

Painful Ageing: Opioids, benzodiazepines and Other Drugs in Older People

Never Stand Still

Medicine

Psychiatry

Conjoint Professor Brian Draper
Prince of Wales Hospital, Randwick

What is old?

There is no single age cut-off that captures the different older populations with substance misuse disorders

Aged Care Services	75+	mainly prescription drugs
Mental Health Services	65+	mainly alcohol & prescription drugs
Drug & Alcohol Services	50+	alcohol, illicit & prescription drugs
General Public	??	alcohol, illicit & prescription drugs

Age Effects, Alcohol, Drugs and Health

Older People - Physiological changes impact tolerance

- Respond to alcohol & drugs differently - Less does more - older adults have a higher sensitivity to alcohol & drugs
- Alcohol & drugs take longer to excrete/ metabolise
- Effects of medications can be drastically different (comorbidities)
- Thus the amount of alcohol that might cause short term risk is much less in older people but exact reduction is unclear and may depend on comorbidities

Geriatric 'Giants'

- Immobility – (frailty)
- Intellectual impairment - (dementia, 9% age 65+)
- Instability – (falls)
- Incontinence
- Iatrogenic – (polypharmacy)

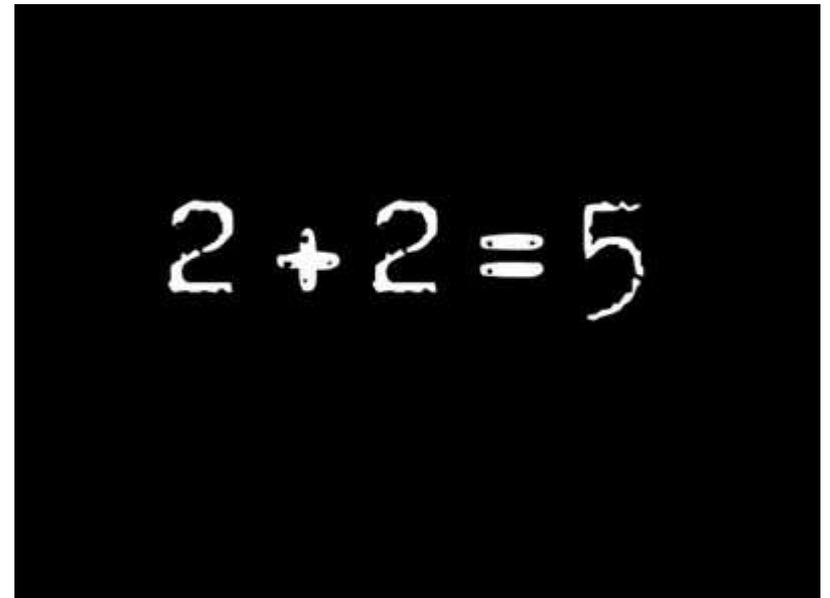
Why does this matter to older people with alcohol and substance use disorders?

Synergistic increase in risk

Earlier development of 'geriatric giants'

Need to recognise the unique needs of geriatric patients

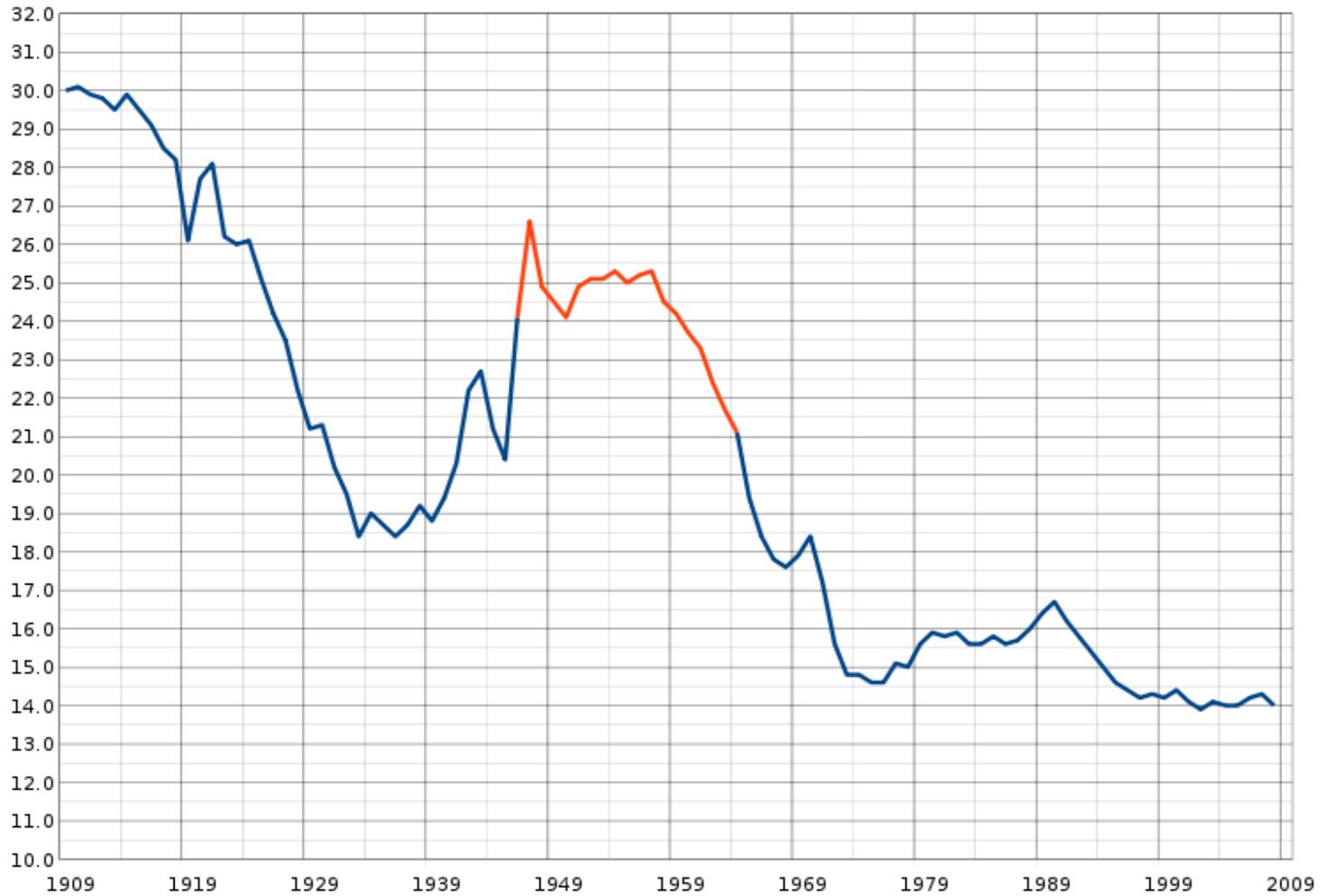
Unusual to find only one specific cause of an acute presentation



The Baby Boomers have arrived!

DOB 1946-1964





US birth rate (births per 1000 population), red segment highlights birth rate 1946 to 1964

The Baby Boomers and Substance Use

- o Substance use disorders in over 50s predicted to double by 2020 (Han et al, 2009)

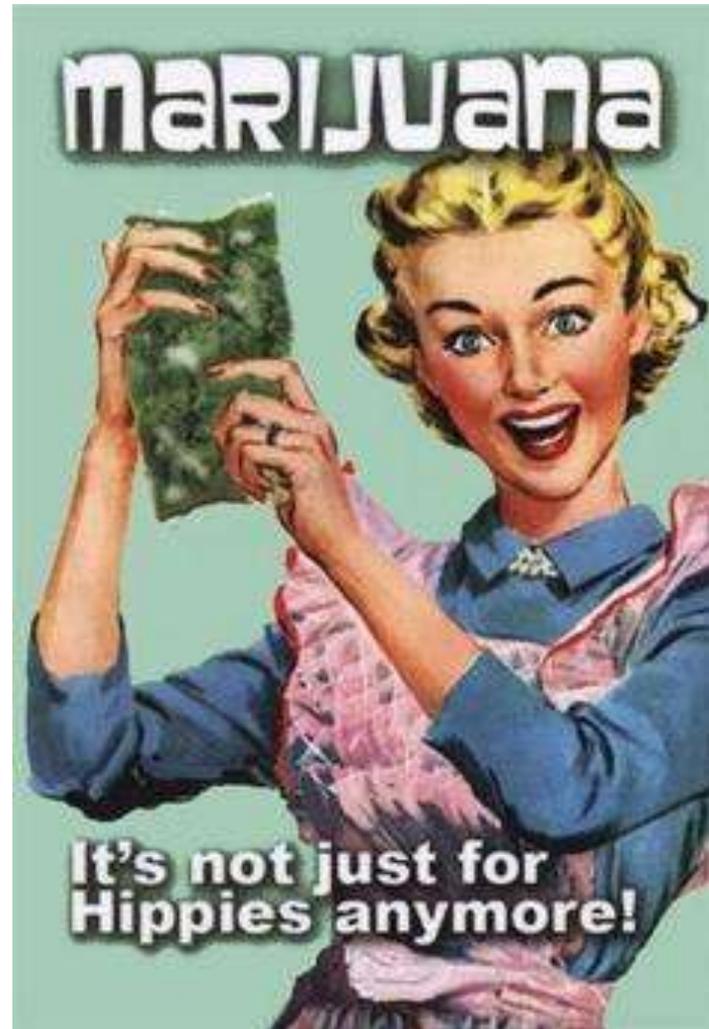
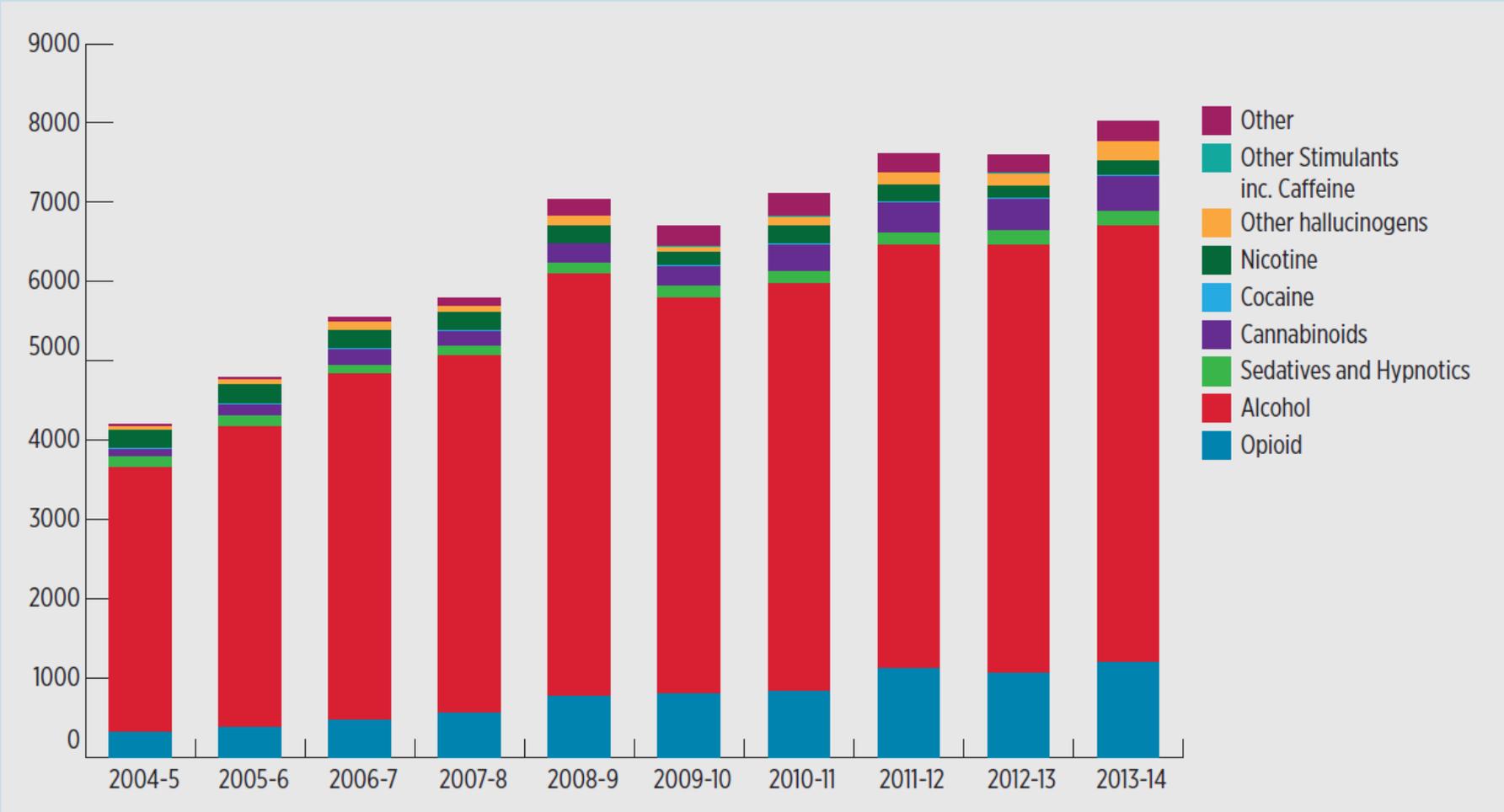


Figure 9: 'Principal drug of concern' for drug and alcohol services closed treatment episodes for clients aged 50+ by year



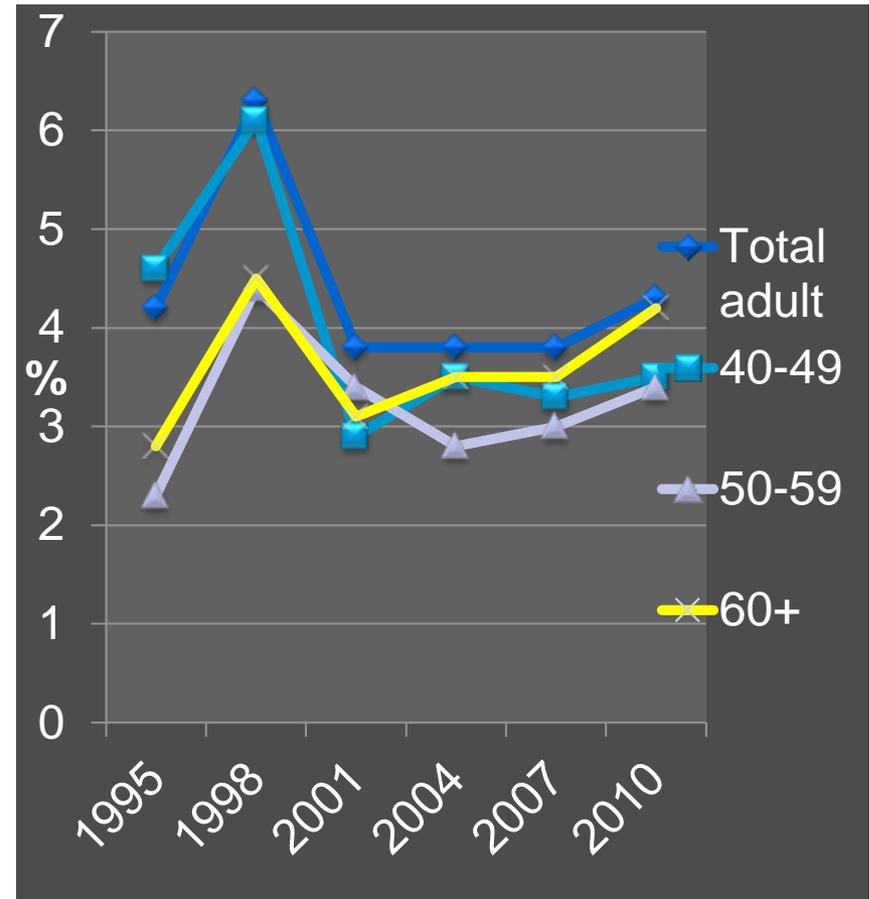
NSW Older People's D&A Report, 2015

Non-medical Pharmaceutical Use

1995-2010 National Household Survey

- Range: sharing medications, higher doses, or longer durations than prescribed, to persistent abuse and dependency issues.
- Main: benzodiazepine sedative-hypnotics and the opioid analgesics

(AIHW, 2011)





Benzodiazepines (BZ)



Recommendation is that BZ be avoided in older adults because of residual sedative effects and an association with falls, MVAs, Overdoses, and worsened memory (Hanlon et al., 1998; Sheahan et al., 1995; Simoni-Wastila & Yang, 2006)

Worse with longer half-life BZ e.g. diazepam, nitrazepam

Increased falls risk

Withdrawal risks: Seizures, Tremors, Hallucinations, Delirium

Quebec Survey on the Health of Older Persons¹

2,782 persons randomly selected persons aged 65 years or older in Quebec



707 (25.4%) report benzodiazepine usage



67 (9.5%) meet DSM-IV criteria for benzodiazepine dependence



304 (43%) consider themselves to be dependent on

benzodiazepines

¹ Voyer et al, Can J Aging 2010



Do BZD cause a typical type of dependence?

DSM-IV criterion	Dependent BZD users (n=67)	None-dependent users (n=639)
1. Tolerance	50 %	7 %
2. Withdrawal	56 %	10 %
3. Increases in quantity or duration/ tolerance	33 %	6 %
4. Ongoing resolution or fruitless efforts to reduce or cease medication	89 %	23 %
5. Takes time to recover from drug effects	35 %	2 %
6. Reduction or abandonment of important activities	17 %	0 %
7. Continued use of drug despite problems caused by use	30%	1 %

¹ Voyer et al, Can J Aging 2010

Why Do Older Adults Use Benzodiazepines?

1. Sleep problems

- Bz appear to be a simple (and initially seemingly effective) remedy for sleep disorders in late life.

2. Anxiety and Stress

- Many older patients have been prescribed low dose Bz for chronic anxiety for many years.
- New prescriptions for acute anxiety (often in the context of an evolving depression or dementia) occur when doctors lack skills/time for non-drug treatments & fail to refer to Mental Health

Benzodiazepines and Cognition in Late Life

- The long term effects of benzodiazepines upon cognition are mixed but mainly suggestive of increasing risk of cognitive impairment (Stewart 2005)
- Some longitudinal studies indicate chronic Bz consumption can increase risk of cognitive decline (e.g. Paterniti et al, 2002) and dementia (e.g. de Gage et al, 2012) in older people
- The extent to which Bz and other sedative/hypnotics are associated with MCI are unclear

Meta-analysis of Benzodiazepine Withdrawal Studies (Gould et al, 2014)

Ten controlled withdrawal studies on achieving BZD abstinence:

Withdrawal with psychotherapy (n=4):	OR = 5.1 [95% CI: 2.7 – 9.6], p<.001
Withdrawal with pharmacotherapy (n=4):	OR = 1.3 [95% CI: 0.7 – 1.5], p=.42
Withdrawal with prescribing intervention (n=2):	OR = 1.4 [95% CI: 1.0 – 2.0], p=.04

Eight prescribing RCTs on achieving BZD abstinence:

Multifaceted intervention (n=5):	OR = 1.4 [95% CI: 1.1 – 1.7], p=.006
Single prescribing intervention (n=3):	OR = 0.9 [95% CI: 0.7 – 1.1], p=.27

¹ Gould et al, Br J Psychiatry 2014

Stepped Care Approach for Benzodiazepine Discontinuation in Primary Care

Based on the BenzoRedux Project in the Netherlands

Step 1 – Discontinuation Letter (Gorgels et al, 2005, 2008)

Main effects of a letter with stop advice (Gorgels et al 2005)

Short-term quitters (6 mths): 24% vs 12% (RR = 2.1 [95% CI: 1.8 – 2.4])

Full abstinence for 21 mths: 13% vs 5% (RR = 2.6 [95% CI: 2.0 – 3.4])

Secondary effects (Gorgels et al 2008)

No increase in medical consumption

No substitution for other (psychotropic) drugs

Age was not a significant predictor of response

Stepped Care Approach for Benzodiazepine Discontinuation in Primary Care

Step 2: Gradual Tapering of Benzodiazepines with & without CBT (Oude Voshaar et al, 2003, 2006)

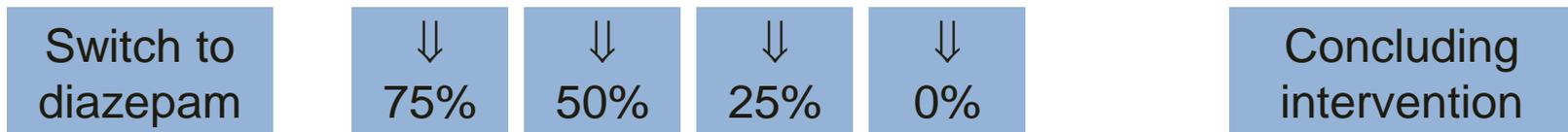
Time span (weeks):



Visits to the GP:



Dose reduction (done by GP):



CBT group meetings:



Stepped Care Approach for Benzodiazepine Discontinuation in Primary Care

Step 2: Gradual Tapering of Benzodiazepines (Oude Voshaar et al, 2003, 2006)

End of treatment Abstinence

Taper 62%, Taper + CBT 58%, Control 21%

18 months Abstinence

Taper 36%, Taper + CBT 29%, Control 15%

Low dose users, those who do not have alcohol problems more likely to be abstinent

Opioids



Risk for opioid-related problems has increased over the past 10-years for all birth cohorts

Increase in older adults receiving pharmacotherapy for opiate dependence in Australia – proportion aged 50+ increased from 8% to 21% between 2006 and 2014, aged 60+ increase from 0.3% in 2006 to 1% in 2010 (AIHW 2015)

Prescription Opioids

Older people (mainly late mid life) misusing painkilling medication have driven the first rise in deaths from heroin and other opioid drugs in more than 10 years

A study of over 19,000 community dwelling Australians aged 60+ found 22% were using opioids regularly & 12% exceeded dose recommendations (Veal et al, 2015)

Increased use of opioids in chronic pain management including nursing home residents with dementia and disturbed behaviour

Deaths from opioids increased from 500 in 2008 to more than 700 in 2010, only 30% due to heroin (NDARC, UNSW 2012); mortality is dose-related with prescription opioids

Opioids used in around 9% unintentional & 5% intentional hospitalised self-poisoning in NSW aged 50+ (Mitchell et al, 2015)

Prescription opioids associated with increased suicide risk (12% opioid deaths in 2016 (n = 123))

Risk Factors for Opioid Misuse in Older People

Park & Lavin (2010) - cross-sectional study from 11 VA outpatient clinics, 163 patients (69% male) being treated for chronic pain with opioid medications – mainly arthritis & lower back pain

High levels of pain severity & depressive symptoms, lower disability scores were associated with increased risk of opioid misuse. No association with alcohol problems, social supports, social networks or spirituality

Roxburgh et al (2011) - Increased prescription of opioids for chronic pain in older people & increased morbidity & mortality

Older people with non-cancer pain 2.5 times more likely to become long term users than 18-44 yr olds (Lalic et al, 2018)

Opioids for Chronic Non-Cancer Pain

Despite the increased use of opioids for chronic non-cancer pain in older people there is:

- i) a dearth of evidence for efficacy, particularly as few RCTs include older people;
- ii) few older people with chronic pain attend pain clinics;
- iii) few guidelines for treating chronic pain in older people

O'Brien et al 2019

Opioids and cognition

Immediate effects – drowsiness, slurred and slow speech, reduced coordination, impaired concentration

Evidence for mild cognitive deficits in attention, working memory and verbal memory in chronic cases/

Persistent impairment with abstinence only found in executive (higher-order) functions

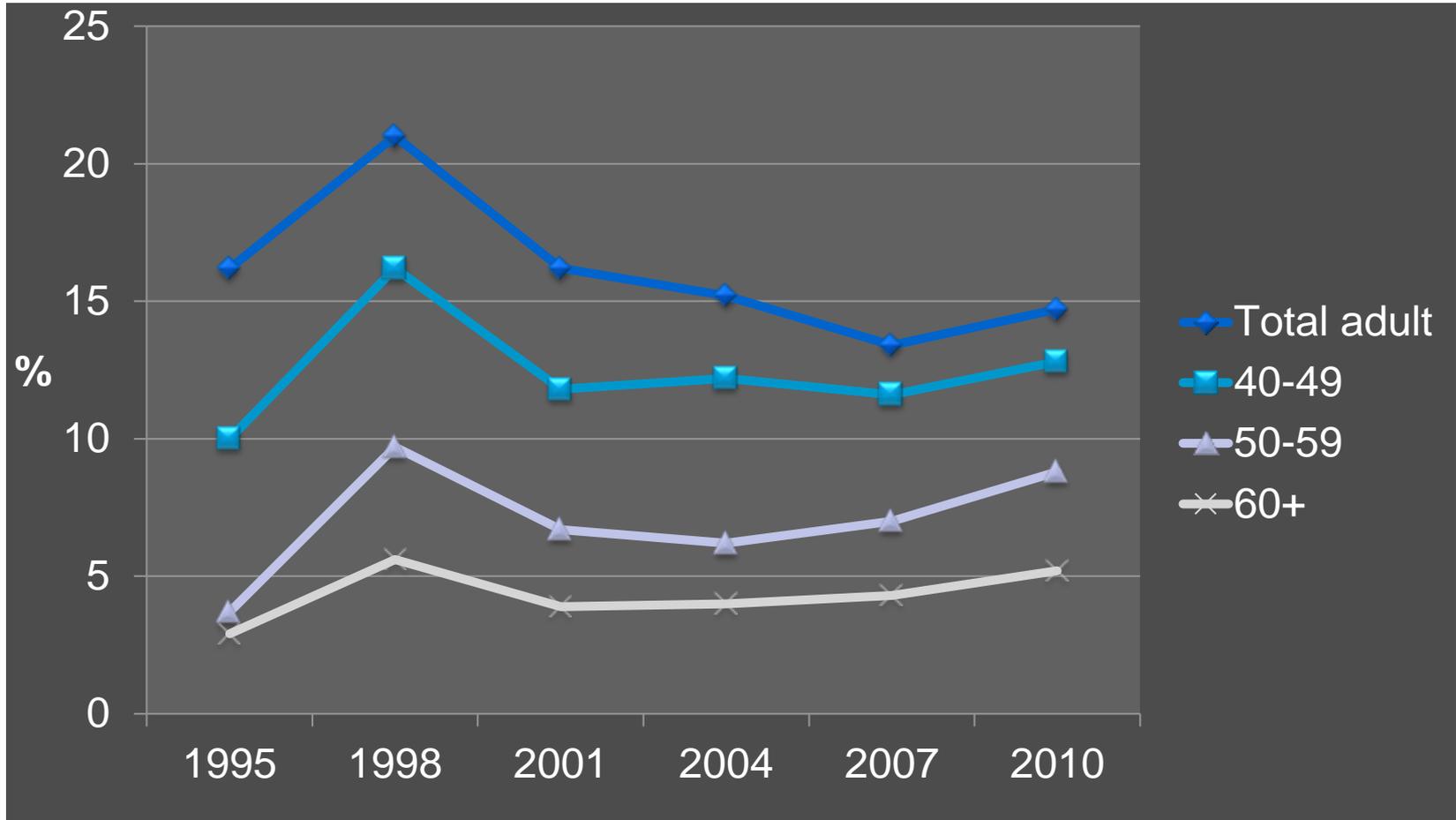
Reversible structural changes with abstinence

Some evidence that Suboxone is associated with less cognitive impairment than heroin/methadone but may reflect group selection

Rapeli et al., 2006; Mitrovic et al., 2011; Darke et al 2012

Trends in Illicit drug use past 12 months

Australian National Household Surveys 1995-2010



CANNABIS

Table 2: Cannabis use patterns by age group: 2004 and 2013 Australia

Cannabis use patterns		2004			
		50–59 years (<i>n</i> = 4730)†, %	60–69 years (<i>n</i> = 3613), %	70+ years (<i>n</i> = 3357), %	All 50+ (<i>n</i> = 11 700), %
Cannabis use in past year	No	96.8	99.5	100.0	98.5
	Yes	3.2	0.5	0.0	1.5
Frequency of use	Occasional	48.7	53.2	49.5	49.1
	Regular	51.3	46.8	50.5	50.9
Age of first use	<50 years	97.4	89.2	69.2	94.9
	≥50 years	2.6	10.8	30.8	5.1

Cannabis use patterns		2013			
		50–59 years (<i>n</i> = 3831), %	60–69 years (<i>n</i> = 4013), %	70+ years (<i>n</i> = 3328), %	All 50+ (<i>n</i> = 11 172), %
Cannabis use in past year	No	92.7	98.0	99.7	96.4
	Yes	7.3	2.0	0.3	3.6
Frequency of use	Occasional	43.8	44.9	45.4	44.0
	Regular	56.2	55.1	54.6	56.0
Age of first use	<50 years	99.7	95.4	84.6	98.0
	≥50 years	0.3	4.6	15.4	2.0

Kostadinov & Roche, 2017

Long Term Effects of Cannabis Use

adapted from Hall (2014)

Condition	Evidence	Level of Evidence	Strength of Effect
Dependence	+++	Cohort studies	1 in 10 users
Education outcome	++	Cohort & Case Control	2x in regular users
Cognitive impairment	++	Cohort & Case Control	Difficult to quantify
Psychosis	++	Cohort studies	2x in regular users
Depression	+?	Cohort studies	Confounded
Suicide	+?	Cohort studies	2x in regular users
Chronic bronchitis	++	Cohort studies	2x in regular users
Cardiovascular	++	Cohort & Case Control	3-4 times in MI
Testicular cancer	++	Case-control	2-3x
Respiratory cancer	+?	Case-control	Confounded by smoking

Long Term Effects of Cannabis Use

Most research has focused on people who are in midlife and have been using since adolescence or early adulthood

Unclear whether the reported long term effects are amplified in later life

From a psychiatric perspective, in the US reports of comorbid cannabis use in older people with depression e.g. 12% depressed & 4% depressed women aged 60+ in a psych OP clinic had used cannabis in previous 30 days, wit higher scores on BDS associated with cannabis use (Satre et al, 2011)

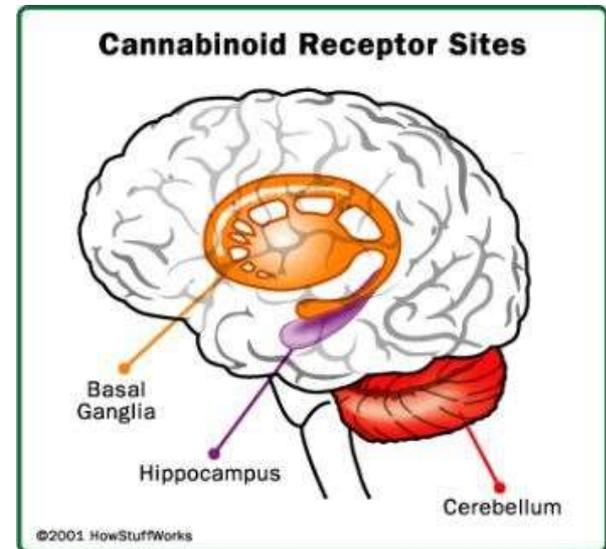
Cannabis and Cognition

Multiple effects on the brain

- Cannabinoid receptors prominent in hippocampus (memory) and basal ganglia and cerebellum (movement control)

Acute and sub-acute effects:

- Attentional and memory (particularly verbal), decision-making and inhibitory control deficits
- Basic motor coordination
- ‘False’ memories and poor recall
- Diminished capacity for behaviour monitoring and error-awareness



Crean et al., 2011, Journal of Addiction Medicine

Cannabis and cognition in older people

There is mounting evidence that long-term cannabis use has deleterious effects on attention & memory

Impairment appears to increase with earlier age of onset, dose, frequency & duration of use. Studies thus far are methodologically poor & really only extend to midlife

However, 12-year follow up of heavy, light & non-users in ECA study – no effects noted on MMSE in persons under 65 (Lyketsos et al, 1999)

Other studies have found cognitive impairments but attribute them to personality factors (Meier et al, 2012) or comorbidities (Sanchez-Torres et al, 2013)

Medicinal Cannabis

In older people, main contexts for use of medicinal cannabis are in chronic pain & behavioural symptoms associated with dementia (BPSD)

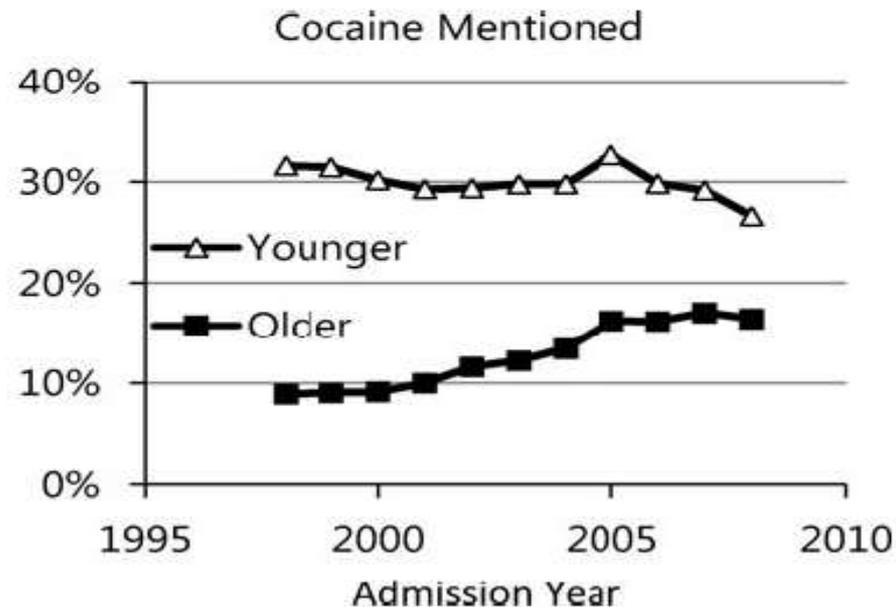
Cannabidiol (CBD), rather than tetrahydrocannabinol (THC), main therapeutic ingredient though CBD/THC combinations might be more efficacious

Also some consideration for use in preventing cognitive decline in dementia but only rodent models so far (Watt & Karl, 2017)

To date, there is very low quality evidence of efficacy for either pain or BPSD – adequately powered RCTs are needed but in 12 month study, serious AEs same as controls, but non-serious AEs higher (Ware et al 2015)

Older Adult First Time Admissions for Substance Use in the US – Cocaine (Arndt et al 2011)

FIGURE 4. Cocaine Mentioned as a Problem Substance for First-Time Admissions From 1998 to 2008 Broken Down by Age Group, Younger (age 30–54 years; N = 3,547,733) Versus Older (age 55 and Older; N = 258,542)



New Jersey Record, May 2013

Elderly residents at senior citizens home in New Jersey 'used cocaine and ran a prostitution ring from their unit'

75 year old man, 'provided prostitutes to his younger neighbors'

66 year old woman, 'had crack cocaine and drug paraphernalia'

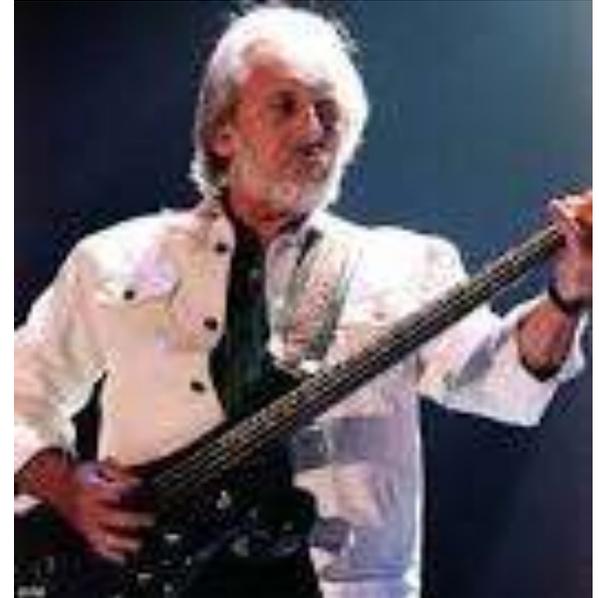
Arrests came after fearful elderly residents complained about drunks and addicts invading the building

In a suburban US hospital, 2.3% of drug screens from 2004-2009 in patients aged 65+ were positive for cocaine (Chait et al, 2010)



Health Effects of Cocaine

- Cardiac, chest pain, respiratory failure, strokes, seizures, headaches, and GIT complications.
- Snorting cocaine can lead to loss of the sense of smell, nosebleeds, problems with swallowing, hoarseness, and chronically runny nose.
- Ingesting cocaine can cause severe bowel gangrene due to reduced BF.
- People who inject cocaine can experience severe allergic reactions and are at increased risk for contracting HIV, viral hepatitis and other blood-borne diseases.
- Cocaine-related deaths are often a result of cardiac arrest or seizure followed by respiratory arrest.



John Entwistle of The Who died of a cardiac arrest age 57 while intoxicated with cocaine

Methamphetamine Abuse in Older People

There are no Australian data & little internationally

Most studies of long term methamphetamine abuse are of people in mid-life – 40s or 50s, with older ages showing worse effects

Reports of 50-60% reduction of brain dopamine levels

Neuropsychological deficits including attention, working memory and executive function which persist for at least a year after abstinence

Up to 30% have persistent psychosis

(Searby et al, 2015)

Health Needs & Services of Older Drug & Alcohol Clients

(Lintzeris et al 2016)

99 subjects (77% male) from SE Sydney D&A services aged 50+ (mean 55 years; range 50-71)

64% live alone, only 7% with partner

7% employed, 79% unemployed/perm. unable to work

Opiate dependence n = 69 (70%)

– 70% on methadone, 30% suboxone

Alcohol dependence n = 30 (30%)

Many were polysubstance users (esp those with opiate dependence) – 40% benzodiazepines, 38% cannabis, 10% amphetamines, 5% cocaine

Substance Use in Past Month

Lintzeris et al, 2016

SUBSTANCE	% OF SAMPLE USING	MEAN DAYS OF USE(SD)
ALCOHOL	45	6.16 (9.73)
HEROIN	13	0.82 (3.27)
COCAINE	5	0.33 (2.82)
AMPHETAMINE TYPE	10	0.40 (1.68)
CANNABIS	38	5.76 (9.75)
BENZODIAZEPINES	40	6.55 (10.93)
OTHER OPIATES*	10	0.30 (1.11)
OTHER PROBLEM SUBSTANCE**	2	0.30 (2.81)

•OTHER OPIATES= TRAMADOL, STREET METHADONE, OXYCODONE, OXYNORM

** OTHER SUBSTANCES= NEUROFEN PLUS, KRONIC

18% STILL INJECTING (MEAN DAYS 7.0; SD 8.4) – NONE SHARING INJECTING PARAPHERNALIA
2% EXPERIENCED VIOLENCE – NONE REPORTED BEING ARRESTED OR CHILD PROTECTION ISSUES

HEALTH STATUS - (Lintzeris et al, 2016)

CONDITIONS	PERCENTAGE OF SAMPLE (N = 99)
DIABETES	7.1%
HYPERTENSION	18.2%
STROKE/TIA	3.0%
HEART PROBLEMS	18.2%
DEFICIENT LEG CIRCULATION	32.3%
RESPIRATORY TRACK PROBLEMS	23.2%
FALLS INJURY	40.0%
HEPATITIS/LIVER CIRRHOSIS/FATTY LIVER	57.6%
GIT ULCERS/PROBLEMS	23.2%
EPILEPSY/CONVULSIONS/FITS	14.1%
DEPRESSION, ANXIETY, SKIN CONDITIONS	14.1% (however 87% scored in depression range on Geriatric Depression Scale)
HEAD INJURY/LOSS OF CONSCIOUSNESS	50.5%

MEDICATIONS		
MEAN (SD)	RANGE	% SAMPLE WITH >4 MEDS
1.73 (1.55)	0 TO 7	15.1%

Depression & Social Isolation - (Lintzeris et al 2016)

Geriatric Depression Scale

OST (n=69) Mean (SD)	EtOH (n=30) Mean (SD)	Total (n=99) Mean (SD)	% score > 6
7.55 (1.8)	7.0 (1.85)	7.38 (1.82)	79%

On Lubben Social Network Scale, around 20% were very isolated

Cognitive Performance - MMSE & ACE-R ($n = 99$)

Lintzeris et al 2016; Monds et al 2017

TOOL	MEAN (SD)	MED	RANGE	Cut-off	<i>n</i>	%
MINI MENTAL STATE EXAM	27.76 (2.55)	29	16 – 30	<24	8	8.1
ADDENBROOKE'S COGNITIVE EXAMINATION-R (ACE-R)	82.43 (9.58)	84	46 - 97	<82	44	44.4

- ACE-R total score had a significant negative correlation with GDS symptoms, $r_s(98) = -.252, p = .012$

What service delivery models are required?

Service Delivery Models for older people with substance misuse will need to change from models currently in use for younger adults

Collaborative models with specialist aged care services (geriatric and old age psychiatry) are likely to be required

Consideration of D&A outreach to the homes of older people with D&A problems

Further research needed – especially in addressing the needs of older cognitively impaired people with substance misuse

Thank you.....

Any questions?

Brian Draper:

b.draper@unsw.edu.au



Alcohol and the Adult Brain

Edited by JENNY SVANBERG,
ADRIENNE WITHALL, BRIAN DRAPER
and STEPHEN BOWDEN

