

Severe mental illness and dementia

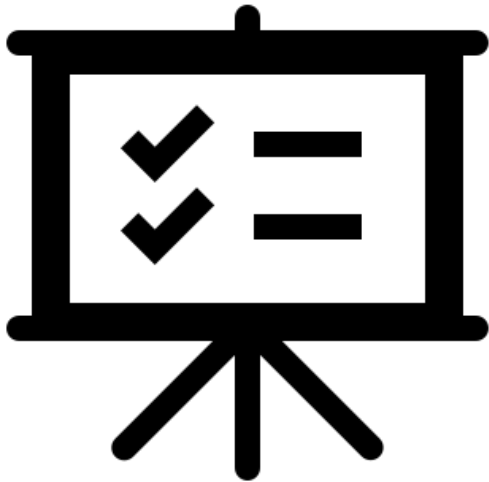
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Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Learning objectives



- appreciate the increased risk of dementia in persons with schizophrenia, bipolar disorder, major depressive disorder and substance use disorder
- describe the relationship between psychotropic medications and dementia

Chronic mental illness & risk of dementia

- schizophrenia
- bipolar disorder
- major depressive disorder
- alcohol
- medications

Schizophrenia (1)

- people with schizophrenia have roughly twice the risk of developing dementia as those without (RR*=2.29)¹
- they may develop dementia earlier²:
 - by age 65: 1.8% had dementia (vs 0.6% for people w/o schizophrenia)
 - by age 80: 7.5% (vs 5.8%)

Schizophrenia (2)

- why?
 - tobacco → vascular disease
 - other medical comorbidities (diabetes, heart disease)
 - alcohol & other substances
 - low physical activity
 - poor access to medical care (?)
 - lower cognitive reserve (?)
 - shared genetic risk (?)

Bipolar disorder

- people with bipolar disorder have roughly twice the risk of developing dementia as those without (OR*=2.36)
- why?
 - tobacco, alcohol & other substances
 - medical comorbidities (obesity, diabetes, sleep apnea)
 - risky behaviors
 - diet & exercise
 - neuroinflammation & decreased neuroplasticity
 - unclear if number of episodes correlated with dementia

Major depressive disorder (1)

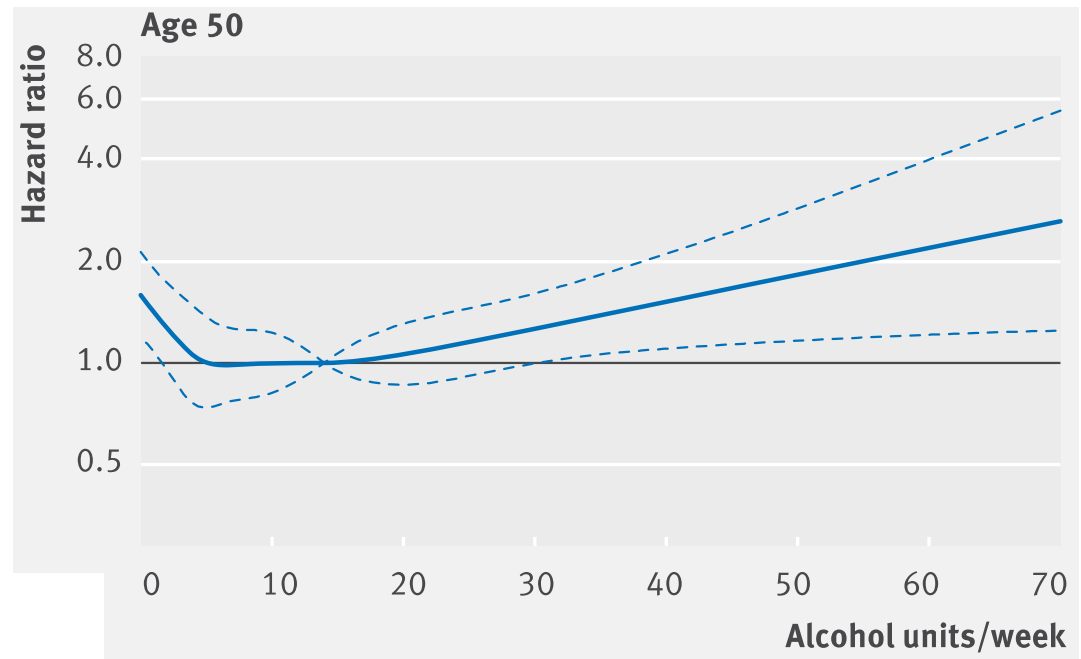
- people with MDD have roughly twice the risk of developing dementia as those without (OR* either 1.90 or 2.03, depending on type of study)
- risk of vascular dementia (2.52) slightly higher than risk of Alzheimer's disease (1.65)
- late-onset depression may represent prodrome of dementia
- contradictory evidence regarding whether early-onset or late-onset depression confers greater risk
- depression increases risk of progression from MCI to dementia

Major depressive disorder (2)

- why?
 - neuroinflammation
 - chronic HPA axis activation
 - dysfunctional neural networks
 - tobacco, alcohol
 - diet & exercise
 - shared risk: genetics, social determinants of health, chronic medical problems

Alcohol & risk of dementia

- in general, studies have shown that light alcohol use may reduce risk of dementia
- high alcohol use increases risk of dementia and results in smaller hippocampi



10 units = five 12-oz beers

Medications & risk of dementia

- lithium¹: may be neuroprotective and reduce risk of dementia
- valproic acid²: in people with dementia, may increase the rate of shrinkage of the brain
- anticholinergic medications³: can cause reversible cognitive impairment in people with schizophrenia ≥ 50 years old
- benzodiazepines⁴: conflicting evidence about risk of dementia; do cause reversible cognitive impairment
- antipsychotics: ?

¹Diniz et al., *Neuropsychiatr Dis Treat* 2013; ²Tariot et al., *Arch Gen Psychiatry* 2011;

³Tsoutsoulas et al., *J Clin Psychiatry* 2017; ⁴Grossi et al., *BMC Geriatr* 2019

Psychotropic medications on the Beers list

Potentially inappropriate

- antidepressants
 - ami-/nortriptyline
 - clomipramine
 - desi-/imipramine
 - doxepin > 6 mg/d
 - paroxetine
- all antipsychotics
- all benzodiazepines
- z-drugs
- also: other medications with anticholinergic effects

Use with caution

- antipsychotics
- carbamazepine/oxcarbazepine
- SSRIs
- SNRIs
- mirtazapine
- TCAs
- dextromethorphan-quinidine

Drug-drug interactions

- lithium
- and others

What to do about psychotropic medications

- consider dose reduction or discontinuation of medications for pre-existing mental illness, especially valproate, benzodiazepines, anticholinergics, antipsychotics
- consider cognitive enhancer to delay progression of dementia
- use medications for BPSD only if imminent dangerousness or severe distress (start low, go slow)