# Rational prescribing in the older adult
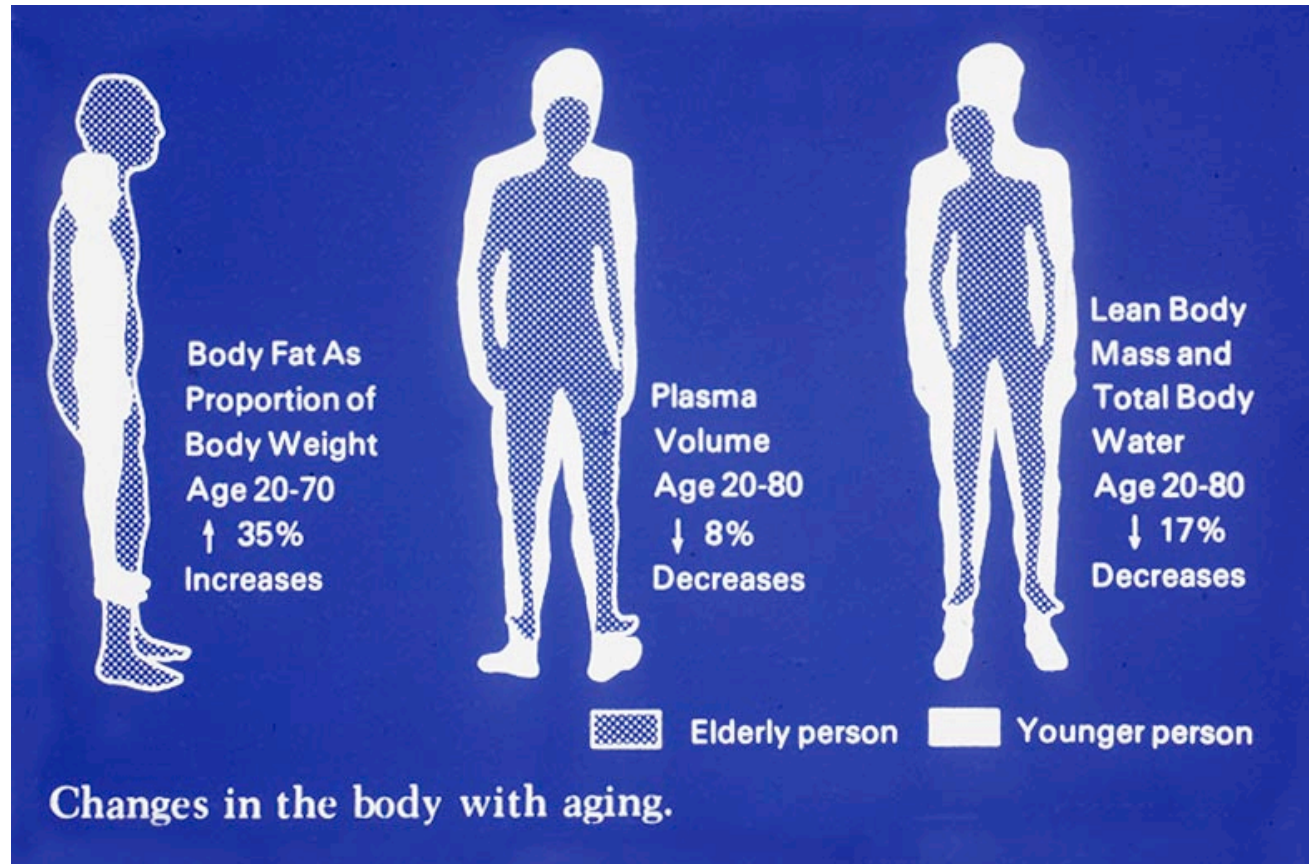
Assoc Prof Craig Whitehead

# Introduction

- Physioloical ageing and frailty
- Medication risks in older adults
- Drug Burden
- Anticholinergic and sedative drug burden
- Cascade prescribing
- Underprescribing
- Possible solutions

# Physiological ageing



Body Fat As Proportion of Body Weight Age 20-70 ↑ 35% Increases

Plasma Volume Age 20-80 ↓ 8% Decreases

Lean Body Mass and Total Body Water Age 20-80 ↓ 17% Decreases

Elderly person    Younger person

Changes in the body with aging.

# Physiological Ageing

- Hard to define
- Rate of ageing is very different from person to person
- Gradual reduction in organ function
- Accumulate risk factors for diseases
- Diseases lead us to become disabled

# Functional Implications of Organ System Aging

**CARDIOVASCULAR**

- **VO2 max (training effects, reversibility)**
- **Systolic/diastolic BP (risk of cardiac/CV disease)**
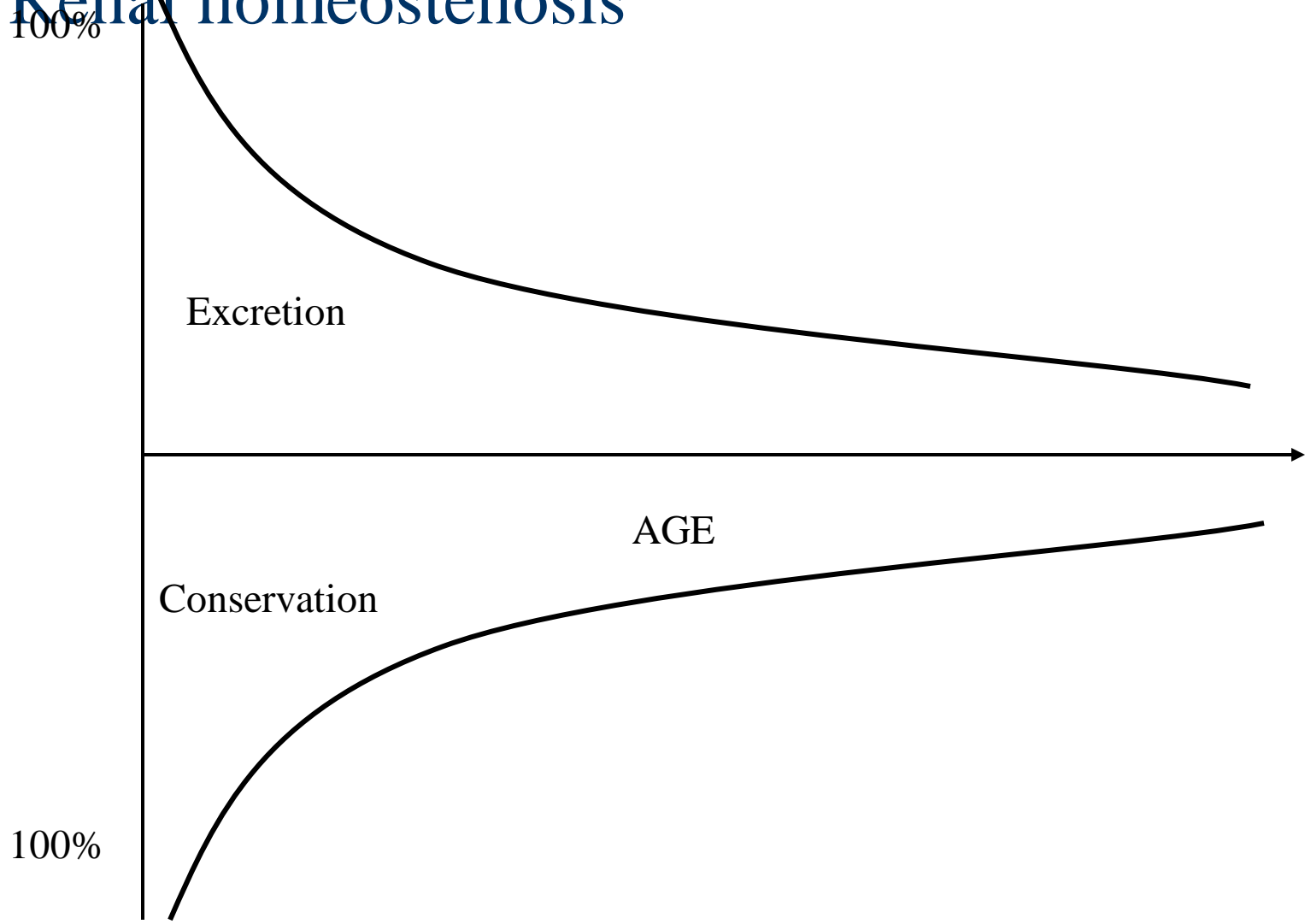- **Baroreceptor sensitivity (risk of orthostatic hypotension)**

# Functional Implications of Organ System Aging

**MUSCULOSKELETAL**

**Decreases in:**

▪ **Number of motor units/myofibrils. Muscle mass**

▪ **Muscle max power output decreases 45% from 50-80**

▪ **Muscle strength decreases 20-30% between 60 and 90 (reversible with high intensity resistance exercises)**
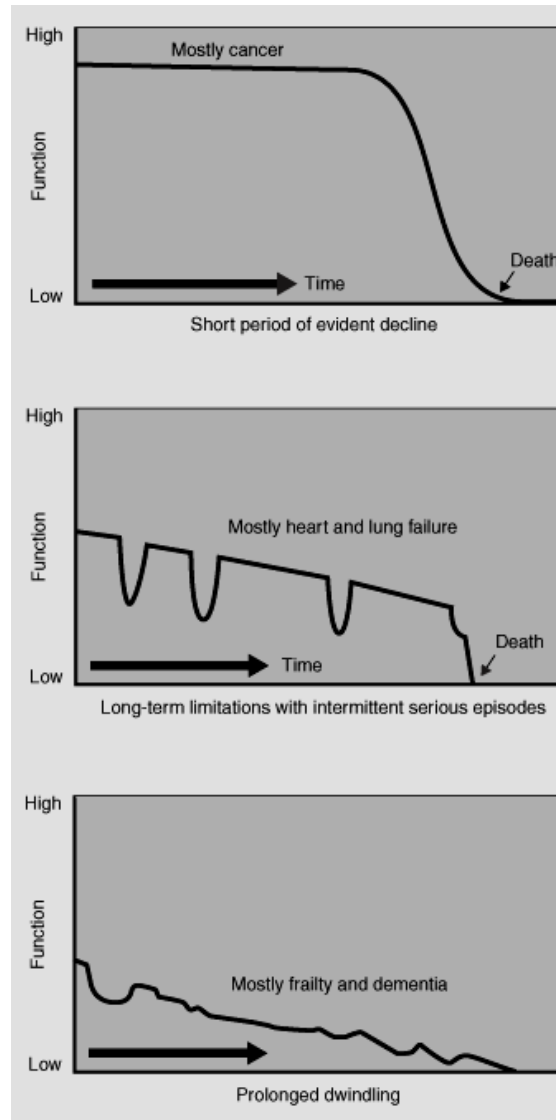
# Renal homeostenosis

# The secret of life

- We are born
- We peak at 30 odd
- We then face a decline in ability
- We become frail and acquire diseases
- Then we become disabled
- Then we die
- Sudden death may intervene at any moment

# End-of-life illness trajectories



- *Lynn J et al. Living well at the end of life. Rand Health 2003*

# "Polypharmacy or poly anticholinergic"

# Medications the good the bad and the ugly

- Modern pharmacology has made peoples lives better
- However 10 to 18% of hospitalisations are related to a medication adverse event
- Beers criteria 20% of older adults are taking medication that are probabaly inappropriate and 3% definitely contraindicated.
- Is it too many ? wrong dose ? Or too few drugs which is the problem ?

# Poly pharmacy

- Traditional teaching dictates that too many drugs are bad
- Are some drugs worse than others
- This statement has rarely been studied
- There is some limited evidence to support that too many drugs are bad for older adults

# ADRs

- **ADRs 2-3x higher in elderly *cf* young**
  - *Cusak et al, 1997*

- **Reportedly 5th leading cause of death in US**
  - *Lazarou et al, JAMA 1998*

- **Contributes to 10% of geriatric admissions**
  - *Williamson and Chopin, 1980*

# ADRs

| No. of drugs | Risk of ADR |
|:---:|:---:|
| 0-5 | 5% |
| 6-10 | 10% |
| 11-15 | 30% |
| 16-20 | 55% |

– *May et al, Clin Pharmacol Ther 1977*

# Falls

# Drugs as a risk factor for falls

- A large body of literature of observational studies/case control

- Few RCTs in older adults measure falls as an adverse event (esp. psychotropic trials)

- A good metaanalysis was published in 1999

# Total number of drugs

- Fairly consistent finding that more than 4 drugs increases risk (OR 2.07-2.91)
- Part of one successful multi-component intervention was to reduce drugs to <4
- Not clear if this definition is only prescription drugs or includes over the counter
- Current evidence base for common conditions start at 4 drug regimes

# Psychotropic drugs

- Neuroleptics OR 1.99
- Anti depressants OR 1.62
- Sedative/Hypnotics OR 1.25
- Benzodiazepines OR 1.4
- TCAs OR of 1.4
- ie Small but significant

# Psychotopic drugs

- Risk probably independent of cofounders
- Risk maybe biased by indication
- Risk goes up probably with
  - More than one
  - Higher dose
  - ? On initiation rather than chronic use

# Psychotropic Drugs

- Short acting BZDs are as risky as Long acting
- New antidepressants may not be safer
- The only study suggested SSRIs maybe worse than TCAs but ? patient selection

# Other drugs

- Analgesics inc NSAIDs and Opiates don't increase risk
- Digoxin OR 1.59 and Diuretics OR 1.09 may increase falls
- Other antihypertensives don't increase risk
- Postural hypotension as a rule doesn't increase falls risk ( but maybe important for an individual)

# Drugs and nutritional status

- Loss of weight typically involves loss of muscle mass
- Muscular weakness has been shown to be a risk factor for falls
- Weight loss is a big risk factor for disability

# Drugs and Nutritional status

- Anorexient: Digoxin, SSRIs, perhexiline, Amiodarone other cardiovascular drugs, metformin

- Metabolically active: Thyroxine, Insulin, Cortico steroids

- Cognitive Impairment/ sedative: antipsychotics, benzodiazepines

- Swallowing/mastication anticholinergic drugs, EPSE from antipsychotics
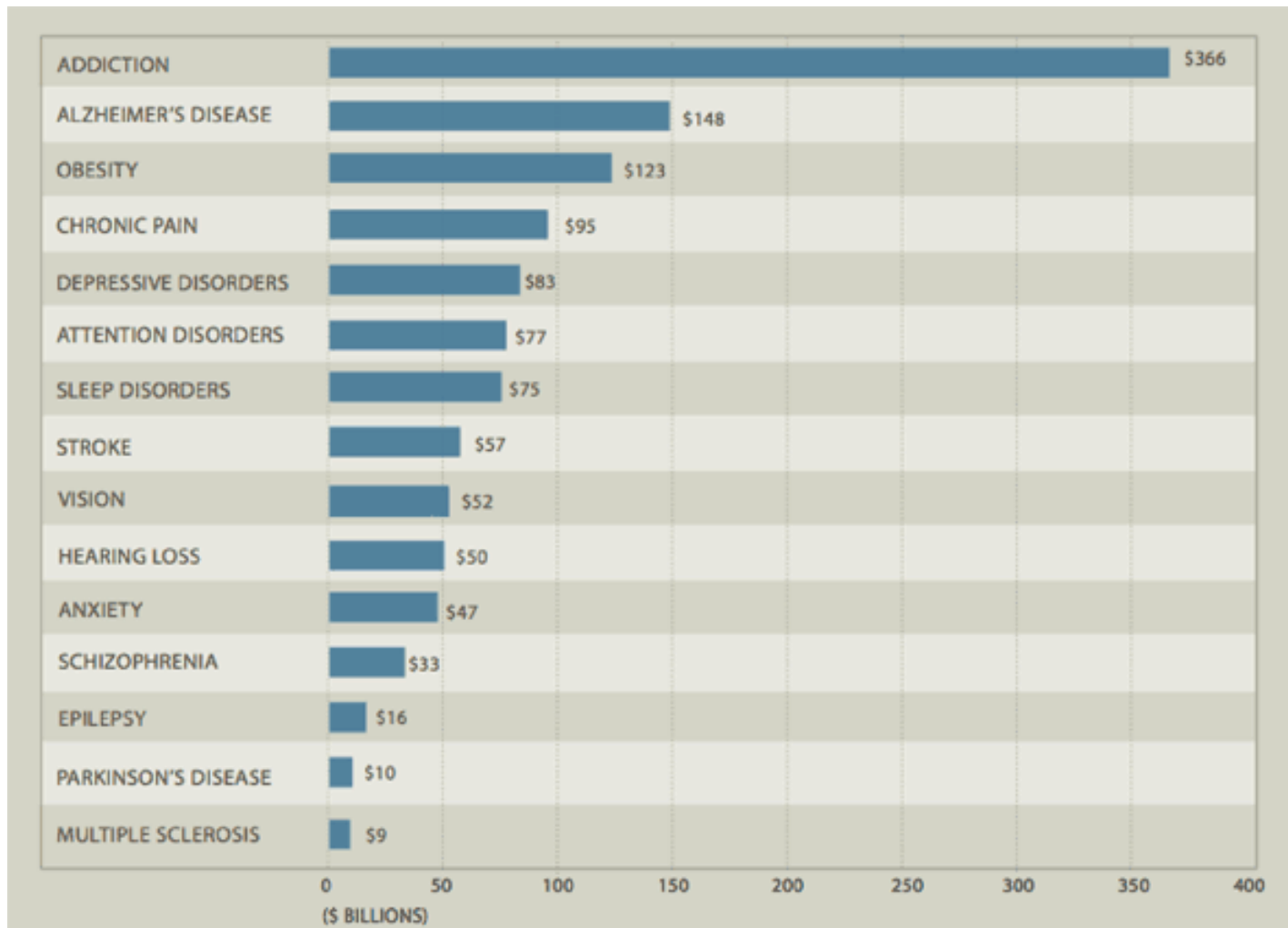
# Drugs and Delirium

- Psychoactive drugs
  - Withdrawal/Discontinuation syndromes
  - Toxicity (serotonin syndrome)

- Non-psychoactive drugs
  - H2 blockers, steroids, cardiac drugs, NSAIDs, antibiotics, opiods

- Drugs with anticholinergic effects

# Anticholinergic drugs and delirium

- Moderate to high anticholinergic activity
  - atropine, benzhexol, hyoscine, oxybutinin, propantheline, tricyclic antidepressants, some antipsychotics

- Medications not usually associated with anticholinergic activity

# Drug burden



| | ($ BILLIONS) |
|---|---|
| ADDICTION | $366 |
| ALZHEIMER'S DISEASE | $148 |
| OBESITY | $123 |
| CHRONIC PAIN | $95 |
| DEPRESSIVE DISORDERS | $83 |
| ATTENTION DISORDERS | $77 |
| SLEEP DISORDERS | $75 |
| STROKE | $57 |
| VISION | $52 |
| HEARING LOSS | $50 |
| ANXIETY | $47 |
| SCHIZOPHRENIA | $33 |
| EPILEPSY | $16 |
| PARKINSON'S DISEASE | $10 |
| MULTIPLE SCLEROSIS | $9 |

# Drug Burden Index

$$DB = \sum \frac{D_{AC}}{\delta_{AC} + D_{AC}} + \sum \frac{D_S}{\delta_S + D_S}$$

DB       Drug Burden

AC       Medications with anticholinergic properties

S       Medications with sedative properties

D       Daily dose

δ       Minimum recommended daily dose approved by US Food and Drug Administration; estimate of $DR_{50}$

# Correlate Drug Burden Index with Function in the Health, Aging and Body Composition (Health ABC) Study Participants

## Population

Random sample of 3075 Medicare recipients

Pittsburgh, Pennsylvania and Memphis, Tennessee

70-79 years, high functioning, community dwelling

## Medication Inventory

"Brown Bag"

All medications actually taken in past 2 weeks

## Objective Functional Measures

# Longitudinal Association Between Drug Burden and Function in Health ABC Study Participants

Association of

– Drug Burden Index at each time point

– Cumulative drug burden exposure

with function over 5 years

# Health ABC Study Participants with Longitudinal Functional Measures

| Baseline (Year 1) Characteristics | Included | Excluded |
|---|---|---|
| n | 2172 | 903 (501 dead) |
| Age* | 73 ± 3 | 74 ± 3 |
| Sex (% female) | 53 | 48 |
| Race (% black)* | 37 | 53 |
| Drug burden Index over zero (%) | 34 | 37 |
| Mean number of physical comorbidities* | 1.9 ± 1.3 | 2.3 ± 1.4 |
| % with significant depression, anxiety or cognitive impairment* | 25 | 29 |

*p<0.01 for difference between included and excluded participants

# Covariates

- Socio-demographics
- Cumulative physical comorbidities
- Cumulative significant depression, anxiety or cognitive impairment
- Significant sleep disturbance
- Body Mass Index (BMI)

# Objective Functional Outcomes

- **Short Physical Performance Battery (SPPB)**
  - Observed measures for:
    - Gait speed on 4 or 6 m walk
    - Chair stands
    - Standing balance
- **Gait Speed on 4 or 6 m walk**
  - Component of SPPB
- **Grip Strength**
  - Isometric dynamometer
  - Loss of grip strength:
    - strong predictor of disability and mortality in older people
    - associated with frailty

# Association between Drug Burden Index and 4 m or 6 m Walk Speed at Year 6
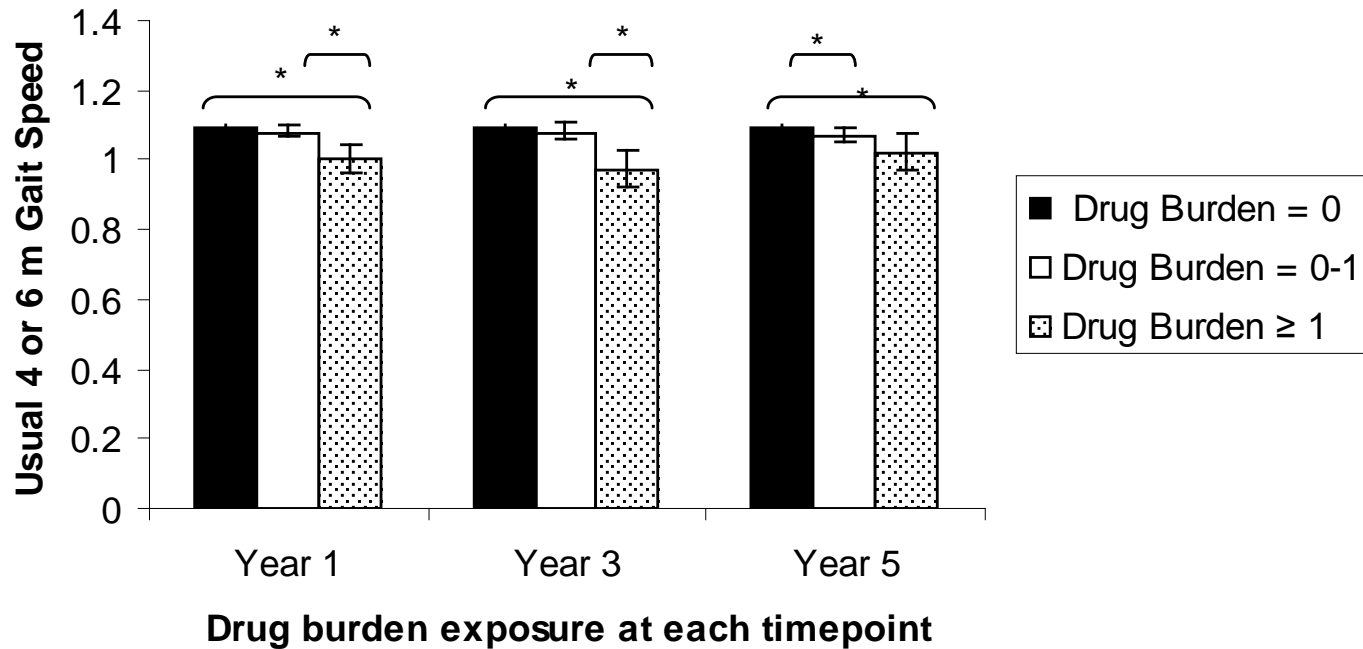


| | Subjects with four or six meter gait speed at year 6 (n=2192) | | |
|---|---|---|---|
| Drug burden | Year 1 | Year 3 | Year 5 |
| 0 | 1457 | 1619 | 1566 |
| 0-1 | 624 | 516 | 556 |
| ≥ 1 | 111 | 57 | 70 |

# Association between Drug Burden Index and Grip Strength at Year 6
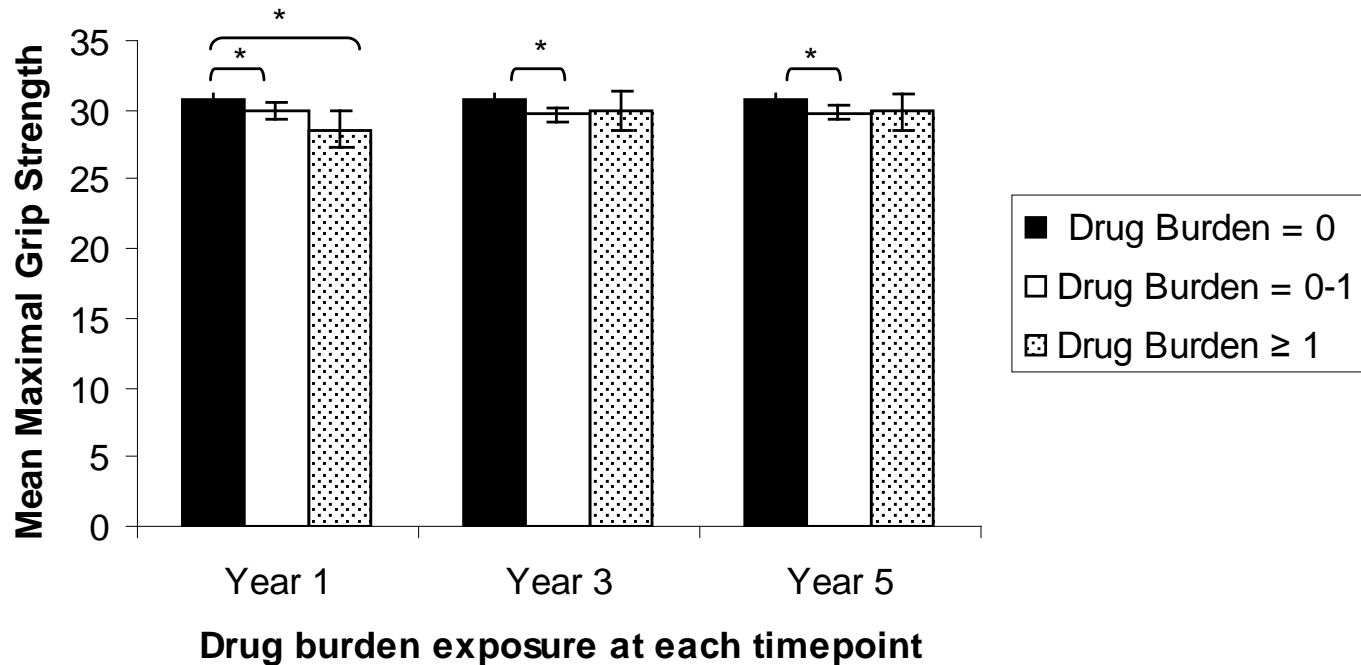


| | Subjects with grip strength at year 6 (n=2099) | | |
|---|---|---|---|
| Drug burden | Year 1 | Year 3 | Year 5 |
| 0 | 1397 | 1550 | 1506 |
| 0-1 | 600 | 495 | 530 |
| ≥ 1 | 102 | 54 | 63 |

# Higher Baseline Drug Burden Index Associated with Lower Function Year 6

- Multivariate regression analysis
- One unit increase in drug burden in year 1 would predict at year 6 an independent decrease in:
  - SPPB of 0.32 (p < 0.005)
  - Gait speed of 0.05 (p < 0.0005)
  - Grip strength of 0.62 (p=0.05)
- Degree of change
  - > that of 2 additional physical or mental comorbidities for each outcome

# Substance abuse in older adults

- Poorly studied
- In my experience benzodiazepine abuse and alcohol abuse are common problems
- Dementia can predispose to alcohol abuse in particular
  - They forget that they have been drinking

# Substance abuse in older adults

- The issues of psychological and physical dependency plague prescribing
- Common in therapeutic doses of benzodiazepines
- Also common with drugs like Protpn Pump Inhibitors and Diuretics for example

# Conclusions

- The therapeutic risks of prescribing in late life centres on nutrition, falls and cognition
- Worse in misuse
- Alcohol is the worse drug
- The issues of psychological and physical dependency are common in older adults