Multi-morbidity in Dementia: A 21st Century Challenge’

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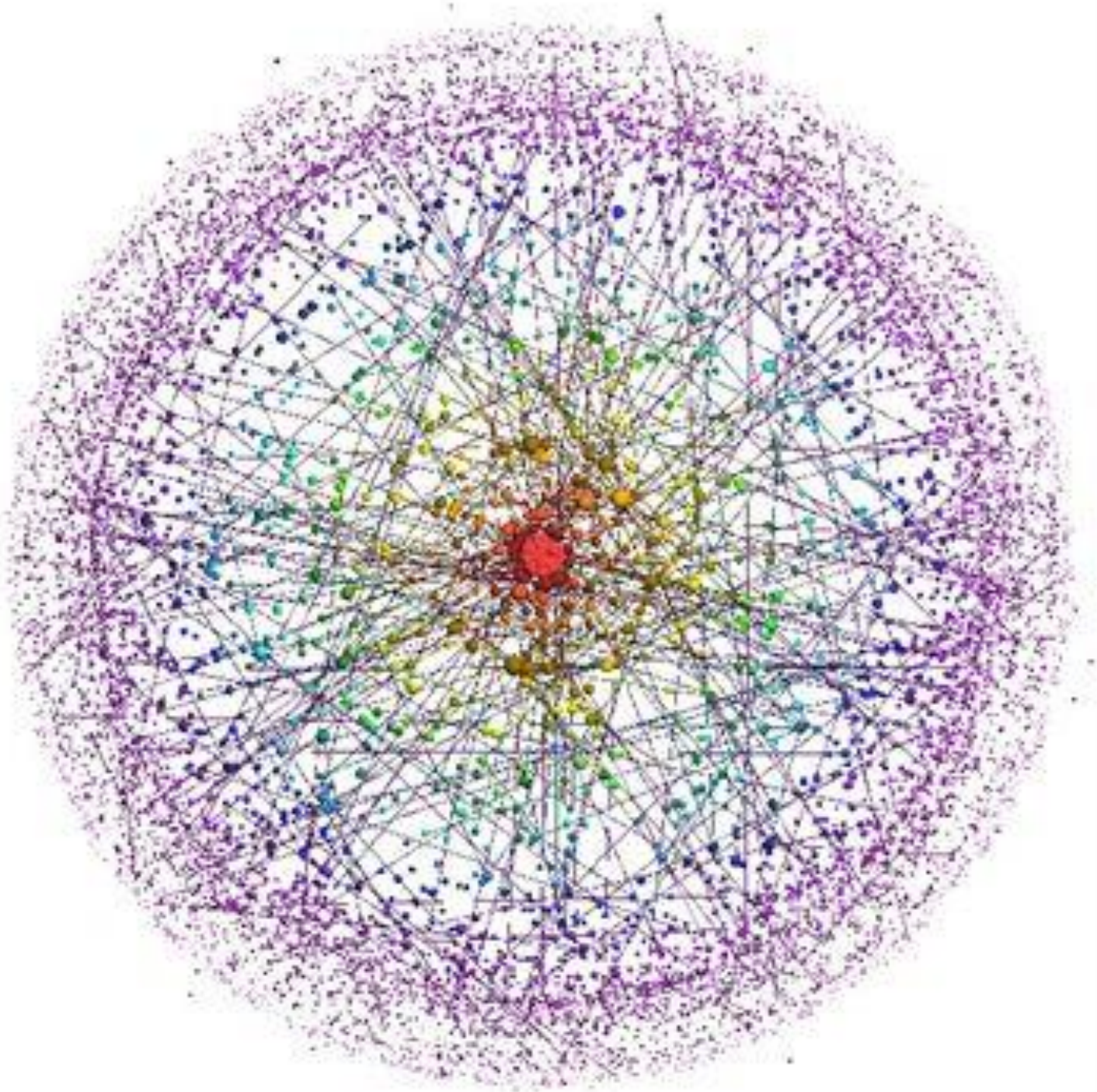
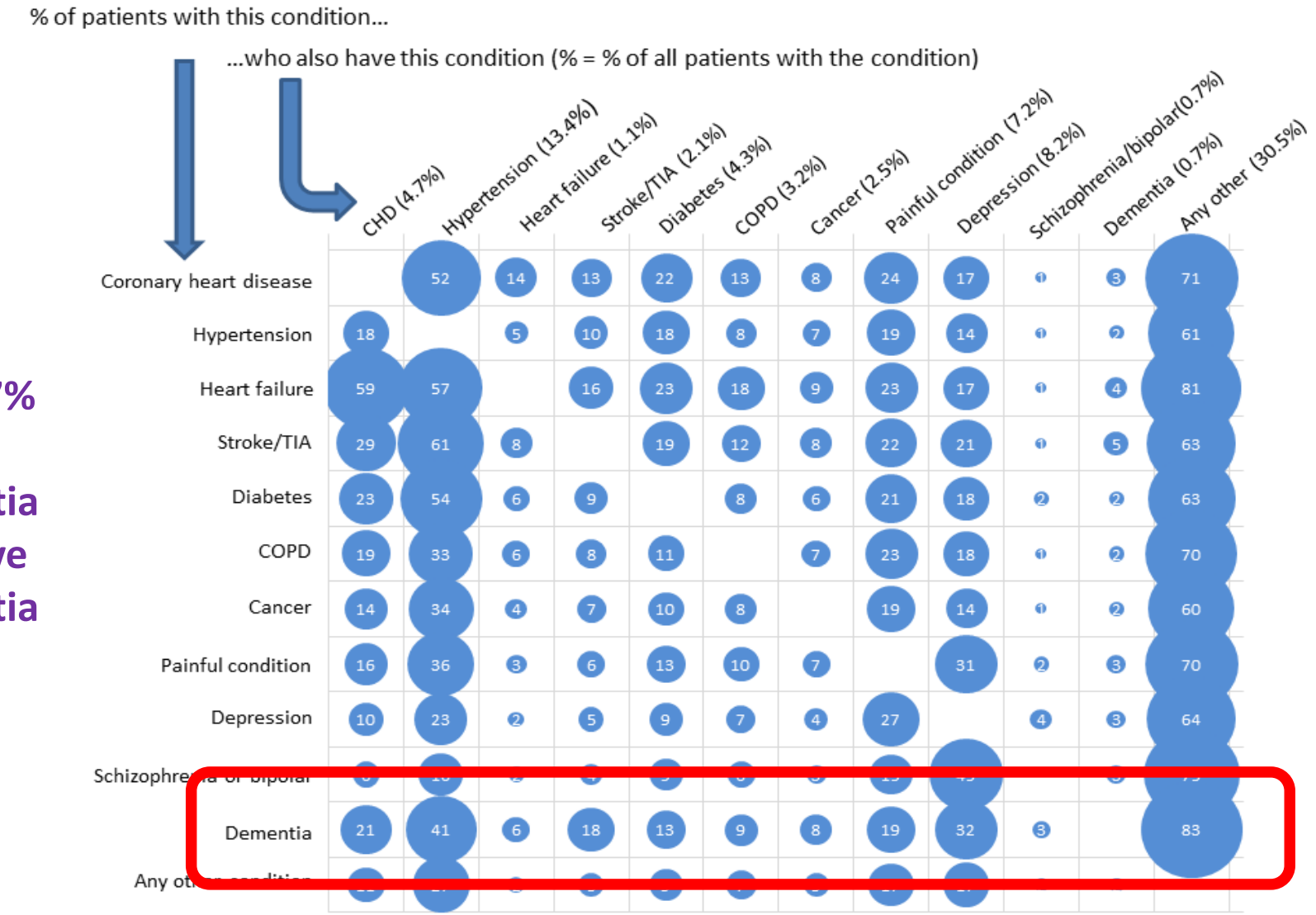
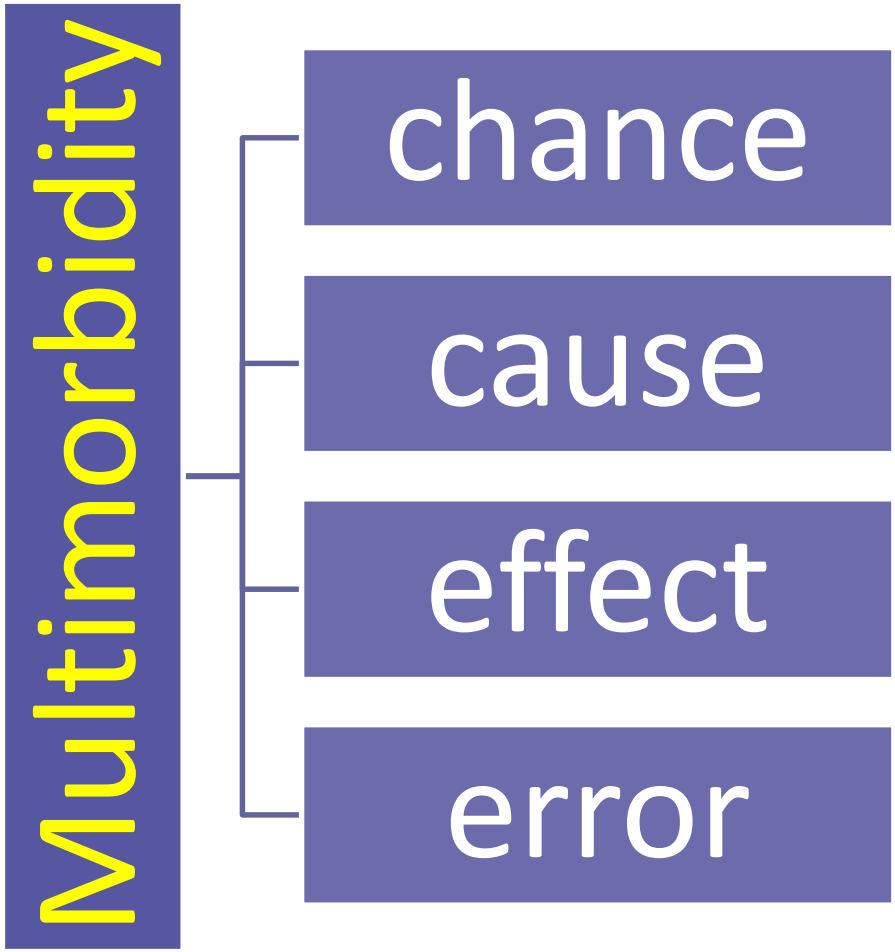


Most people of any age with any long term condition have multiple conditions *(Scottish School of Primary Care, 2012)*



Only 17% with dementia *just* have dementia

Multimorbidity – two or more things happening together - mechanism?



Dementia cause and effect – some subtypes require comorbidity (or lack of it)

Alzheimer's disease

- Nothing

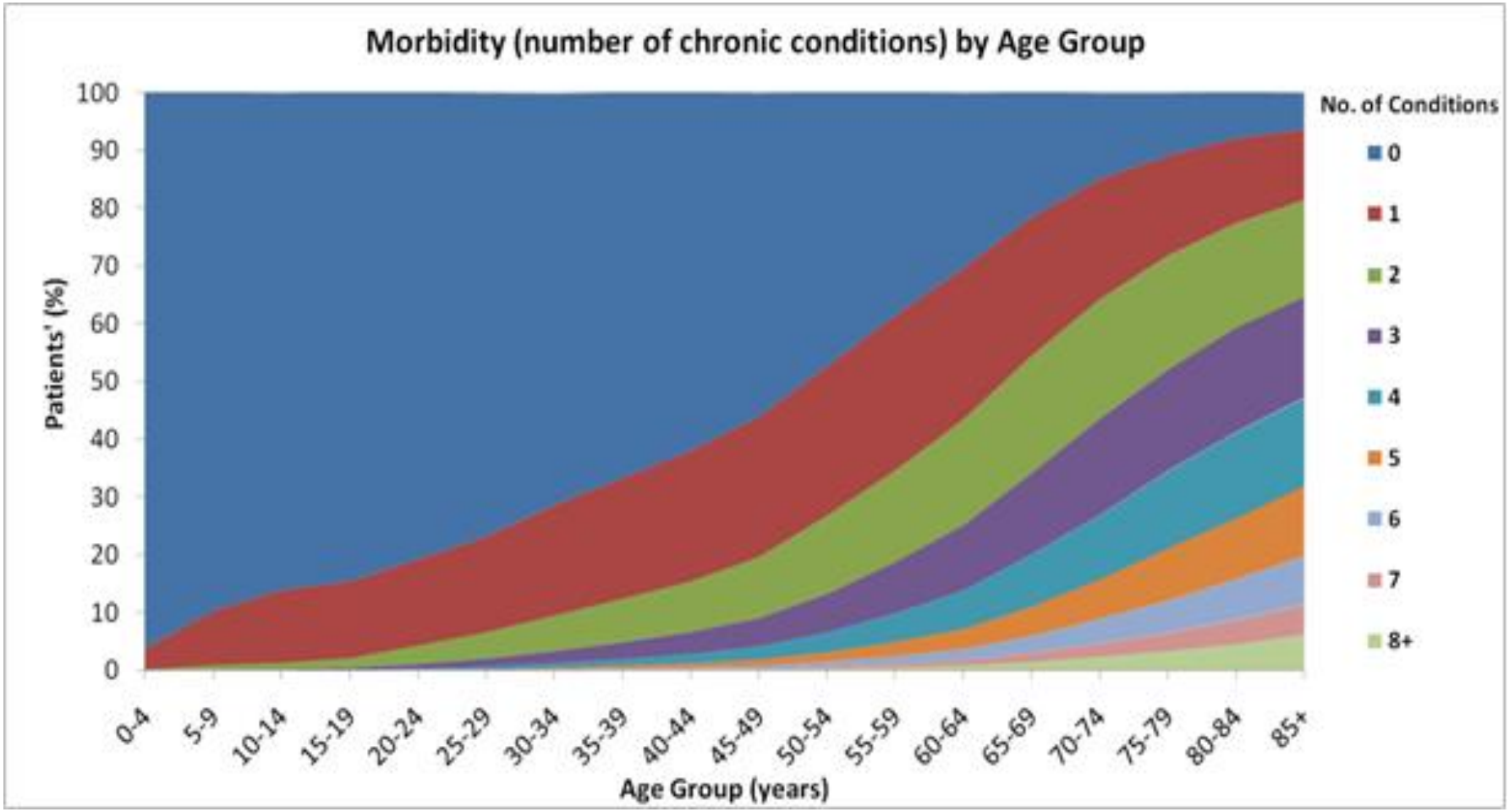
Vascular dementia

- Vascular disease

Lewy body dementia

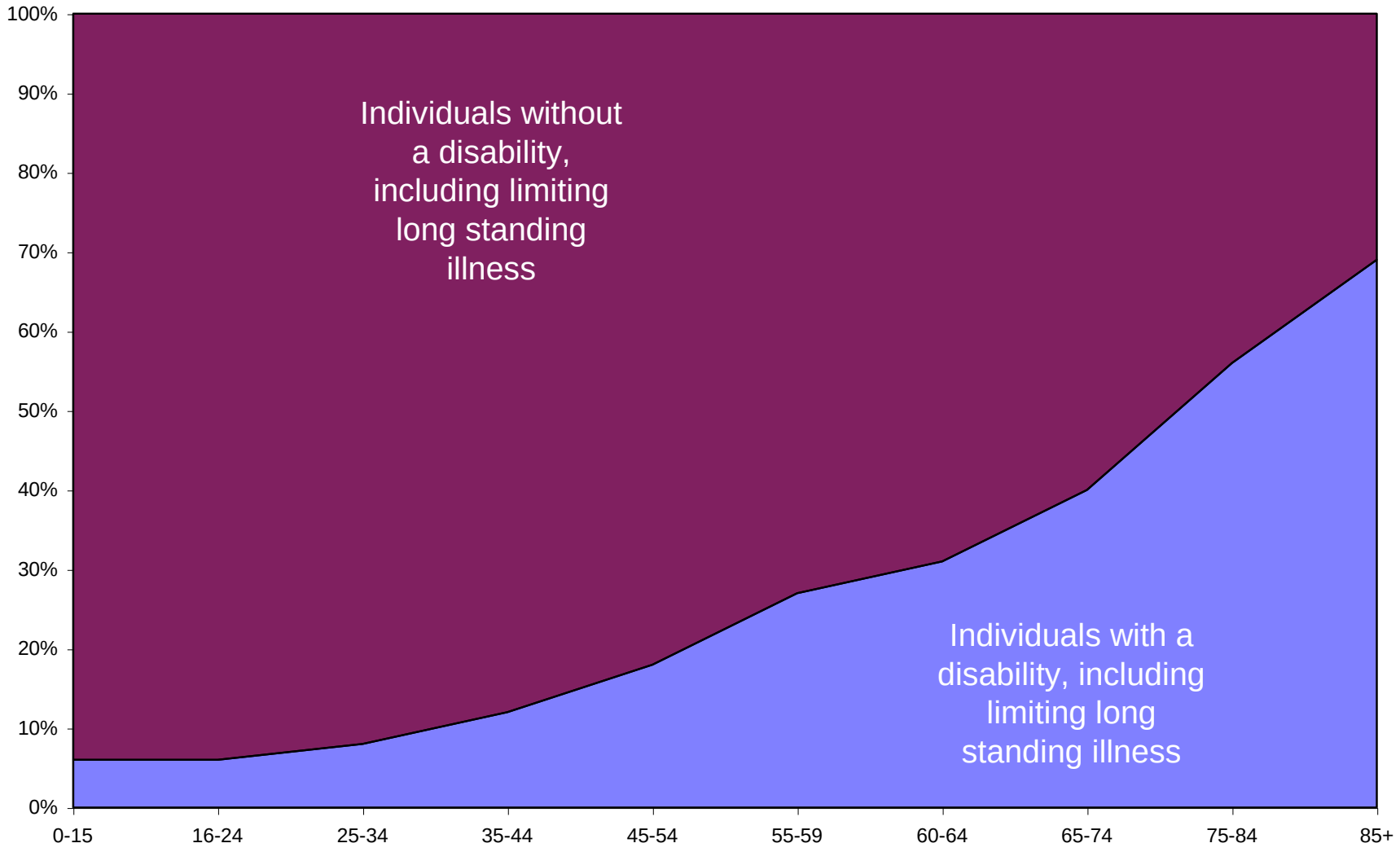
- Parkinson's disease

Dementia chance – stuff happens to older people - multimorbidity (*Barnett et al, 2012*)



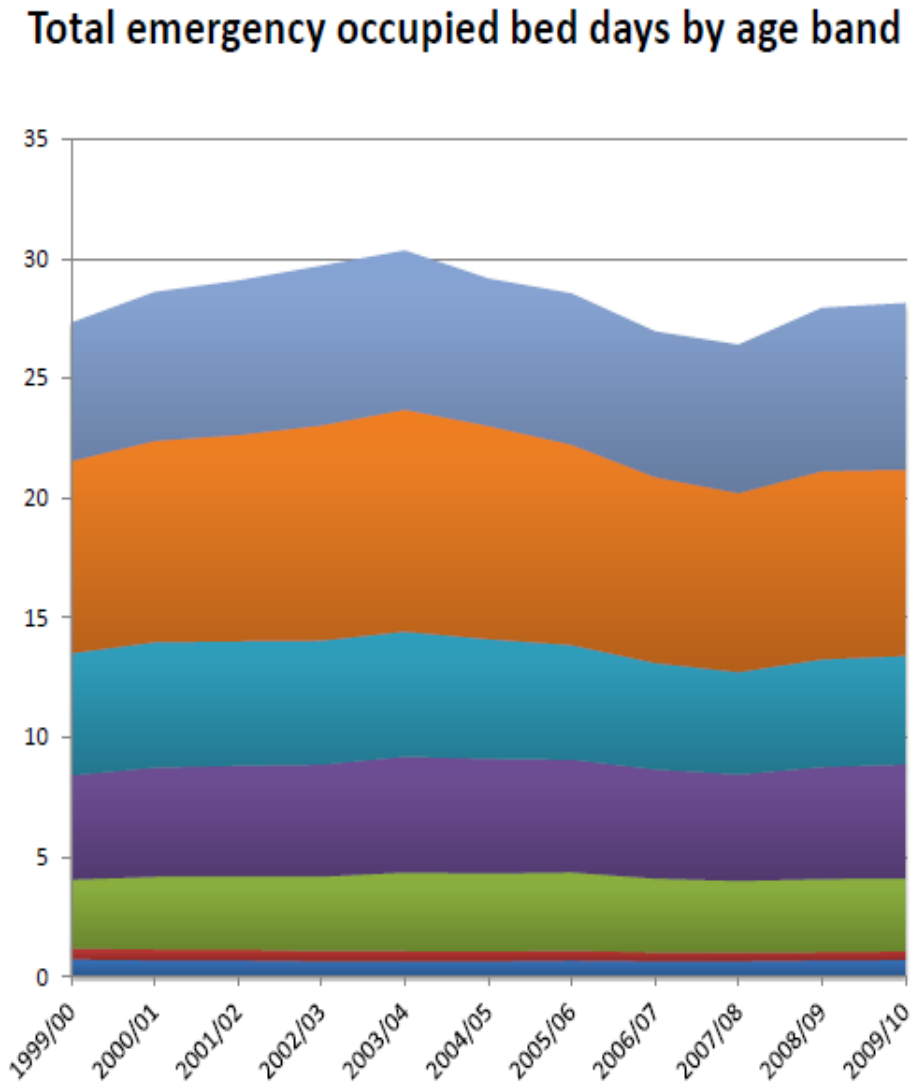
- Most over-65s have 2 or more conditions
- Most over-75s have 3 or more conditions

Prevalence of disability rises with age



Family Resources Survey 2007

Over 65s in hospital in England – older people are the NHS's customers (HES data)



- 60% admissions
- 70% bed days
- 85% delayed transfers
- 65% emergency readmissions
- 75% deaths in hospital
- 25% bed days are in over 85s

Comorbidity in primary care

- People with dementia report fewer symptoms (McCormick et al, 1994)
- Undiagnosed but treatable medical disease in almost half (Larson et al, 1984)
- Wishard Health Services, Indiana US (Schubert et al, 2006) people with dementia n=107/3,013
  - **Mean 4 chronic medical conditions**
  - **Prescribed 5.1 medications**
  - **82% hypertension**
  - **39% diabetes mellitus**

US Health and Retirement Survey (Cigolle et al, 2007)

Respondents with an Index Geriatric Condition Who Have Other Geriatric Conditions*

Condition	≥1 Other Geriatric Conditions (95% CI), *weighted* %†	≥2 Other Geriatric Conditions (95% CI), *weighted* %†	≥3 Other Geriatric Conditions (95% CI), *weighted* %†
Cognitive impairment (*n* = 1012)	78.7 (75.5–81.6)	46.3 (42.3–50.4)	20.1 (17.1–23.4)
Injurious falls (*n* = 1084)	63.5 (60.0–66.8)	32.9 (30.2–35.7)	14.3 (11.8–17.3)
Incontinence (use of pads) (*n* = 1439)	60.2 (57.8–62.5)	29.3 (26.7–32.0)	12.7 (10.3–15.5)
Low BMI (*n* = 334)	63.1 (57.7–68.2)	38.8 (32.4–45.8)	22.5 (18.2–27.6)
Dizziness (*n* = 1540)	69.7 (66.9–72.5)	31.2 (28.7–33.7)	12.2 (9.9–15.0)
Vision impairment (*n* = 973)	74.5 (71.0–77.7)	43.3 (39.5–47.3)	19.8 (17.0–22.9)
Hearing impairment (*n* = 2884)	48.7 (46.6–50.9)	20.4 (18.8–22.2)	7.7 (6.4–9.3)

* BMI = body mass index.

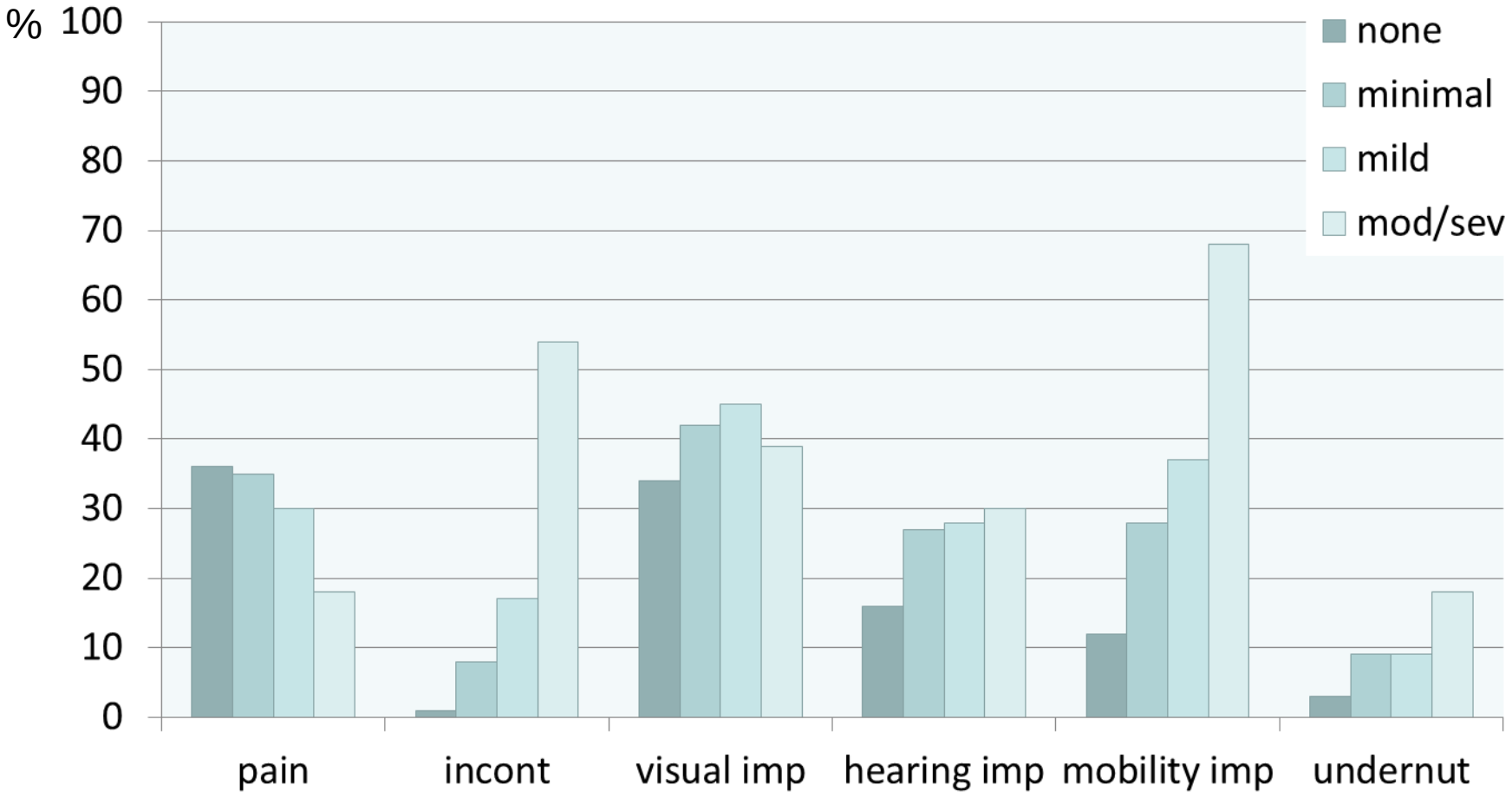
† Weighted percentage derived by using the Health and Retirement Study (HRS) respondent population weights to adjust for the complex sampling design of the HRS.

- **50% of total sample had 1+ 'geriatric conditions'**
- **Cognitive impairment - highest level of comorbidity**
  - **46% having two or more**
  - **20% having three or more of the other conditions**

Data from low to middle income countries (Prince at al 2010)

- multicentre cross-sectional 65y+ (n=15,022)
- 11 areas: China, India, Cuba, Dominican Republic, Venezuela, Mexico and Peru

The prevalence of physical impairments, by dementia diagnosis and severity – Latin America



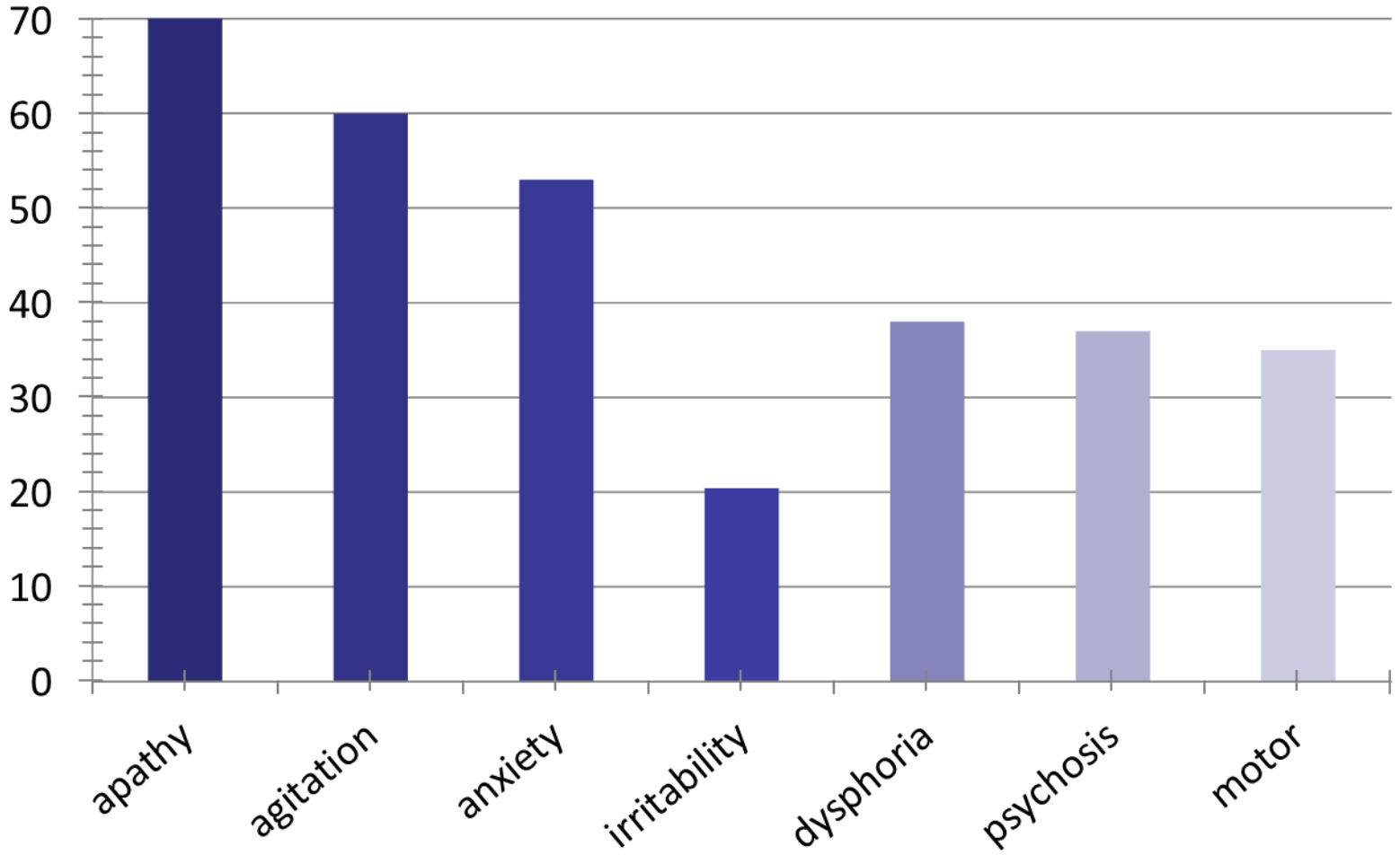
Summary

MULTIMORBIDITY IS COMMON IN DEMENTIA
MULTIMORBIDITY IS A COMPLEX PHENOMENON
CO-MORBIDITIES OFTEN POORLY MANAGED

COMORBIDITY WITH MENTAL DISORDER

BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS IN DEMENTIA

Frequency of BPSD in dementia



Lyketsos CG et al. Am J Psychiatry 2000 May;157(5):708-14

Management of BPSD – a lack of specificity – evidence of difference in dementia

Treatments

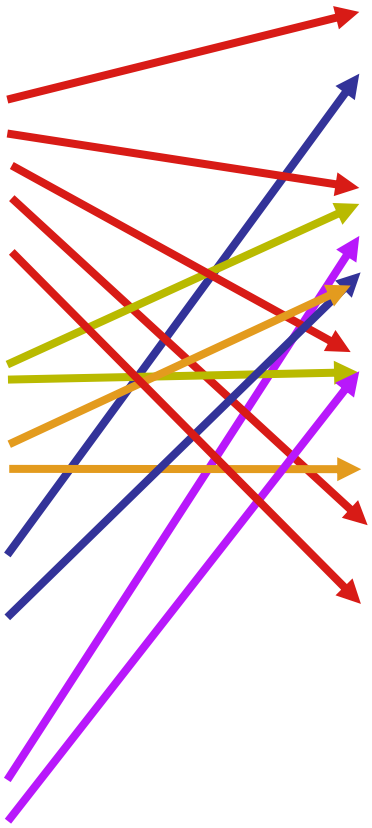
Anti-dementia drugs
Cholinesterase inhibitors
i.e.Donepezil, Rivastigmine, Galantamine
Glutamatergic drugs i.e Memantine

Antidepressants

Antipsychotics

Behavioural techniques Memory retraining
ABC approach

Novel interventions
Bright light therapy
Aromatherapy
Exercise



Symptoms

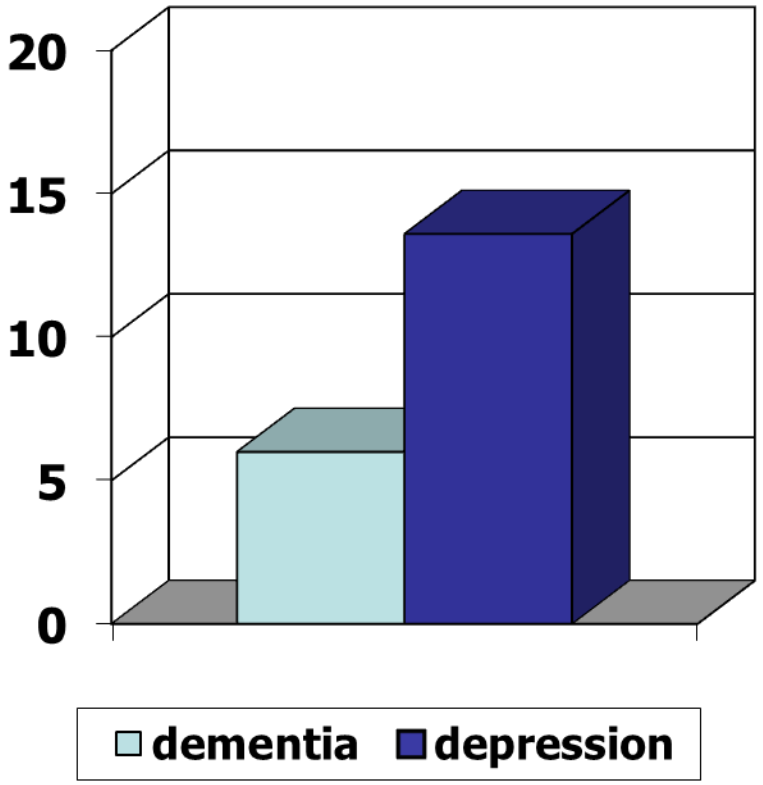
Memory loss, executive dysfunction, aphasia
Behavioural problems e.g. agitation

Depression

Psychosis eg delusions, hallucinations
Activities of daily living

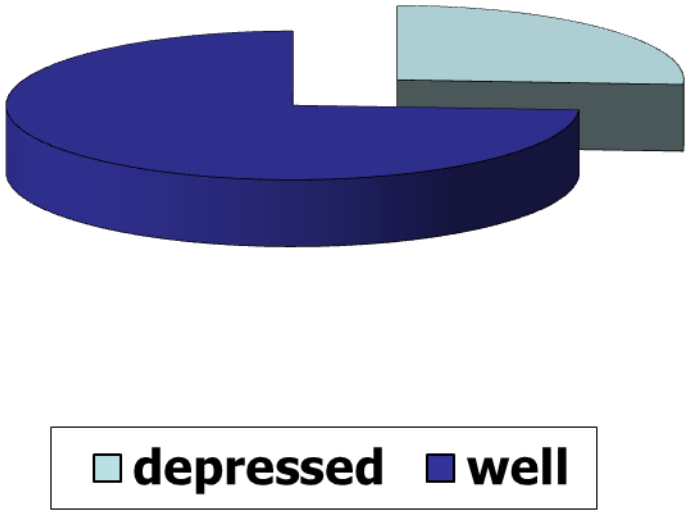
DEPRESSION IN DEMENTIA – AN EXEMPLAR

Epidemiology



- Both common in later life
  - 6% dementia
  - 14% depression
- Assorted randomly expect 1% co-morbidity

Epidemiology II



- Prevalence: 0-86% of people with dementia depressed
- Incidence: 12% per year (Steinberg et al, J Neuropsych 2003)
- Depends on:
  - Study group
  - Diagnostic criteria for depression
- Unstable and poor estimates for clinical practice

Depression in dementia – not a good thing

- High distress
- Low quality of life
- High carer stress and burden
- High carer depression
- Lowers cognition
- Lowers functional ability
- Placement
- Death
- Often not treated

Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial

Sube Banerjee, Jennifer Hellier, Michael Dewey, Renee Romeo, Clive Ballard, Robert Baldwin, Peter Bentham, Chris Fox, Clive Holmes, Cornelius Katona, Martin Knapp, Claire Lawton, James Lindesay, Gill Livingston, Niall McCrae, Esme Moniz-Cook, Joanna Murray, Shirley Nurock, Martin Orrell, John O'Brien, Michaela Poppe, Alan Thomas, Rebecca Walwyn, Kenneth Wilson, Alistair Burns

Summary

Background Depression is common in dementia but the evidence base for appropriate drug treatment is sparse and equivocal. We aimed to assess efficacy and safety of two of the most commonly prescribed drugs, sertraline and mirtazapine, compared with placebo.

Methods We undertook the parallel-group, double-blind, placebo-controlled, Health Technology Assessment Study of the Use of Antidepressants for Depression in Dementia (HTA-SADD) trial in participants from old-age psychiatry services in nine centres in England. Participants were eligible if they had probable or possible Alzheimer's disease, depression (lasting ≥4 weeks), and a Cornell scale for depression in dementia (CSDD) score of 8 or more. Participants were ineligible if they were clinically critical (eg, suicide risk), contraindicated to study drugs, on antidepressants, in another trial, or had no carer. The clinical trials unit at King's College London (UK) randomly allocated participants with a computer-generated block randomisation sequence, stratified by centre, with varying block sizes, in a 1:1:1 ratio to receive sertraline (target dose 150 mg per day), mirtazapine (45 mg), or placebo (control group), all with standard care. The primary outcome was reduction in depression (CSDD score) at 13 weeks (outcomes to 39 weeks were also assessed), assessed with a mixed linear-regression model adjusted for baseline CSDD, time, and treatment centre. This study is registered, number ISRCTN88882979 and EudraCT 2006-000105-38.

Findings Decreases in depression scores at 13 weeks did not differ between 111 controls and 107 participants allocated

Lancet 2011; 378: 403–11

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See Comment page 375

Institute of Psychiatry, Health Services and Population Research Department (Prof S Banerjee MD, M Dewey PhD, R Romeo PhD, M Knapp PhD, N McCrae PhD, J Murray MA, M Poppe PhD), **Mental Health and Neuroscience Clinical Trials Unit** (J Hellier MSc, R Walwyn PhD), **and Wolfson Centre for Age-Related Disease** (C Ballard MD), **King's College London, London, UK;**

CSDD scores by treatment group, unadjusted means with 95% CI (a lower CSDD score means less depressive symptoms)

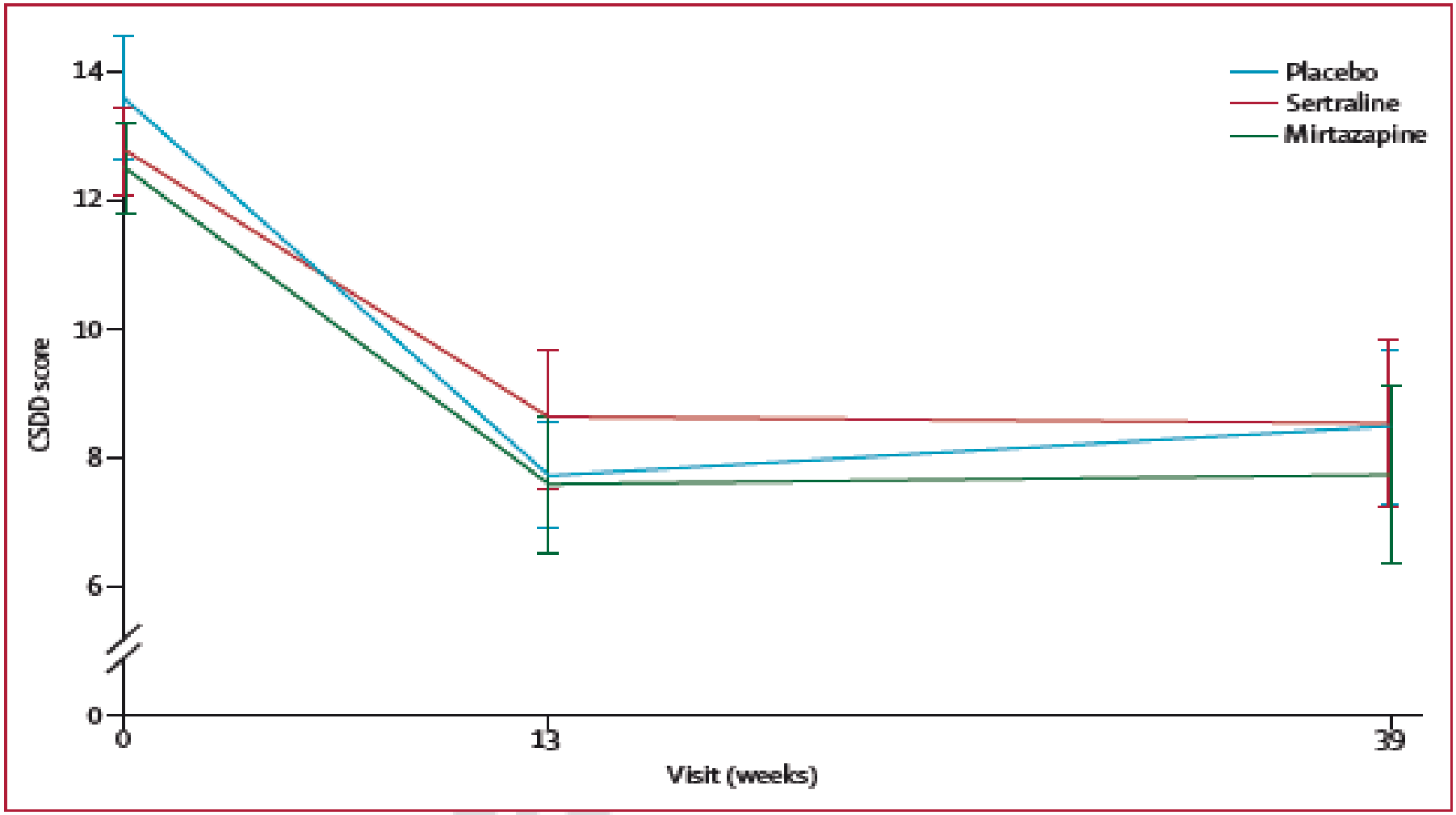


Figure 2: **Unadjusted mean CSDD scores by treatment group**
Lowest score is best. Error bars show 95% CIs. CSDD=Cornell scale for depression in dementia.

Adverse Reactions by week 39

	Treatment Group			Total
	Placebo	Sertraline	Mirtazipine	
Adverse Reaction				
Yes	29	46	44	119
No	82	61	64	207
Total	111	107	108	326

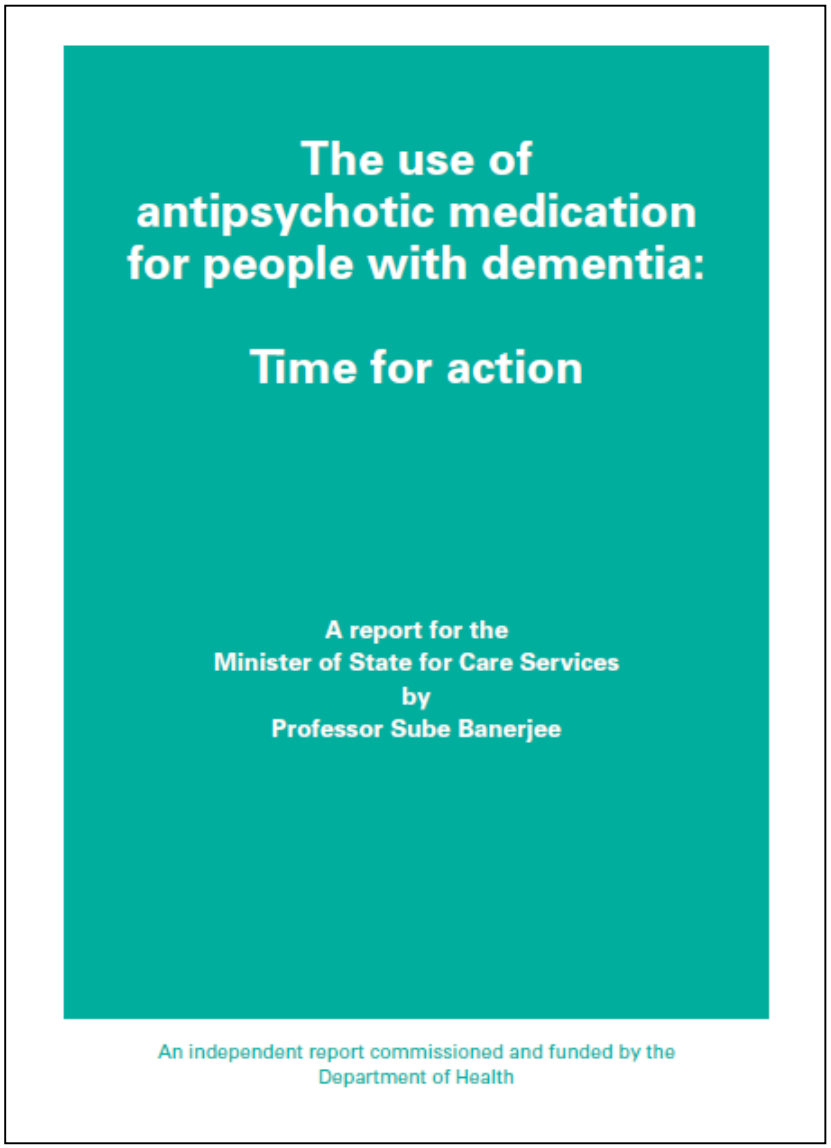
Fisher's Exact p=0.017

HTA-SADD - conclusions

- What do we know?
  - That the evidence has changed
- No superiority of drugs on primary endpoints
- Not
  - Dementia severity
  - Depression severity
  - Depression type
  - Dose reached
  - Drop-out
- Depression is different in dementia

ANTIPSYCHOTIC MEDICATION IN DEMENTIA

UK Ministerial review of use of antipsychotics in dementia



- Published November 2009
- Comprehensive review
  - Negative effects
  - Positive effects
- Analysis of reasons for current clinical behaviour
- Practical clinical plan to deal with problems found

Summary of risks and benefits at a population level of the use of atypical antipsychotics for BPSD in people with dementia

- data suggest that treating 1,000 people with BPSD with an atypical antipsychotic drug for around 12 weeks would result in
  - an additional 91–200 patients with behaviour disturbance showing clinically significant improvement
  - an additional 10 deaths;
  - an additional 18 CVAEs,
    - » around half of which may be severe;
  - no additional falls or fractures; and
  - an additional 58–94 patients with gait disturbance.

- For UK
  - **1,800 deaths per year**
  - **1,620 severe CVAEs per year**

Just because it flies it doesn't make it a bird

All that looks like depression is not necessarily so

- Heterogeneity in depression in dementia
  - (i) a group situationally determined as a reaction to the impacts of dementia and may respond to problem solving and support
  - (ii) a homophenotypic group where the syndrome looks like depression but may have a different biological basis and a different (poor) response to antidepressant treatment
  - (iii) a group of people who carry depression into dementia or who develop a ‘true’ episode of MDD in dementia where response may be similar to MDD but where there may also be impairment in the treatment response due to the neurochemical changes in dementia.

What does this mean?

- Depression (and psychosis) are different in dementia
- Psychopharmacology is different in dementia

- Need to be very careful in generalising findings from non-demented populations to people with dementia
  - **Effects**
  - **Harms**

CO-MORBIDITY IS ALL ABOUT COMPLEXITY – DIFFERENT RULES APPLY

Treatment (Condition A + Condition B + Condition C)

$\neq$

Treatment A + Treatment B + Treatment C

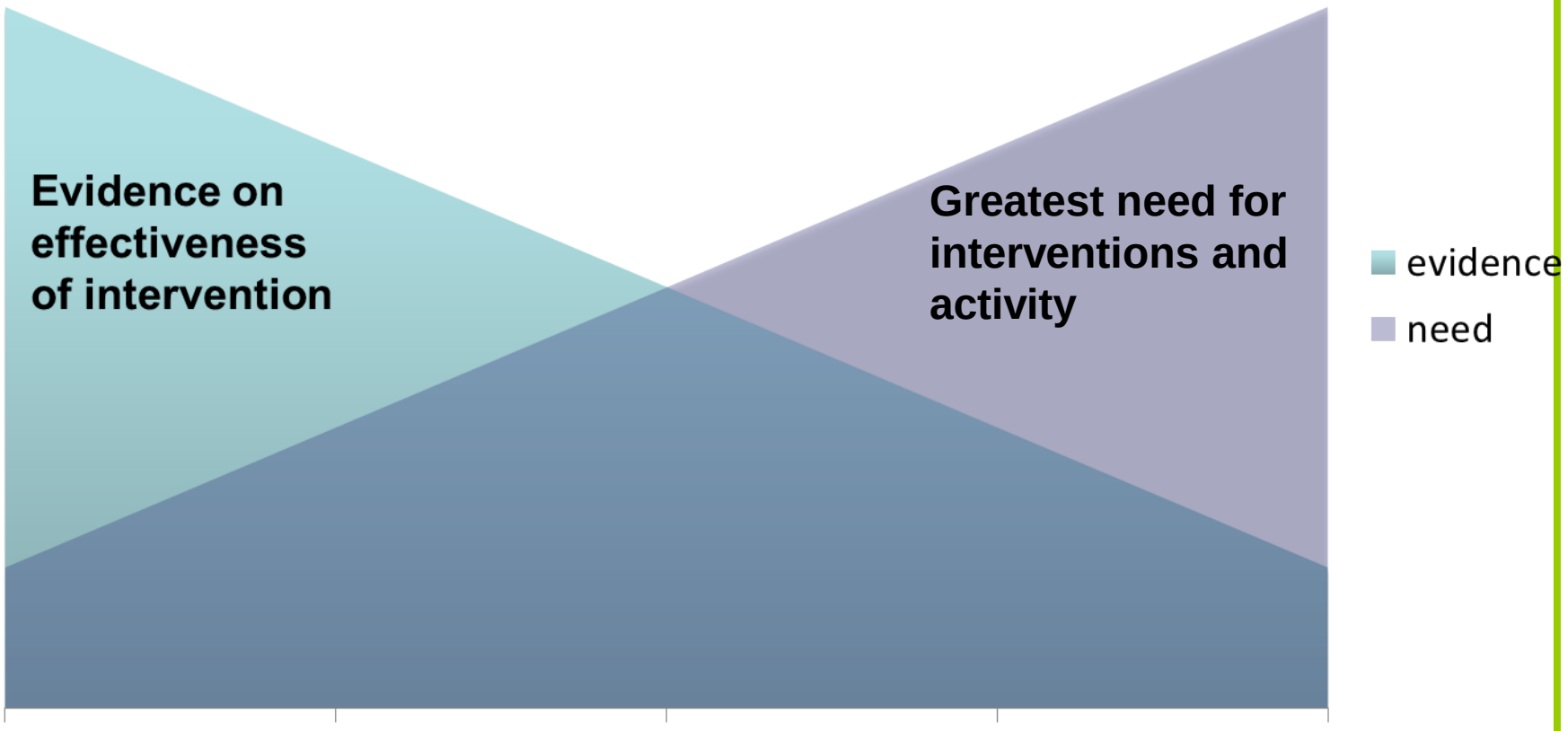
Summary

- Dangers in generalising data from non-demented populations to those with dementia
  - Research
  - Practice
  - Services
- We need evidence that relates to treatment in the complex populations we actually serve

The paradox of evidence and need

Single conditions
simplicity

Multimorbidity
complexity



Final thoughts – our simple paradigms lead to failures in research, services and systems

*If we design **services** for people with one thing wrong at once but people with many things wrong turn up, the fault lies not with the users but with the service, yet all too often these patients are labelled as inappropriate and presented as a problem* (Rockwood, 2005)

***Systems** designed to treat occasional episodes of care for normally healthy people are being used to deliver care for people who have complex and long term conditions. The result is often that they are passed from silo to silo without the system having ability to co-ordinate different providers* (Dorrell, 2009)

Thank you!