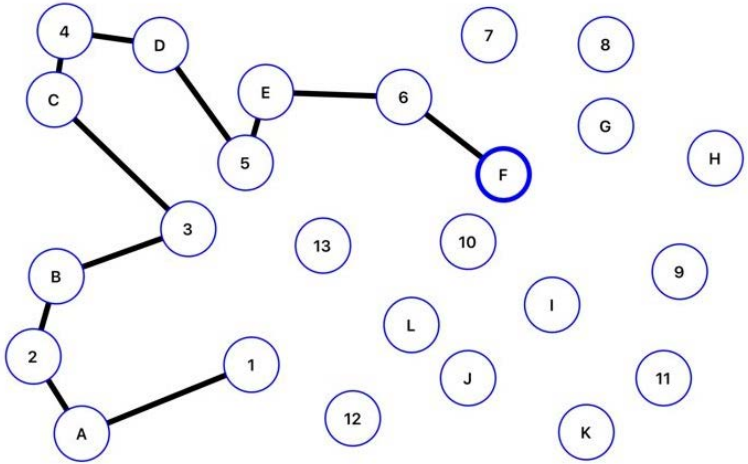


*P<0.05 (Wilcoxon signed-rank test); † P=0.095 at 0h and P=0.099 at 2h (Wilcoxon signed-rank tests).

Results: Cognitive tests

Cognitive testing

- 10 tasks
  - Divided attention*
  - Working memory
  - Executive control
  - Visual attention
  - Speed of processing
- Alertness+
- Visit order



Significant treatment effect only found for one cognitive test- elevator counting with distraction (assesses divided attention), n = 13

Conclusions

- Inflammatory markers good response
- FMD good response, of clinical significance
- Microvascular benefits
- Potential effect of 4 day run in period?
- Baseline BP and lipids- less effect of anthocyanins
- No adverse effects

Queensland Government
Department of Agriculture and Fisheries

QGP fruit and analyses (in-kind)

Challenges with measuring dietary flavonoid intake

Nutrition & Dietetics 2018; **75**: 106–116 DOI: 10.1111/1747-0080.12371

ORIGINAL RESEARCH

Development, validation and reproducibility of a food frequency questionnaire to measure flavonoid intake in older Australian adults

Katherine KENT [1,2] and Karen E. CHARLTON [2,3]

[1]Centre for Rural Health, School of Health Sciences, Faculty of Health, University of Tasmania, Launceston, Tasmania, [2]School of Medicine, Faculty of Science, Medicine and Health, University of Wollongong and [3]Illawarra Health and Medical Research Institute, Wollongong, New South Wales, Australia

Kent & Charlton Food Frequency Questionnaire

Fruit

How many pieces of fresh fruit do you usually eat per day?

- ☐ NEVER (go to question 37)
- ☐ less than 1 piece of fruit per day
- ☐ 1 piece of fruit per day
- ☐ 2 pieces of fruit per day
- ☐ 3 pieces of fruit per day
- ☐ 4 or more pieces of fruit per day

15. Over the past 12 months, when in season, how often did you eat blueberries?

- ○ 6 or more times per day
- ○ 4 to 6 times per day
- ○ 2 to 3 times per day
- ○ 1 time per day
- ○ 5 to 6 times per week
- ○ 3 to 4 times per week
- ○ 1 to 2 times per week
- ○ 2 to 3 times per month
- ○ 1 time per month or less
- ○ NEVER *(go to the next question)*

Each time you ate blueberries, how much did you usually eat?

- ☐ less than ¼ cup
- ○ ¼ a cup
- ○ ½ a cup
- ○ More than ½ a cup

Kent K, Charlton KE, 'Development, validation and reproducibility of a food frequency questionnaire to measure flavonoid intake in older Australian adults', *Nutr Diet* 2018; 75: 106-116.

Measuring Dietary Anthocyanins: Food Composition Tables

Journal of Food Composition and Analysis 64 (2017) 33–38

Contents lists available at ScienceDirect

Journal of Food Composition and Analysis

journal homepage: www.elsevier.com/locate/jfca

Original research article

First stage development of an Australian anthocyanin food composition database for dietary studies – A systematic process and its challenges☆

Ezinne Igwe*, Elizabeth Neale, Karen E. Charlton, Kurt Morton, Yasmine C. Probst

School of Medicine, University of Wollongong, NSW 2522, Australia

Fruit/vegetable	USDA database (mg/100 g)	Phenol-Explorer database (mg/100 g)	Australian data (mg/100 g)
Strawberry	2.24	73.01	2.02
Blueberry	163.3	133.99	381.75
Plum	56.05	47.79	89.8
Red cabbage	209.95	- [a]	57.4

[a] Not reported.

Sources of anthocyanins in Australians

Top 10 food sources (%) of total anthocyanin intake

Age (y) N	31–50 3565		51–70 2907		71 + 1277	
1.	Eggplant[§]	8.1	Eggplant[§]	23.1	Eggplant[§]	26.4
2.	Blackberry, raw	7.4	Grape, raw[‡]	9.1	Wine, red,	10.3
3.	Cherry, raw	5.7	Blackberry, raw	8.4	Cherry, raw	8.3
4.	Blueberry, raw	5.1	Wine, red	7.8	Blueberry, raw	7.1
5.	Raspberry, raw	4.9	Blueberry, raw	7.1	Blackberry, raw	5.1
6.	Cranberry, raw	4.8	Cherry, raw	6.3	Plum, unpeeled, raw	4.9
7.	Grape, black sultana, raw	4.6	Plum, unpeeled, raw	4.7	Raspberry, purchased frozen	4.7
8.	Radish, peeled or unpeeled, raw	4.4	Raspberry, raw	2.9	Grape, Thompson,	3.4
9.	Raspberry, purchased frozen	4.3	Blueberry, purchased frozen	2.6	Radish, raw	3.2
10.	Wine, red, sparkling	4.1	Cabbage, red, raw	2.4	Raspberry, raw	2.9
TOTAL		53.5		74.4		76.3

Secondary analysis of National Nutrition and Physical Activity component of the Australian Health Survey, 2011-12

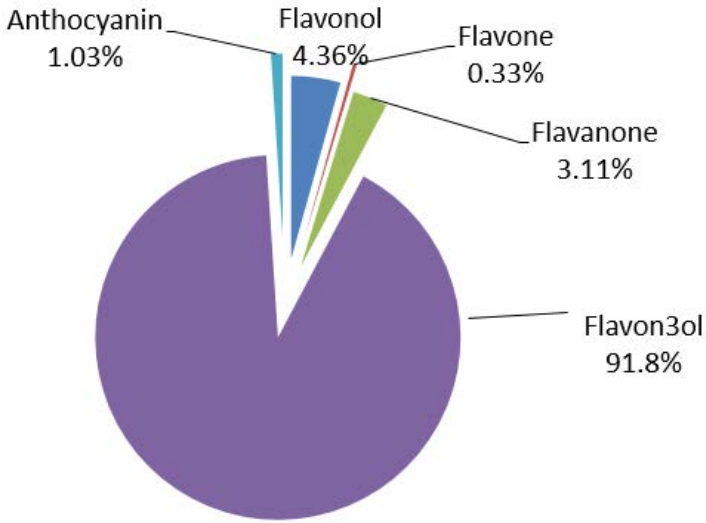
Mean anthocyanin intake was **24.2 (0.3) mg day**.

Significant inverse association between anthocyanin intake and **systolic BP** ($b = 0.04, F = 16.8$, d.f. = 6, $r_2 = 0.05$, $P < 0.01$) and **diastolic BP** ($b = 0.01$, $F = 5.35$, d.f. = 6, $R_2 = 0.013$, $P < 0.01$), in models that adjusted for covariates.

Igwe, Charlton & Probst. *J Hum Nutr Diet* 2019; Early view. https://doi.org/10.1111/jhn.12647

Sources of flavonoids in older Australians

Flavonoid Subclass	Food	% Contribution to Subclass
Flavan-3-ols	Tea, black	94.55
	Tea, green	3.52
	Apple	0.40
	Banana	0.39
	Wine, red	0.155
Flavonols	Tea, black	68.59
	Onion	7.73
	Apple	3.39
	Tea, green	2.78
	Beans	2.76
Flavones	Parsley	98.52
	Tomato	0.69
	Celery	0.27
	Pumpkin	0.23
	Watercress	0.13
Flavanones	Oranges	44.47
	Orange juice	36.78
	Mandarin	4.07
	Tomato	3.06
	Grapefruit juice	2.80
Anthocyanins	Blueberry	29.56
	Banana	22.81
	Radish	9.14
	Wine, red	8.19
	Cabbage, red	7.71



% Contribution to overall flavonoid intake according to 12 days of WFRs (n=79) from participants in the Blue Mountains Eye Study

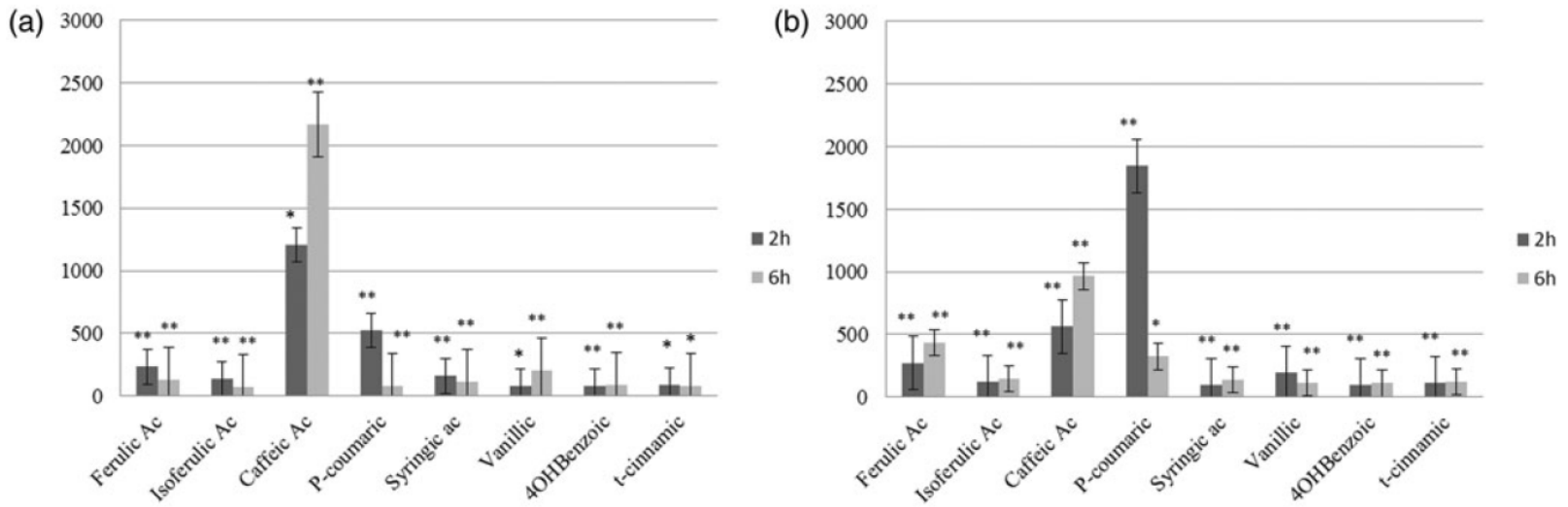
Kent, Charlton et al. *J Nutr Gerontology and Geriatrics* **2015; 34: 388-398,**

Measuring Anthocyanins: Biomarkers

Acute cross over study – 300ml cherry juice; percentage change in plasma concentrations of polyphenolic and aromatic acids over 2 and 6 hours

Young, n = 6; 21.8 (0.97)y; BMI 26.3 (4.2)

Old, n =7; 77.5 (6.2)y; BMI 28.6 (3.8)



P>0.05, **p<0.001, Bonferroni post-hoc analyses for differences between 0 and 2 h, or 0 and 6 h.

Kent K, Charlton KE, Jenner A, Roodenrys S, *Int J Food Sci Nutr* **2015; 67: 47-52.**

Effect of cold storage on QGP puree

Anthocyanin contents (mg cyanidin-3-glucoside equivalents/100 g FW) for two types of puree samples, AOAC-based spectrophotometric method together with the % decrease when compared to the value at Day 1.

Day	Storage	Sample type	ANTH mg.C3G eq./100g FW	% Decrease from Day 1
1	Fridge	Puree	114.3	
4	Fridge	Puree	104.8	8.2
7	Fridge	Puree	101.4	11.2
14	Fridge	Puree	86.2	24.6
14	Freezer	Puree	113.8	0.4
30	Freezer	Puree	110.5	3.3
1	Fridge	Puree+Water	94.0	
4	Fridge	Puree+Water	87.9	6.6
7	Fridge	Puree+Water	87.1	7.4
14	Fridge	Puree+Water	78.4	16.7
14	Freezer	Puree+Water	93.1	1.1
30	Freezer	Puree+Water	91.7	2.5

Food components, foods and whole diets

Flavonoids (food components) and hypertension

Middle-aged (n = 6630), 15y hypertension incidence 24.9%.
Lower risk associated with higher intakes of:
Flavones (adjusted relative risk (ARR) for quintile 5 vs 1: 0.82, 95% CI: 0.70-0.97);
Flavanones (0.83, 0.69-1.00)
Isoflavones (0.86, 0.75-0.99);
(orange, orange juice, apples and soy milk)

Reproductive-aged (n = 6099), 12y hypertension incidence 5.5%
Lower risk associated with higher intakes of:
Flavanols (ARR for quintile 4 vs 1: 0.70, 95% CI: 0.49-0.99);
Total flavonoids (0.68, 0.46-1.01, p=0.058)
(orange juice, red wine, apples and onions)





do Rosario VA, Shoenaker DAJM, Kent K, Weston-Green K, Charlton K. Association between flavonoid intake and risk of hypertension in two cohorts of Australian women: a longitudinal study. *Eur J Nutr*. In review.

Chocolate…

Intermediate (520 mg) or high (993 mg) cocoa flavanols. Aim for 200 mg/day of cocoa flavanols

Reference	Participants	Flavanols amount	Cognitive measures	Principal findings
Francis et al. (31)	16 subjects (all females; 18–30 years)	Cocoa drinks containing 172 and 13 mg flavanols daily over a 5-day period	Task switching paradigm	Increased BOLD signal in response to the task switching paradigm after the higher flavanol drink, with no significant behavioral effect
Crews et al. (34)	101 subjects (41 males, 60 females; mean age: 69 years)	Chocolate bar containing 397 mg flavanols, chocolate drink containing 357 mg flavanols, or similar placebo	Selective Reminding Test, Stroop Test, Trail Making Test, Wechsler Adult Intelligence Scale-III (Digit Symbol-Coding Subtest), Wechsler Memory Scale-III (Faces I and Faces II Subtests)	No differences in cognitive performance between placebo and polyphenol groups
Camfield et al. (35)	63 subjects (40–65 years)	Cocoa drinks containing 500, 250, and 0 mg flavanols (placebo) over a 30-day period	Spatial Working Memory Test	SSVEP changes indicating improved working memory function after flavanol treatment, with no significant behavioral effect
Desideri et al. (36)	90 subjects with Mild Cognitive Impairment (43 males, 47 females; 64–82 years)	Cocoa drinks containing 993, 520, or 48 mg (low-flavanol) flavanols daily over an 8-week period	Mini-Mental State Examination, Trail Making Test (A–B), Verbal Fluency Test	Improvements in blood pressure, insulin resistance and Tail Making Test (A–B) performance for high and intermediate flavanol groups compared to the low-flavanol group. Improved verbal fluency performance in the high-flavanol group
Sorond et al. (37)	60 subjects with vascular risk factors (29 males, 31 females; mean age: 72.9 years)	Cocoa drinks containing 609 or 13 mg (flavanol-poor) flavanols daily over a 30-day period	Mini-Mental State Examination, Trail Making Test (A–B)	Improvements in neurovascular coupling and Trial Making Test B performance for the flavanols group, only in those with impaired neurovascular coupling at baseline
Brickman et al. (38)	37 subjects (13 males, 24 females; 50–69 years)	Cocoa supplement containing 900 or 10 mg (low-flavanol) flavanols daily over a 3-month period	Modified Benton Task (dentate gyrus-dependent memory task)	Correlation between increased cerebral blood volume in the dentate gyrus and improvements in the Modified Benton Task performance in the high-flavanol group
Mastroiacovo et al. (39)	90 subjects (37 males, 53 females; 65–85 years)	Cocoa drinks containing 993, 520, or 48 mg (low-flavanol) flavanols daily over an 8-week period	Mini-Mental State Examination, Trail Making Test (A–B), Verbal Fluency Test	Improvements in blood pressure, insulin resistance and Tail Making Test (A–B) performance for high and intermediate flavanol groups in comparison to low-flavanol group. Improved verbal fluency performance among all treatment groups
Neshatdoust et al. (40)	40 subjects (22 males, 18 females; 62–75 years, mean age: 68.3 years)	Cocoa drinks containing 494 and 23 mg (low-flavanol) flavanols daily over a 28-day period	Several cognitive tasks measuring executive functions, episodic memory, working memory, spatial memory, implicit memory, attention and processing speed	Higher BDNF serum levels and improvements in global cognition scores following high-flavanol treatment

BDNF, brain-derived neurotrophic factor; BOLD, blood oxygenation level-dependent; SSVEP, steady-state visually evoked potentials.

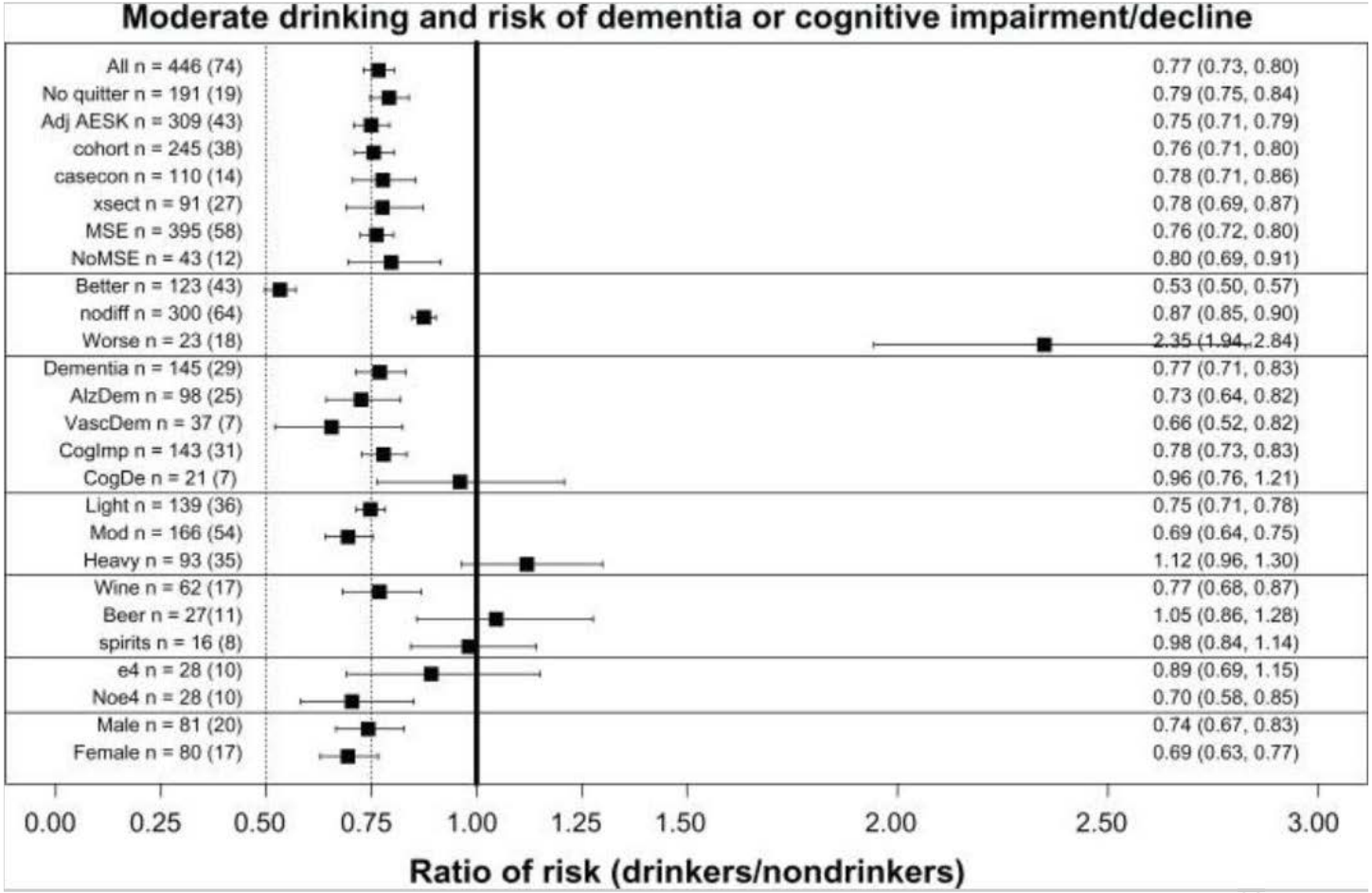
Socci et al. *Front. Nutr* 2017;
| https://doi.org/10.3389/fnut.2017.00019

Chocolate…

- Fermented, roasted, and finely ground seeds of *Theobroma cacao* tree.
- Ground cacao = Cacao butter (natural oil) + ground particles cacao seed.; potent mix of phytochemicals, mostly flavanols and proanthocyanidins.

- Choose chocolate bars labelled "70%" (70% ground cacao and 30% sugar).
- Flavanols often destroyed in the production of chocolate and cocoa powder (Dutch method) – choose natural cocoa powder.
- Aim for 200 mg/day cocoa flavanols.
- Dark chocolate has more flavanols than milk chocolate. Range = 100 mg to 2,000 mg/100g (ave = 170 mg/100g).
- 70–85% cocoa solid chocolate: 604 calories (2525kJ), 8g protein, 43g fat.

Wine?



Neafsey EJ,Collins MA. *Neuropsychiatr Dis Treat*; 2011; 7: 465–484.

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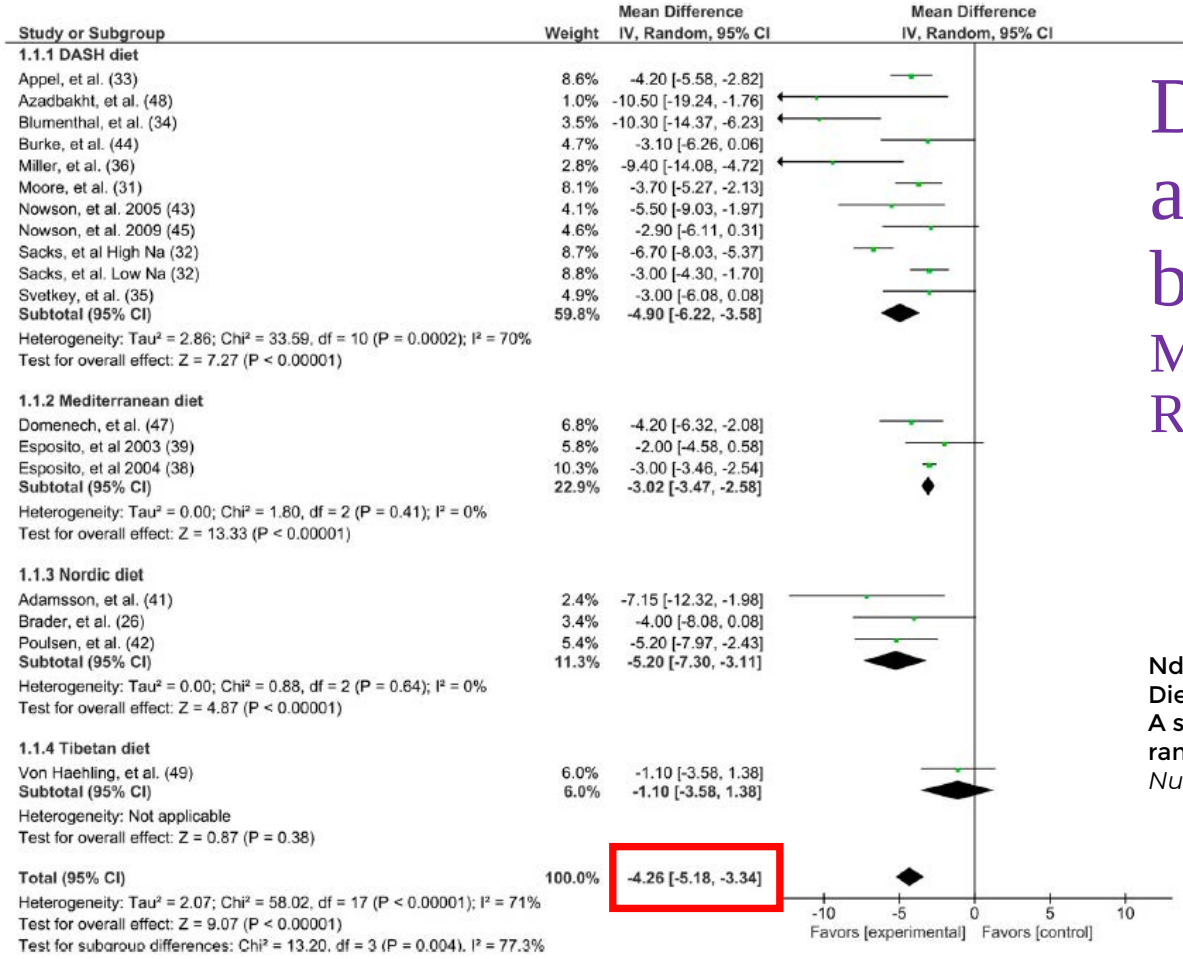
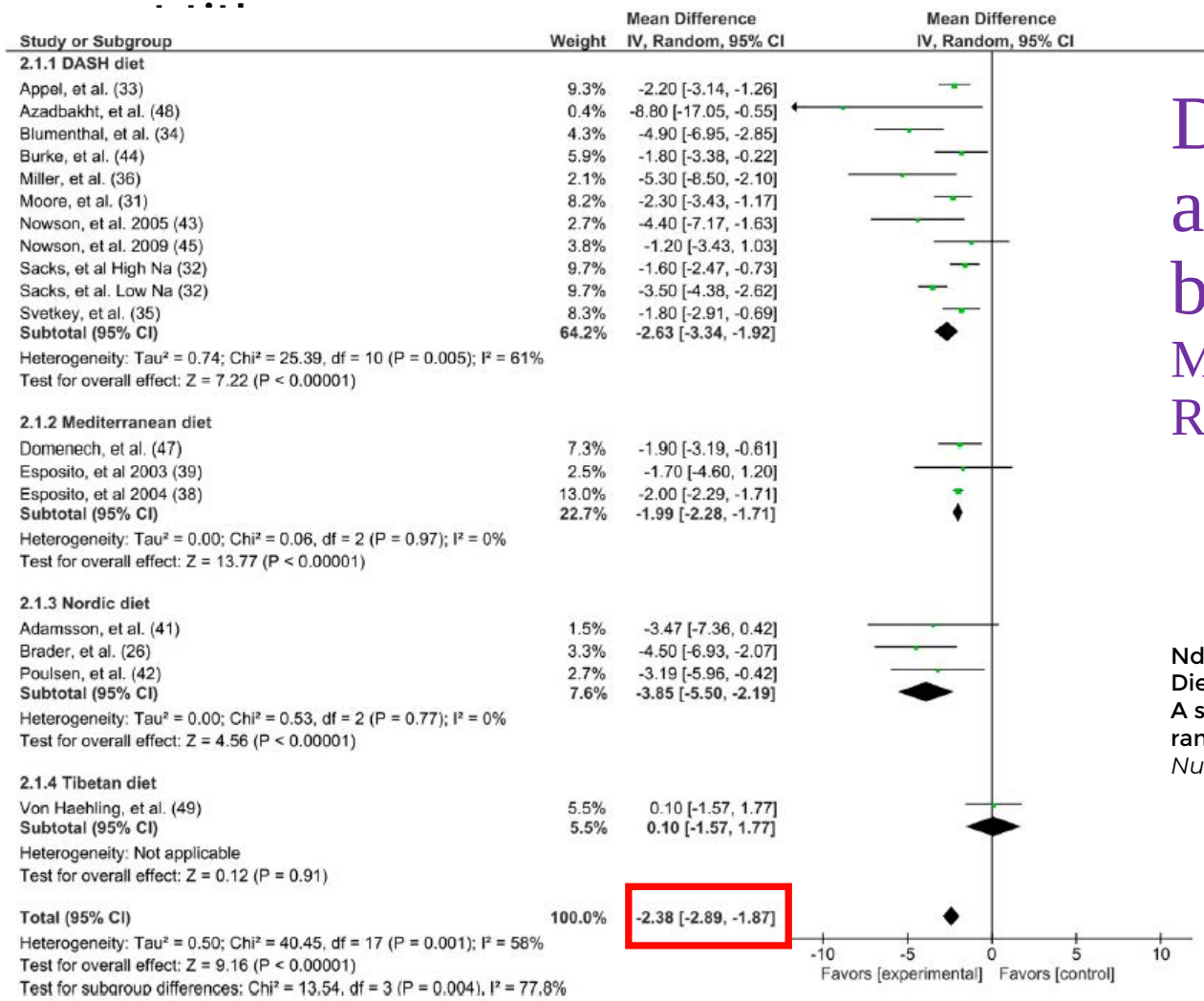


Dietary patterns and systolic blood pressure:

Meta analysis of 17 RCTs

Ndanuko RN, Tapsell LC, Charlton KE. *et al.* **Dietary patterns and blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials.** *Advances In Nutrition*. **2016;7:76-89.**



Dietary patterns and diastolic blood pressure:

Meta analysis of 17 RCTs

Ndanuko RN, Tapsell LC, Charlton KE. *et al.* **Dietary patterns and blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials.** *Advances In Nutrition*. **2016;7:76-89.**

Characteristics of dietary patterns (g food/day)

Food group	DASH diet	Nordic diet	Med diet	Western diet (Control)
Fruit	750 g/d	300 g/d	>300 g/d	300 g/d
Vegetables	300 g/d	375 g/d	>150 g/d	150 g/d
Whole grains	280 g/d	240 g/d	400 g/d	Refined grains 280 g/d
Low fat dairy	500 g/d	500 g/d	Not specified	Nil
Fish	100 g/wk	300 g/wk	>300 g/wk	Nil
Meat	35 g/d	70 g/d	70 g/d	105 g/d
Nuts/ legumes	30g	30g	30g	Nil
Other			Olive oil 8 g/d	
Snacks/ sweets	1 serve/d			4 serves/d

Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J., Dietary patterns and blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials. *Advances In Nutrition*. 2016;7:76-89.

Putting it together

Document title

Author, Country	Dietary interventions	Patient group	Results
Soininen *et al.*, 2017 Finland, Germany, Netherlands, and Sweden	**LipiDiDiet** (Fortasyn Connect; Souvenaid®). RCT 24 months.	N = 311 promodal AD	No change in Neuropsychological Test Battery (low power)
Freund-Levi *et al.*, 2006 Sweden	**OmegAD trial** – 6 month RCT of omega-3 fatty acid supplementation	N = 174 patients with mild to moderate AD	Improved cognition only in patients with very mild AD (MMSE >27).
Estruch *et al.*, 2018 Spain	**PREDIMED:** 1.Mediterranean diet + EVOO 2.Med diet + mixed nuts 3.Control diet	N = 447 cognitively healthy volunteers, mean age, 66.9y at high CVD risk	Med +EVOO associated with higher scores of global cognitive performance after 6.5 year intervention.
Marseglia *et al.*, 2018 France, Italy, UK, Netherlands and Poland.	**NU-AGE** study. 12-month RCT of personally-tailored Med diet.	N = 1250 older adults, 65-79y	Higher adherence to Med diet associated with improvements in overall cognition.
Ngandu *et al.*, 2015 Finland	FINGER study. 24-month: Combination of exercise, diet, cognitive training, management vascular risk factors.	N = 1260 older at-risk individuals aged >60 years	Promising results on overall cognitive outcomes but individual components cannot be separated.
Morris et al., 2015b; Morris et al., 2015c	**MIND** (Mediterranean-DASH Intervention for Neurodegenerative Delay). 3-year intervention	n = 600 individuals 65+ y without cognitive impairment; overweight; sub-optimal diets.	Ongoing

Where to next? Anthocyanin content of Australian foods

Food	Total Anthocyanin mg/100g
Blackberry	438
Blueberry	382
Cherry	210
Tasmanian pepperberry	607
Queen Garnet plum	195
Illawarra plum	557
Burdekin plum	175
Bush Cherry	106

Conclusions

- Anthocyanins in plant foods show promise for cognitive benefits, mediated possibly through effects on vascular function;
- Anti-inflammatory potential;
- Mechanisms yet to be fully elucidated (gut-brain axis); microbiota may influence absorption and metabolism;
- Synergistic effects of combinations of flavonoid-rich foods;
- Mild cognitive impairment or early dementia provide greatest opportunity for intervention;
- Clinical trials are essential, but difficult to conduct.

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- Health Impacts Research Cluster
- University Global Partnership Network

Illawarra Health and Medical Research Institute

AGRITECHNOLOGY

Cherry juice (in-kind)

Nutrafruit
naturally better

QGP juice (in-kind); seed funding

Appledale Processors
Co-operative Ltd

Apple juice (in-kind)

Queensland Government
Department of Agriculture and Fisheries

QGP fruit/analyses (in-kind)