Substance use and cognitive disorders in later life

25 May 2018

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Alcohol related brain injury

- Covers a wide range of presentations
  - Mainly impaired memory, executive function, judgement
  - Umbrella term

Wernicke-Korsakoff Syndrome

- Thiamine deficiency

"Alcohol related Dementia"

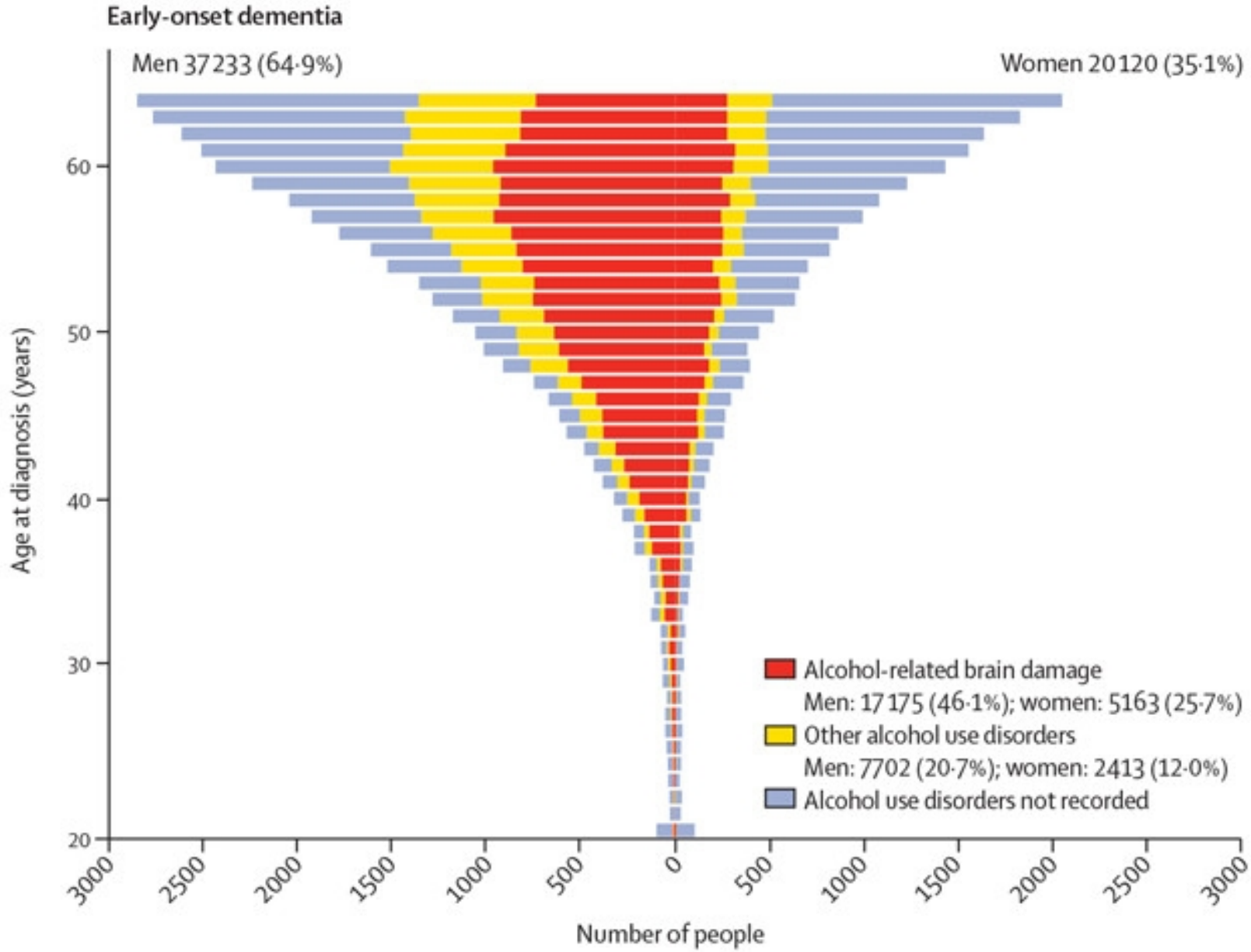
- Alcohol induced toxicity

Other persistent alcohol-related cognitive impairment

- TBI,CVD,depression, effects malnutrition / end organ dysfn etc

Alcohol related brain injury

- There are different considerations in older patients
- Numbers admitted UK with amnestic syndromes a/w alcohol by age
  - 15-59 yrs ↑ <10%
  - 60+ yrs ↑ 140%



**greatest modifiable risk factor.

Alcohol – 56% dementia cases. But is it alcohol or poor diet, lifestyle, concomittant smoking, CVS disease, depression, social isolation, or failure to comply with medical management??

- Compare the projected effect size of the last slide with effect of ApoE4 status in late onset dementia :
  - Estimated around 7%.

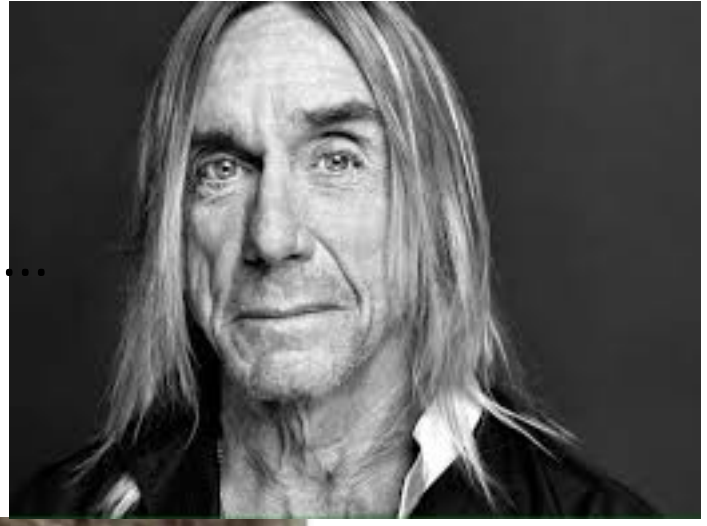
Table 1. Alcohol drinking status, frequency and consumption among older Australians and all Australian adults, 2013 [5]

Age group	Abstainers (%)	Drink daily (%)	Risky drinking (%)*
50-59	19.0	9.0	20.1
60-69	24.4	12.4	18.6
70+	40.3	14.7	10.1
All ages 18+	22.6	6.9	19.1

* at a level to be at risk of alcohol-related harm over a lifetime [4]

Baby Boomers are ageing :

more liberal attitudes to substance use…..



Alcohol in older patients

- Less does more

  Higher sensitivity to effects

  Decreased ability to metabolise

  Balance – Comorbidities, risks, cognitive reserve

The problem of comorbidities

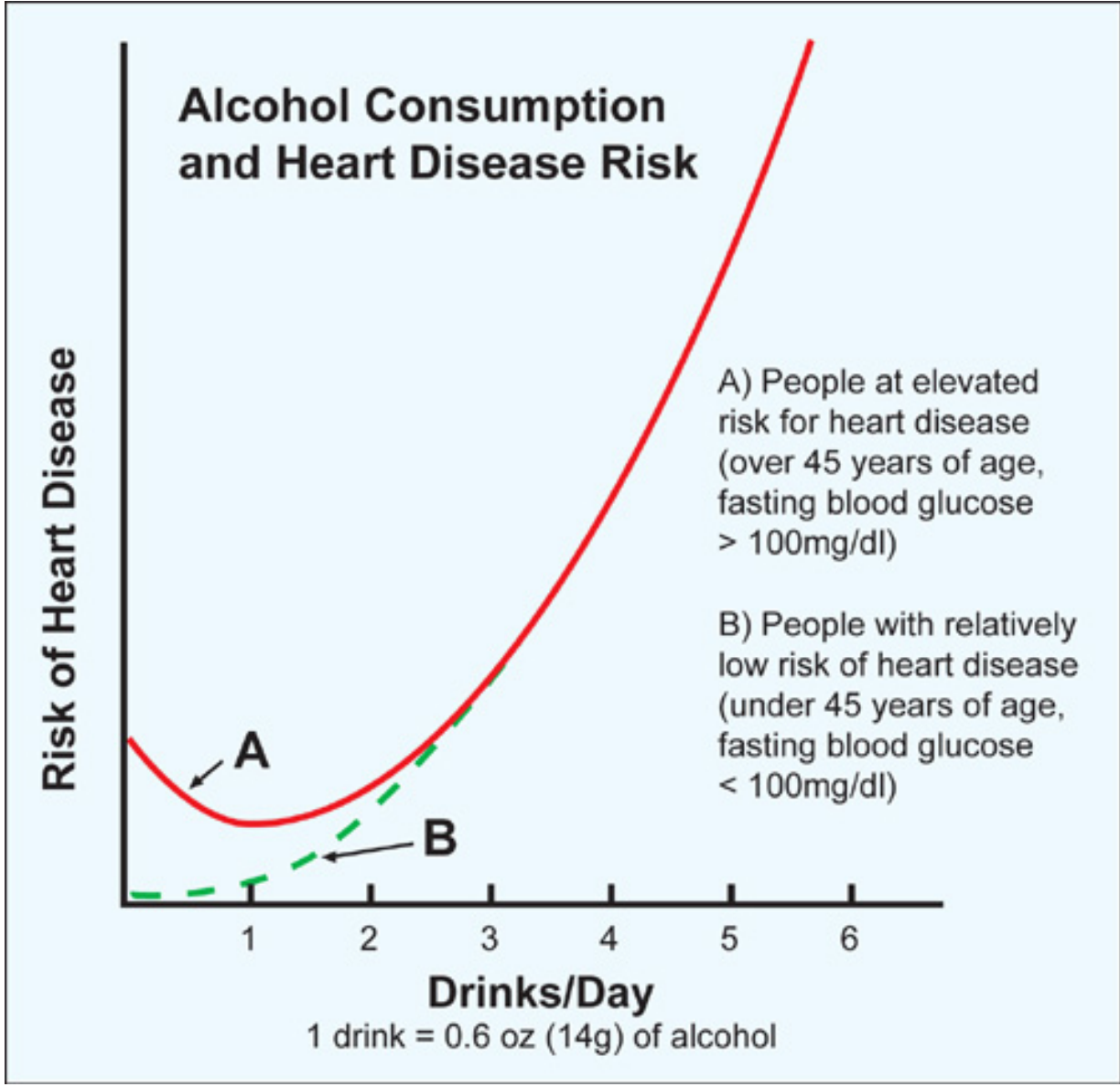
- Often no single presenting problem cf. younger patients
- Frailty
- Increased risk for cognitive change
- Falls
- Iatrogenic harm – polypharmacy /hosp
- Metabolic changes

… Same goes for our brains as the rest of us

?Benefits mainly confined to CHD

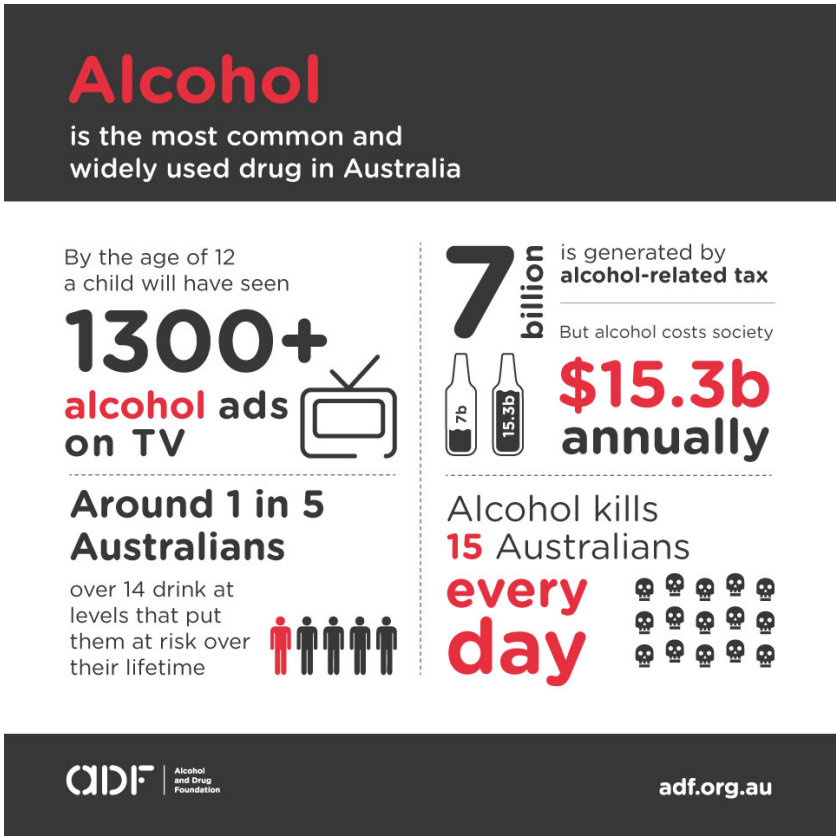
Countries where CHD risk low, Little or no benefit

Recent studies Dementia / alc : mixed



What are ‘safe’ levels of alcohol then?

- NHMRC guidelines (2009)
  - for younger groups
  - UK guidelines
    - <14g = 1.5 units/d
    - <11 units per week
  - Binge defined as
    - >4.5 units for men
    - >3 units for women



Alcohol - comorbidities

- Alcohol affects many organ systems, not just CNS
- Neurological
    - Cerebellar dysfunction, Myopathy, Seizures, cognitive, peripheral neuropathy
- Cardiomyopathy
- Anaemia
- Hypoglycaemia, pancreatitis, hepatic dysfunction
- Nutritional deficiency – thiamine, piridoxine, etc
- Foetal alcohol syndrome
- Secondary – sleep disorders, stroke, depression, suicide

What is cause and what is effect can be unclear

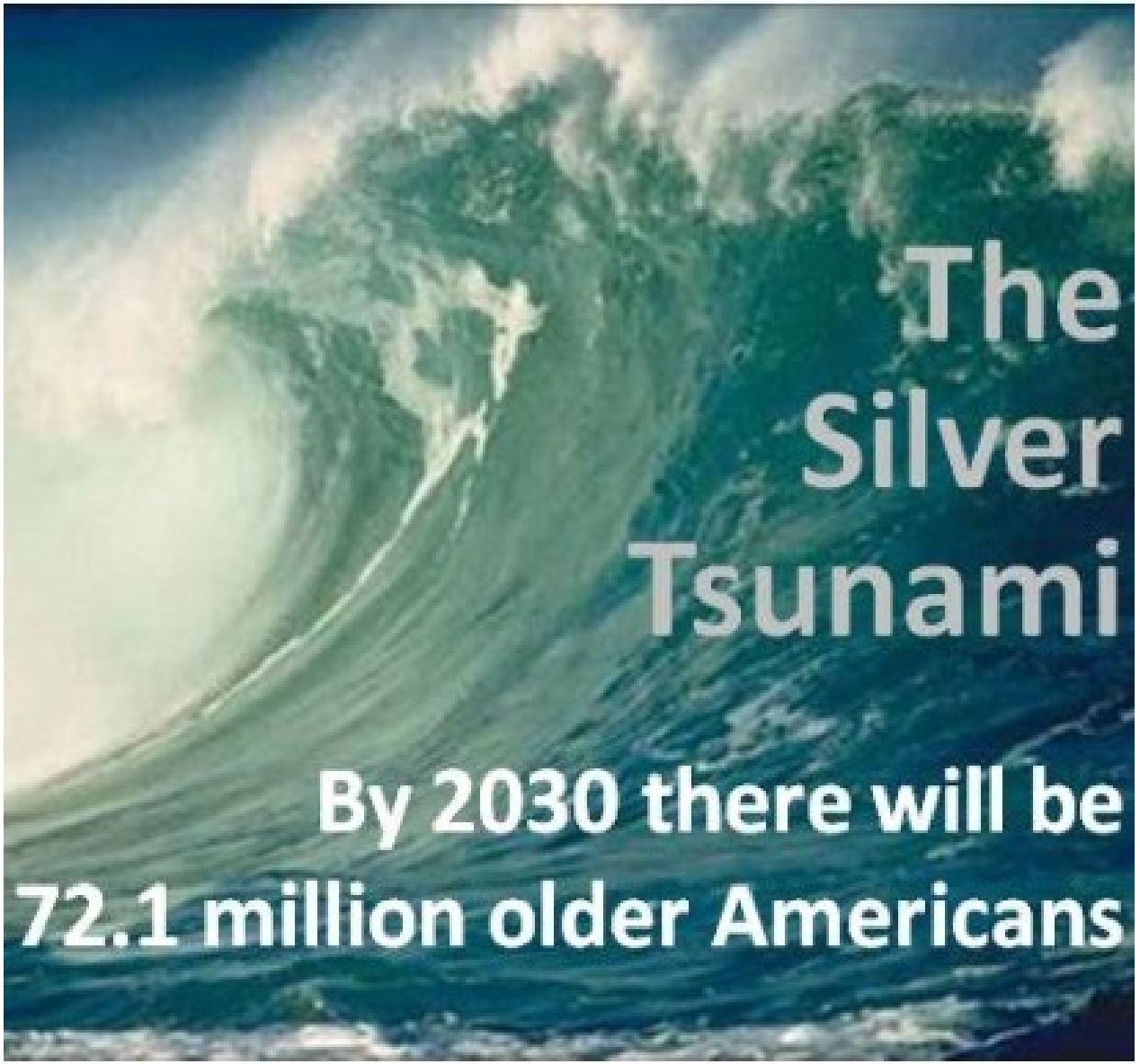
So what is ‘old’ then?

Depends on drug misuse and comorbidities

Different ages depending on services

- Aged care >75
- MH services >65*
- D&A services 50+
- Medical wards UK studies

- General practitioners


The
Silver
Tsunami
By 2030 there will be
72.1 million older Americans

AOD use, depression, and suicide

- Older people self report drinking for pain, meaningless life, anxiety / mood, loneliness, sleep problems
- Psychological autopsy 261 suicides aged 35+ and 73 aged 70+ De Leo and Draper 2013
  - 22% alcohol abuse
  - 18% other substances

Pattern of use in later life

- Long history which persists into older age ("survivors"), 2/3 of US problem drinkers
  - Often mult comorbidities
  - Less intact relationships, more likely depression etc
  - Might have better understanding of psych / AOD services but less success utilising these on their own

Pattern of use in later life

- About 1/3 commence in later life ("reactors")
  - Adjustment (retirement, bereavement, illness)
  - Collateral info from families – often unaware
  - Underestimate harms given older age
  - May forget amounts if early dementia
- Cf survivors – less knowledge of available help but better prognosis

Pattern of use in later life

- Previously “unproblematic” use continues into older age but now with complications – “maintainers”

- E.g. 66 yo lady, 6 years bereaved, always 2 glasses wine /d over 40 years, lives by self, now p/w falls while at social functions. GP finds abnormal liver function and hypertension, poor balance

Acute alcohol use disorders

Think of if confused / agitated, sleep/wake disturbance, hallucinations

- Intoxication / withdrawal
- Wernicke's
- Delirium - DT's or delirium due to another medical illness
- Treat as urgent, high rates morbidity / mortality
- Other - Hallucinosis
    - AH, VH, paranoid delusions
  - Higher morbid jealousy

Wernicke's

- Severe thiamine deficiency : malnutrition, persistent vomiting, GIT / bariatric surgery, anorexia
  - Caine's criteria (1997) : at least 2 of
    - Dietary deficiency
    - Oculomotor signs (nystagmus, palsies)
    - Cerebellar dysfunction
    - Either altered mental state or mild memory imparment
  - Increases diagnostic sensitivity from 20% to 85%

Wernicke's

- Only a minority suspected during life : 20%
- 10 – 20% only with classic triad of signs
- Of those cases suspected,
  - 30% alcohol dependent
  - 6% non-alcohol dependent
- Untreated : up to 20% mortality, 85% survivors develop KS

- Developed world : decreasing population prevalence (thiamine in bread); increasing frequency in patients with previous AUDs (e.g. 19% forensic patients)

Korsakoff's psychosis

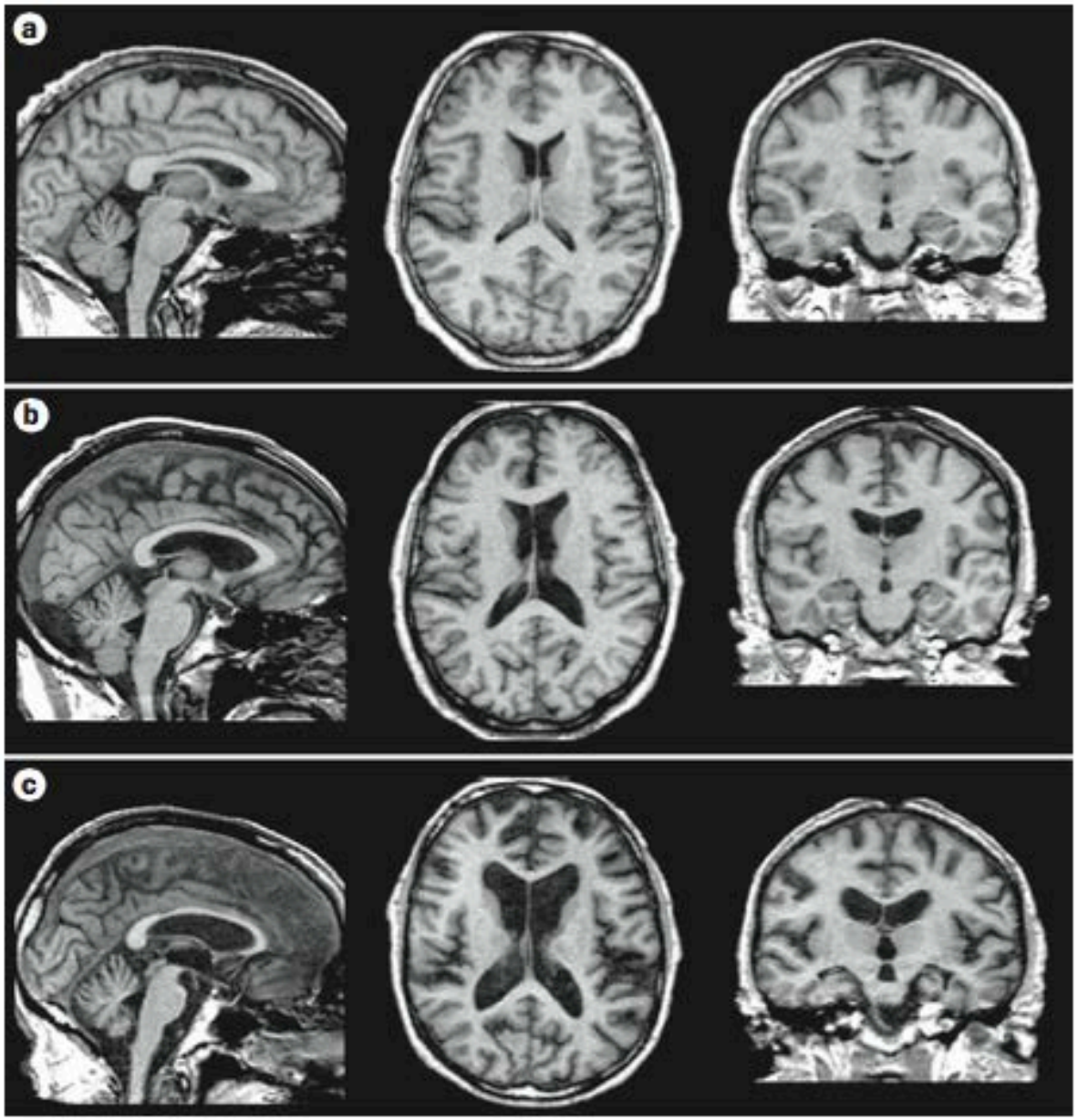
Originally described in 30 patients alcohol abuse, and 16 cases unrelated to alcohol

- Spectrum with ARBD
- Arises from WE
- Confusion, oculomotor abnormalities, ataxia
- MRI – graded volume loss
  - "uncomplicated" acoholism : milder; frontal cortical volume loss
  - WE : Neuronal loss and haemorrhagic lesions periaqueductal grey matter and paravntricular lesions, mamillary bodies
  - KS : thalamus as well
- Heterogenous group so incidence unclear

63 yo man,
Normal control

59 yo man,
alcoholism

63 yo man,
WKS

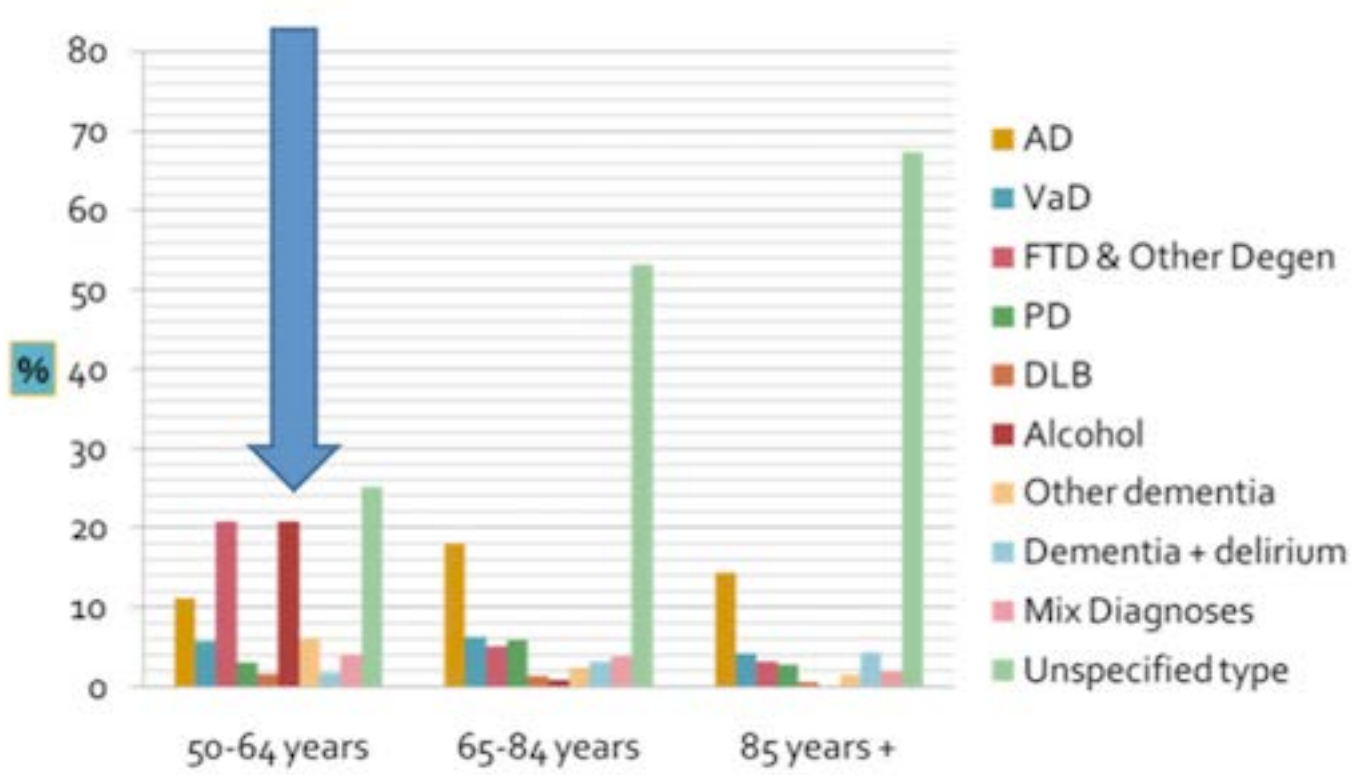


Alcohol related dementia

Rare by itself; more common in YOD – 4th most common

- Recognised in ICD 10 / DSM 5
- But debate whether it is separate entity or not
  - Course often fluctuates
  - Effects alcohol neurotoxicity rare in isolation cf effects thiamine / vasc / HI / liver disease
  - ECA study : OR 1.5 or Liverpool longditudinal study OR 4.5 for cog disorders in general
  - Outpatient consecutive diagnoses neurdegen clinic : 1.1%
  - Draper 2011 : 20000 consecutive dementia admissions for patients > 50 yo : 1.4%
  - YOD – between 5 - 10 % of cases; “reversible dementias” 5%

Draper et al 2011 : Dementia diagnosis by age in NSW hospitals – 2006/7



ARD 1.4% of total

Not all alcohol dependent people develop lasting cog impairment

- Bouts of thiamine deficiency likely in 80% alcoholics yet only about 13% of these develop WKS
- Female : increased vulnerability
  - Males × 1.7 despite 3 – 4 increased rates dependence
  - Women – greater frontal grey matter loss on MRI
  - After detox : do men do better??
  - Reduced tolerance and different body composition
- Correlation between WE and per capita alc consumption not found
- Genetic differences tolerating borderline B_1 deficiency, metabolising, B_1 transport, ApoE4…

Outcomes

- ARBD can improve, rule of quarters :
  - ¼ complete recovery
  - ¼ significant recovery
  - ¼ slight recovery
  - ¼ no recovery
- If abstain and good nutrition over 2 years in NH care, only AD or VaD patients had degenerative course

Is there ‘pure’ alcohol dementia?

- Incidence with age
- Pathology : primary ‘toxicity’ (effects of alcohol), or thiamine deficiency?
- ARBD can improve with time in some patients
- In ‘older’ patients cognitive changes likely comorbid with VaD, AD
- The problem is one of comorbidities and what is the main problem in this patient

So…

- Look out for comorbidities : apathy / depression / vascular change and subcortical impairment / end organ effects / frailty and risks of further morbidity e.g. falls
- Physiological changes in older people mean commonly quoted upper limits ‘safe’ consumption are NOT safe
- Treat recent unexplained confusion / mental state changes in an alcoholic as an emergency. Everyone should get thiamine if nutrition status in doubt
- With abstinence cognition can improve
- If on longditudinal assessment there is cog decline think of another primary neurodegenerative process

Benzodiazepines

- Prescribed for sleep, anxiety – often symptoms of depression
- Risk of dependence and withdrawal (seizures, depirium, tremors)
- Slow reduction : <10% /week

Benzos and cognition

Barker et al 2004

- Bias of published results : the ‘file drawer’ problem
- Still, evidence of increased cognitive impairment with LT use

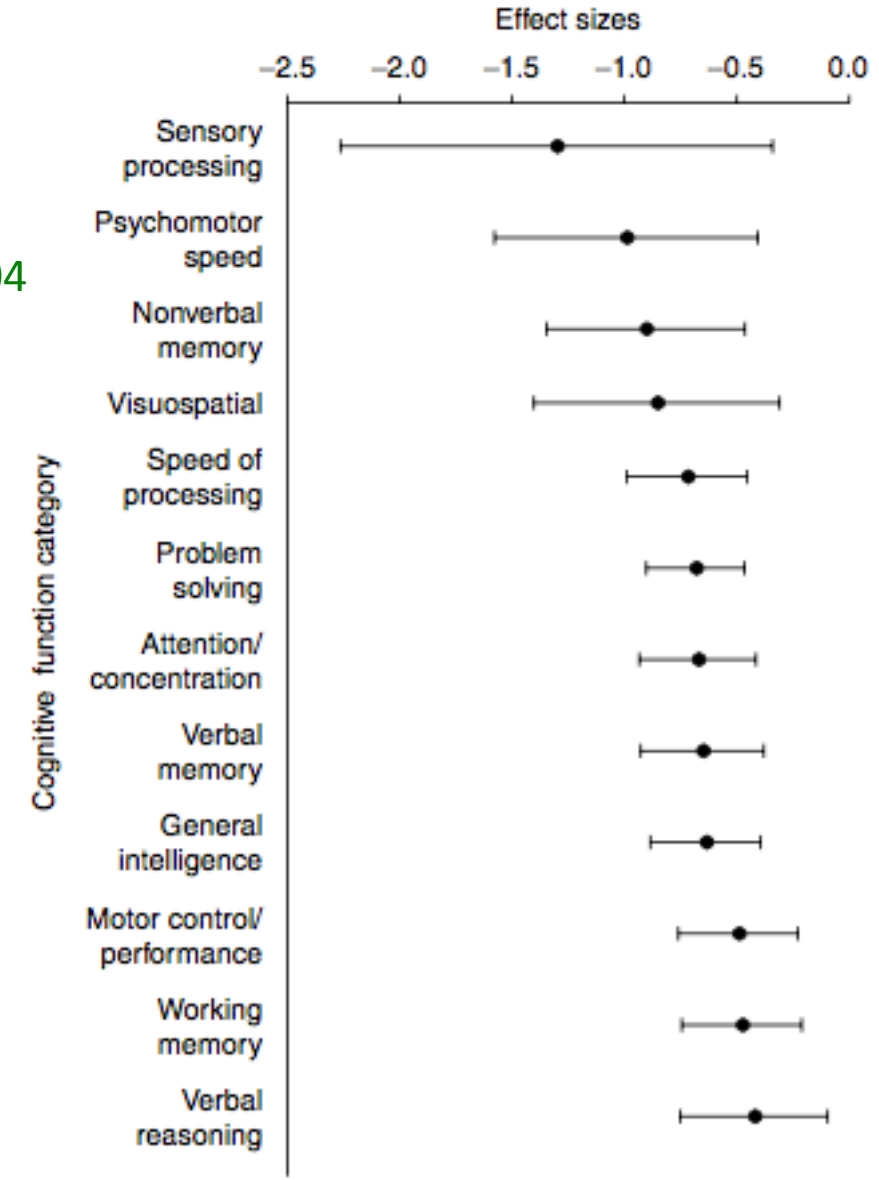


Fig. 1. Weighted mean effect sizes and 95% CIs for the performance of patients who were taking benzodiazepines on tests of various cognitive function categories. A negative effect size indicates that patients were performing worse than controls upon assessment.

opiates

- Increasing use in last 10 years, first rise in death rates in that time in Australia
- Deaths – 500 in NSW in 2008;
  - >700 in NSW in 2010, only 30% due to heroin Draper 2014 and NDARC 2012
- Older : chronic pain management
  - RF :higher pain, depression scores with lower disability levels a/w opioid misuse Park & Lavin 2010
  - Living alone, unemployed, polysubstance use
    - Alcohol, Benzos, THC, other e.g. amphetamines

Opiates – cognitive effects

- Both acute and chronic effects of opiate *abuse* on neuropsychology testing performance
- Attention, concentration, processing speed, spatial skills, recall. Greatest effect (LT) on executive function (flexibility, set shifting, inhibition)
- Chronic pain + LT opiate *therapy* : estimated cog effects in 20 – 62% of patients
- Predictors
  - Depression, degree of pain + distress

Opiates – cognitive effects

- Darke et al 2012 : 125 opoid maintenance, mean age 30
- Impaired executive function, info processing, verbal and non verbal learning
- Lizentaris and Draper 2016 studied health needs of older D+A clients aged 50 – 71
  - Cog changes methadone > suboxone but less than alcohol using the Addenbrooke's (small numbers)
- Predictors
  - depression

Cannabis

- Endocannabinoid system
  - Multiple end receptor effects, second messenger systems (cAMP, K+,Ca, prot-kinase, cFOS,cJun, etc, GABA tansmission)
  - CB_1 – brain, lungs, liver, kidneys ; CB_2 – immune /haematopoetic cells; there are more….

Can't separate "beneficial" from "undesirable" effects

Brain Structure	Regulates	THC Effect on User
Amygdala	emotions, fear, anxiety	panic/paranoia
Basal Ganglia	planning/starting a movement	slowed reaction time
Brain Stem	information between brain and spinal column	antinausea effects
Cerebellum	motor coordination, balance	impaired coordination
Hippocampus	learning new information	impaired memory
Hypothalamus	eating, sexual behavior	increased appetite
Neocortex	complex thinking, feeling, and movement	altered thinking, judgment, and sensation
Nucleus Accumbens	motivation and reward	euphoria (feeling good)
Spinal Cord	transmission of information between body and brain	altered pain sensitivity

THC is perceived as not harmful, even healthy…

Older adults' marijuana use, injuries, and emergency department visits

Namkee G. Choi, PhD[a], C. Nathan Marti, PhD[a], Diana M. DiNitto, PhD[a], and Bryan Y. Choi, MD, MPH[b]

[a]University of Texas at Austin School of Social Work, Austin, TX, USA; [b]Warren Alpert Medical School, Department of Emergency Medicine, Brown University, Providence, RI, USA

- 14 715 patients
- Injury rates 19% controls, 29% THC
- Increased likelihood ED visits because of injury (OR 6)

- Norway study of 40 000 post national service : 40% increased likelihood early mortality

Probable harmful effects of THC – Hall 2014

- A cannabis dependence syndrome (in around 1 in 10 users).
- Chronic bronchitis and impaired respiratory function in regular smokers.
- Psychotic symptoms and disorders in heavy users, especially those with a history of psychotic symptoms or a family history of these disorders.
- Impaired educational attainment among adolescents who use regularly.
- Residual cognitive impairment for up to a month after abstinence.
- Cognitive impairment in those who initiate early and use daily for a decade or more.

Possible

- Respiratory cancers
- Depressive disorders, mania, and suicide
- Use of other illicit drugs by adolescents

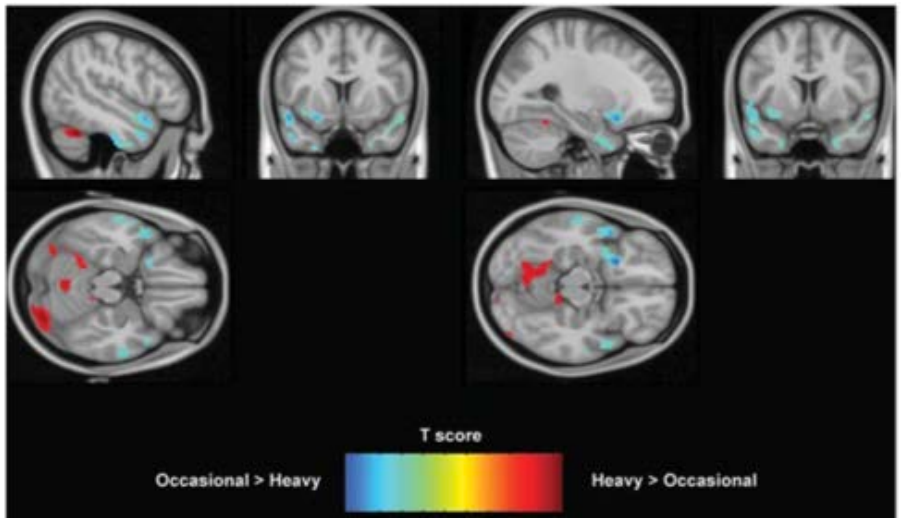
Cannabis and cognition in elders

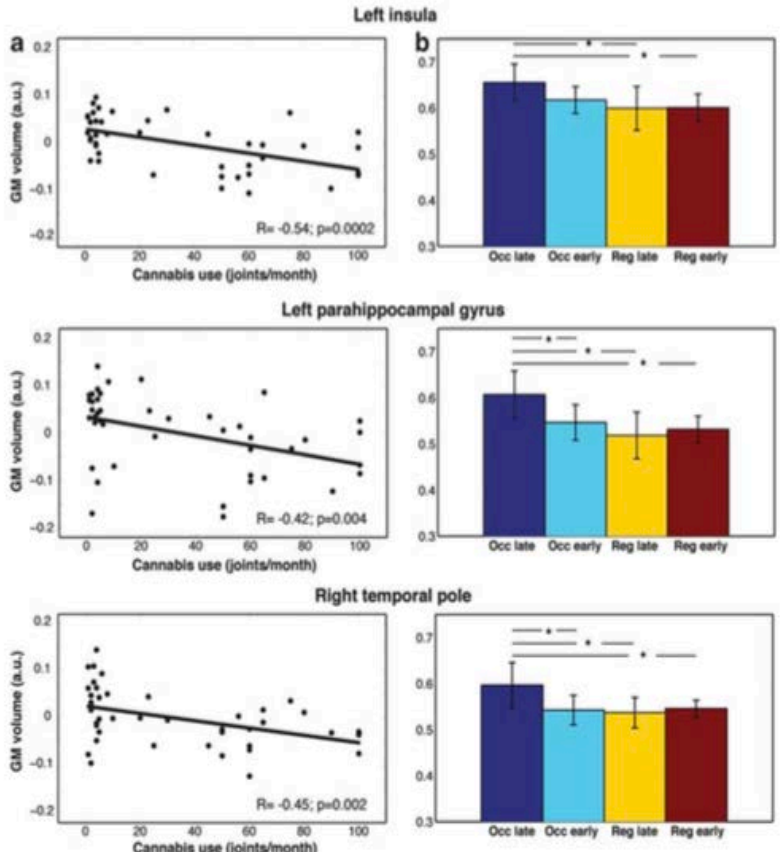
- Attention and memory
- Impairments a/w earlier age of use / frequency / duration
- Studies mainly middle life, not elders
- Mixed findings
  - ECA study : 12 year f/up, no Δ MMSE under 65
  - Are cog changes related to personality? Sanchez-Torres 2013

…. No :

THC and cognition (ctd)

- Comparing heavy users with recreational users
- Decreased grey matter volumes in nearly all areas / networks known to have CBD receptors
  - Motivation, emotion, emotional learning
  - i.e. hippocampus, insula, ventromed + orbitofrontal
- Either starting in adolescence or with heavy use
- Other studies : atrophy of white matter tracts





What about medicinal cannabis?

- Pharmacotherapy or potential drug interactions in elderly not known
- Different strains / mixes of CBD's

- Largest study I found – 2700 pts, Israel
- Largely well tolerated, 18% discontinued

Table 2
Indications for receiving cannabis prescription.

Indication	Number of patients (N = 2736)
Cancer associated pain	1001 (36.6%)
Nonspecific pain	821 (30.0%)
Cancer – chemotherapy treatment	661 (24.2%)
Parkinson's disease	146 (5.3%)
Others	49 (1.8%)
Post-traumatic stress disorder	21 (0.8%)
Crohn's disease	10 (0.4%)
Amyotrophic lateral sclerosis	9 (0.3%)
Compassion treatment	7 (0.3%)
Ulcerative colitis	5 (0.2%)
Alzheimer's disease	4 (0.1%)
Multiple sclerosis	2 (0.1%)

In summary

- Cognitive impairment is common anyway, with increased risk for elder substance users
- Disentagling cause + effect – problem of comorbidity, underlying vulnerabilities

Diagnostic issues – think of pathology

- With chronic use : apathy / depression / vascular change and subcortical impairment
- And the effects of comorbid psych issues

This will inform your engagement and future management for this particular patient