The Challenge of Multimorbidity

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WORLD CHANGING GLASGOW

Acknowledgements:

Katie Gallacher, Carl May and Victor Montori

AND

The International Minimally Disruptive Medicine Workgroup:

Kasey Boehmer, Sara Macdonald, Susan Browne, Bhautesh Jani, Peter Hanlon, David Blane, David Eton, Nilay Shah, Nathan Shippee, Aaron Leppin, Patricia Erwin, Kathleen Yost

Acknowledgements - Funding
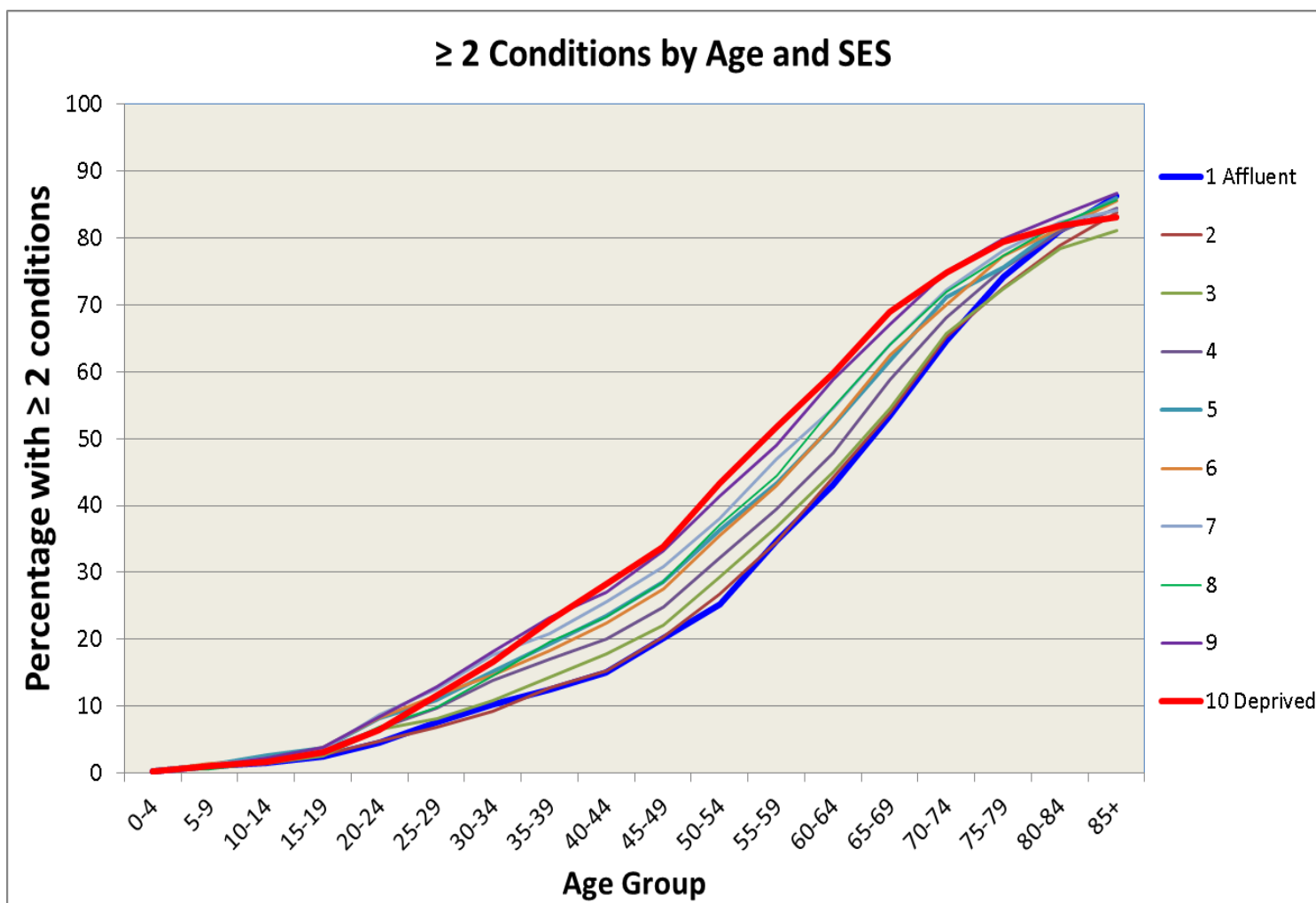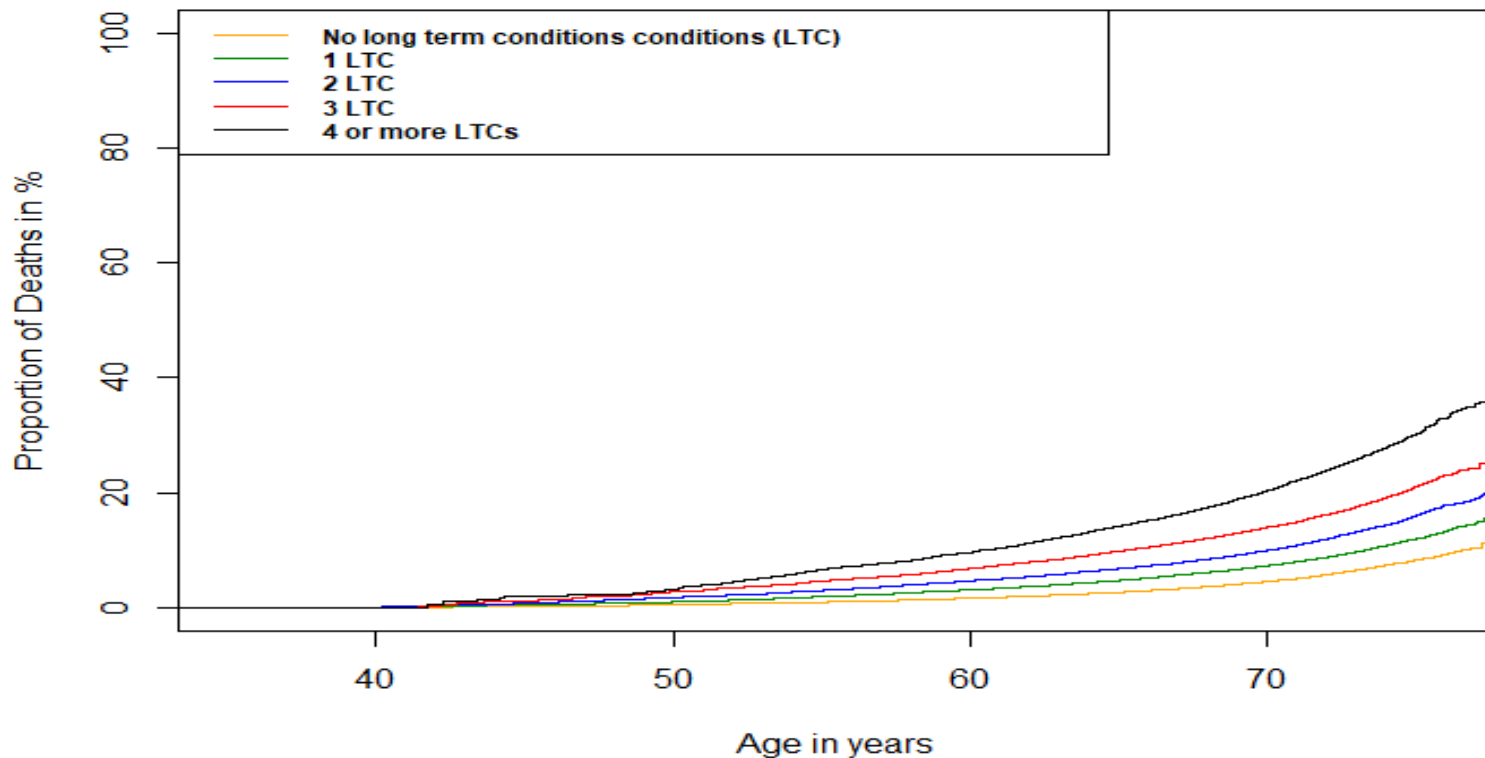
Multiple Morbidity in Scotland

Barnett, K., Mercer SW et al. (2012) Epidemiology of multimorbidity and implications for healthcare, research, and medical education: a cross-sectional study. Lancet, 380 (9836). pp. 37-43

Multimorbidity
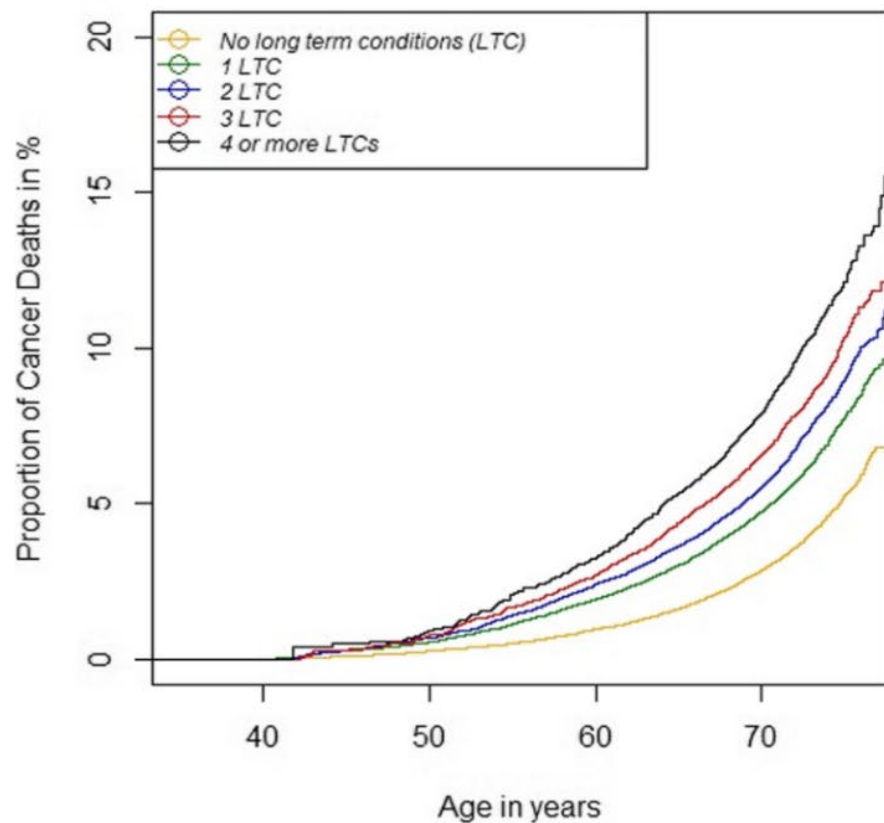# Higher All-cause Mortality

Multimorbidity & All-cause mortality for UK Biobank Participants

Jani B et al. Relationship of Multimorbidity, Demographic Factors and Mortality: Findings from UK Biobank Cohort. BMC Medicine. In Press.

Multimorbidity & Cancer mortality in UK Biobank

Multimorbidity & Vascular mortality in UK Biobank

Legend (both panels):
- No long term conditions (LTC)
- 1 LTC
- 2 LTC
- 3 LTC
- 4 or more LTCs

Left panel: Proportion of Cancer Deaths in % vs Age in years

Right panel: Proportion of Vascular Deaths in % vs Age in years

LTC, long-term conditions. Jani B et al. Relationship of multimorbidity, demographic factors and mortality: findings from UK biobank cohort. BMC Medicine 2019;17:74.
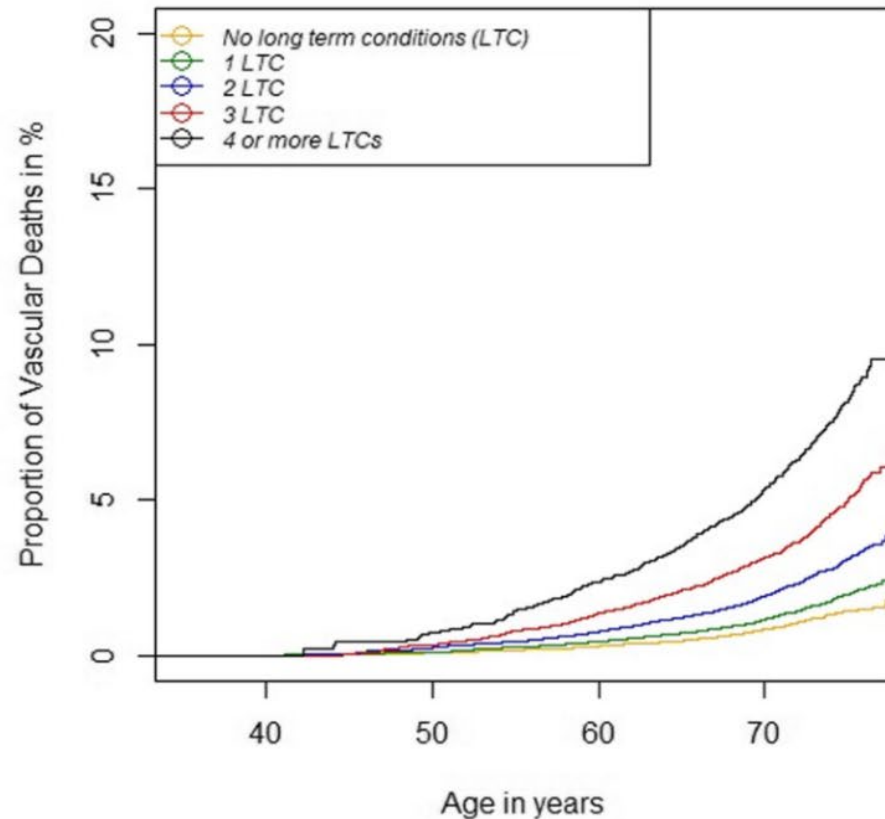
Jani B et al. Relationship of Multimorbidity, Demographic Factors and Mortality: Findings from UK Biobank Cohort. BMC Medicine. In Press.

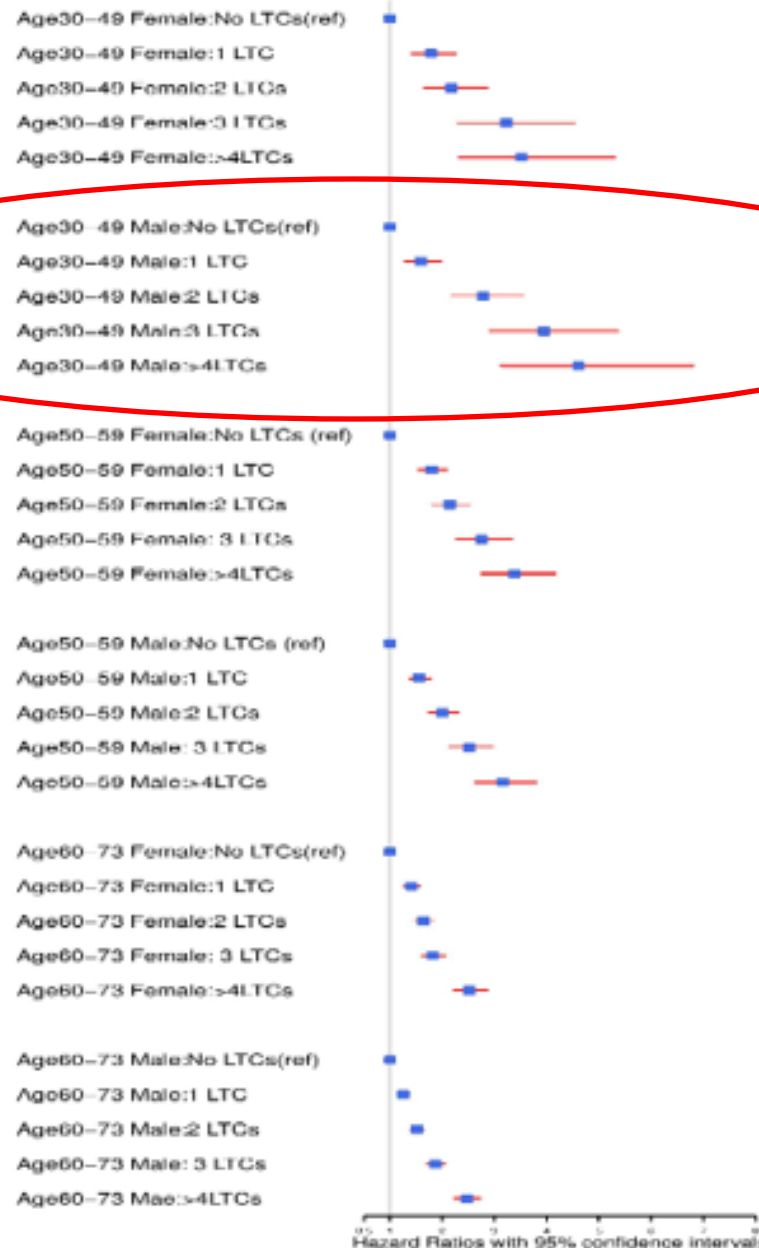The relationship between age, sex and multimorbidity in predicting all-cause mortality. N = 500,769. LTCs long-term conditions. Adjusted for socioeconomic status (Townsend score), smoking status, alcohol consumption, BMI, and physical activity levels at baseline

CV Diseases ➡️ Higher Cancer and Vascular Mortality

Type of LTCs	N=500,769. Adjusted Analyses*(Missing values n=12,045; 2.4%)		
	Hazard Ratios (95% Confidence intervals) for **All-cause Mortality**	Hazard Ratios (95% Confidence intervals) for **Cancer Mortality**	Hazard Ratios (95% Confidence intervals) for **Vascular Mortality**
No cardiometabolic conditions	1	1	1
1 LTC-cardiometabolic	1.19 (1.15-1.24)	1.04 (0.99-1.10)	1.79 (1.63-1.96)
2 LTC-cardiometabolic	1.67 (1.58-1.77)	1.15 (1.06-1.24)	3.42 (3.06-3.82)
3 LTC-cardiometabolic	2.52 (2.31-2.76)	1.23 (1.05-1.44)	7.31 (6.32-8.46)
≥4 LTC-cardiometabolic	3.20 (2.56-4.00)	1.67 (1.12-2.51)	8.20 (5.81-11.58)
No previous cancer	1	1	1
Presence history of Cancer	2.83 (2.71-2.95)	4.26 (4.06-4.47)	0.99 (0.87-1.13)
No non-cardiometabolic condition	1	1	1
1 LTC (excluding cancer and cardiometabolic)	1.08 (1.04-1.12)	0.99 (0.95-1.04)	1.02 (0.94-1.11)
2 LTCs (excluding cancer and cardiometabolic)	1.16 (1.10-1.22)	0.98 (0.92-1.05)	1.15 (1.03-1.29)
3 LTCs (excluding cancer and cardiometabolic)	1.25 (1.16-1.35)	0.96 (0.86-1.07)	1.29 (1.10-1.52)
4 LTCs (excluding cancer and cardiometabolic)	1.50 (1.36-1.67)	0.89 (0.75-1.05)	1.62 (1.31-1.99)

Age as time scale for both analyses. LTC=Long-term conditions; *Adjusted for sex, socioeconomic status based on Townsend score, smoking status, alcohol status, Body Mass Index, and physical activity levels reported at base line.

Jani B et al. Relationship of Multimorbidity, Demographic Factors and Mortality: Findings from UK Biobank Cohort. BMC Medicine. In Press.
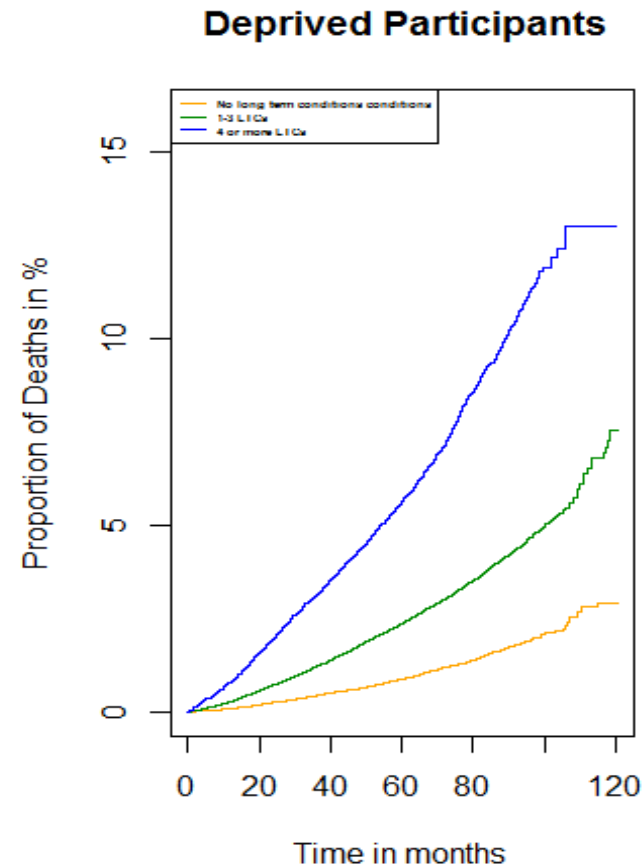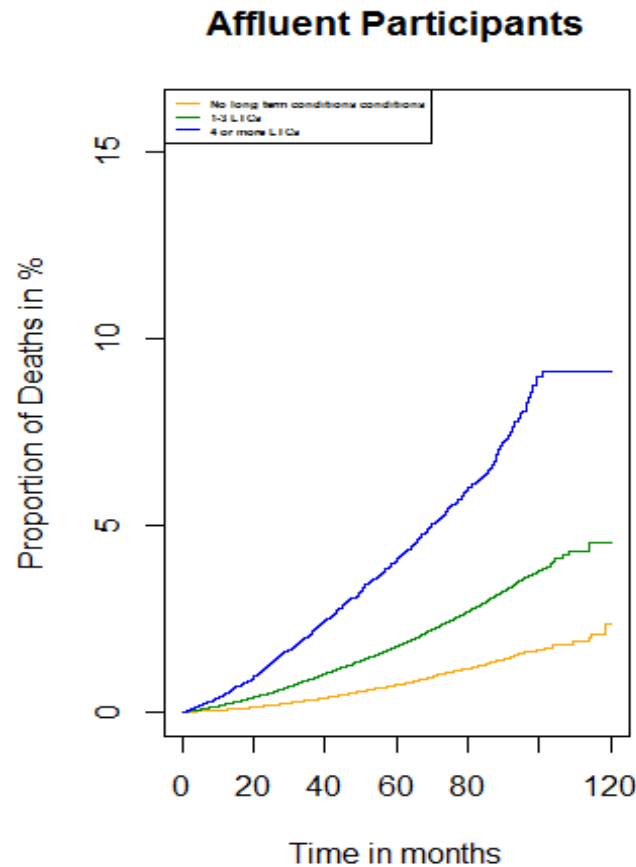
Polypharmacy

Increases in complexity of treatment regimens have been associated with substantially lower adherence, further impairing effective treatment (WHO 2003)

Panel: Key messages in Right Care Series

Overuse and underuse coexist within populations, within systems, and even within patients around the world.

Underuse of proven medical care and overuse of unproven services causes suffering to millions of people around the world. The costs are serious: physical, psychological, and social harms for patients and wasteful misallocation of resources for society.

Because most care falls in a grey zone in which benefits and harms are not clear, attention to preferences of patients is essential. The medical community needs to do what patients want rather than what health professionals know how to do.

Overuse and underuse are symptoms of a health-care system that does not reflect the ethics of medicine. They undermine the capacity of countries to achieve sustainable universal health coverage and to ensure that health care is a human right. Action is possible and necessary.

University
of Glasgow
VIA VERITAS VITA

"There was a chemist I had to go down and see at the health centre one day and he wanted to discuss my medication... he said you need to be on aspirin, I said no I think from what they said that caused me the problem, oh no you definitely need to be on aspirin...I said you better go and check up on that so he went ...he came back and he said you are right you shouldn't be on aspirin. Because I had a bleed. And that would have made it worse." (P2)

BMJ Open

Examining patterns of multimorbidity, polypharmacy and risk of adverse drug reactions in chronic obstructive pulmonary disease: a cross-sectional UK Biobank study

Peter Hanlon,[1] Barbara I Nicholl,[1] Bhautesh Dinesh Jani,[1] Ross McQueenie,[1] Duncan Lee,[2] Katie I Gallacher,[1] Frances S Mair[1]

Methods

- Comparison: COPD vs No COPD

- Outcome: risk of adverse drug reactions (3 or more medications)
  - Falls
  - CNS depression
  - Urinary retention
  - Constipation
  - Bleeding
  - Renal injury

- Logistic regression analyses
- Adjusted for age, sex and socioeconomic status, BMI, smoking, alcohol

Odds ratios (with 95% CI) for taking 3 of more medications associated with similar ADRs

ADR	Self-report COPD compared with no COPD N=502,640	
	OR	95% CI
Falls	1.83 ***	(1.71-1.96)
Constipation	2.66 ***	(2.39-2.96)
Urinary retention	2.59 ***	(2.22-3.0)
Sedation	2.81 ***	(2.45-3.22)
Bleeding	3.39 ***	(2.40-4.66)
Renal injury	1.84 ***	(1.53-2.19)
*** : p<0.001		

Hanlon P et al. Examining Patterns of multimorbidity, polypharmacy and risk of adverse drug reactions in chronic obstructive pulmonary disease: a cross sectional study.. BMJ Open 2018;8(1):e01840

COPD Comorbidity and Adverse Drug Reactions

Bubble plot of showing percentage of participants in each comorbidity category
taking 3 or more concomitant medications associated with specific adverse drug reactions
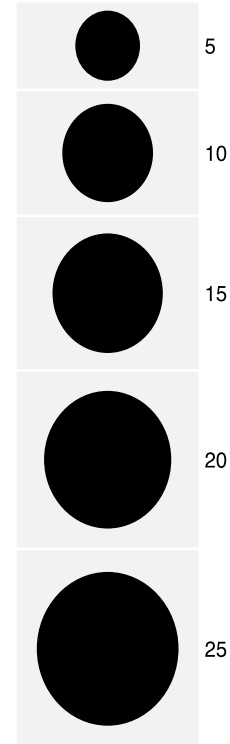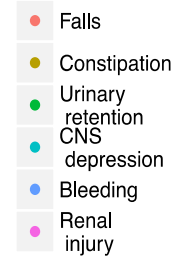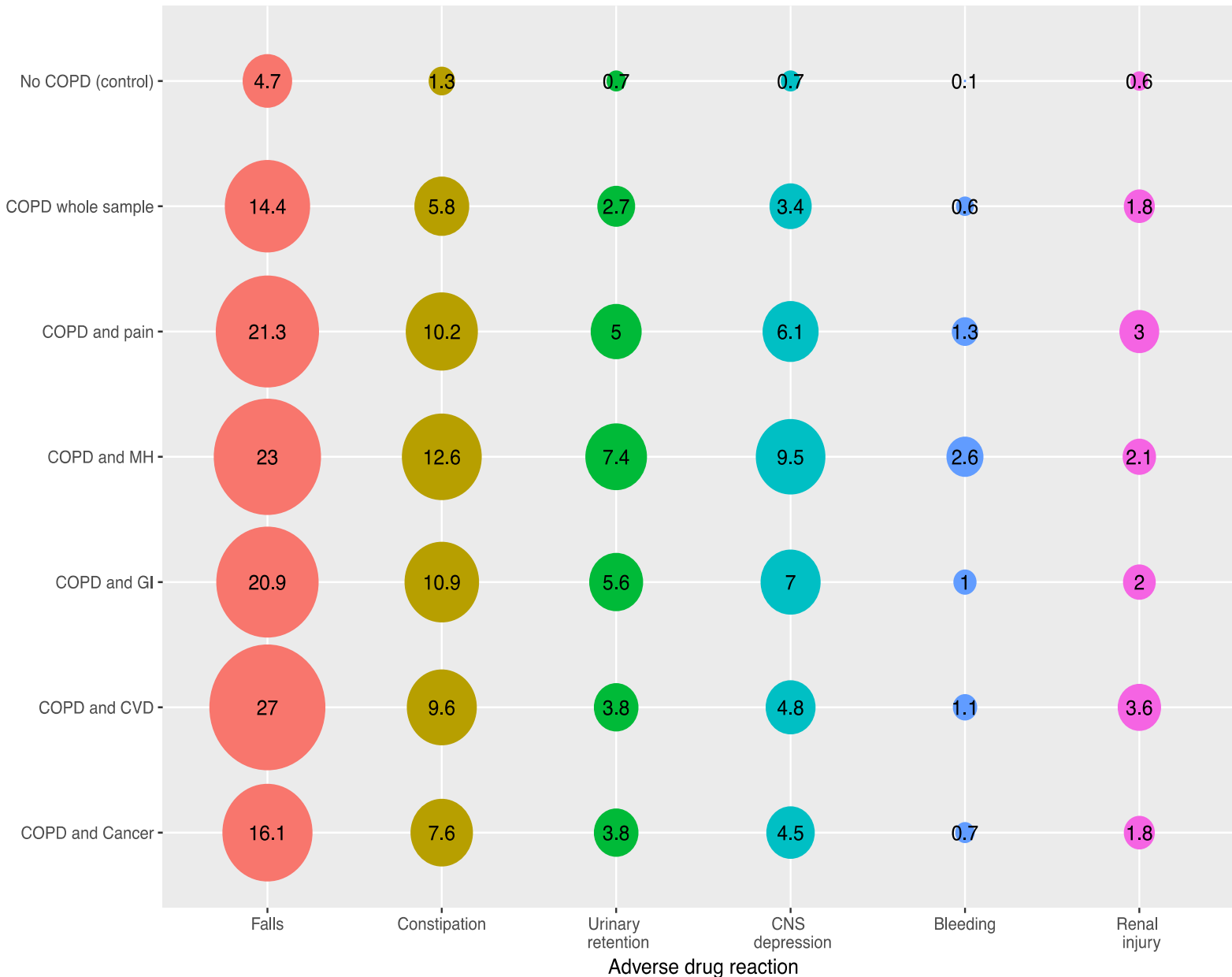
ADR = Adverse Drug Reaction, COPD = Chronic Obstructive Pulmonary Disease, CVS = Cardiovascular disease, GI = Gastrointestinal disease, MH – Mental health conditions. The size of each bubble represents the percentage of participants in each comorbidity group taking 3 or more concomitant medications associated with specific ADRs according to the Scottish Government Polypharmacy Guideline

Conclusion

- Comorbid cardiovascular disease most strongly associated with taking multiple drugs causing falls/fractures and renal injury

- Comorbid mental health conditions most strongly associated with taking multiple drugs causing CNS depression, constipation, urinary retention and bleeding

- Clinical guidelines should emphasize assessment of comorbidities, prescribing and ADR risk

Polypharmacy is Common

- **Co-prescription of drugs with similar ADRs common**

- **Medications contributing to ADR risk indicated for the treatment of comorbidities**

- **Future research should examine the impact of these patterns of prescribing on outcomes**

Hanlon P et al. Examining Patterns of multimorbidity, polypharmacy and risk of adverse drug reactions in chronic obstructive pulmonary disease: a cross sectional study.. BMJ Open 2018;8(1):e01840

Acute kidney injury risk 5 years
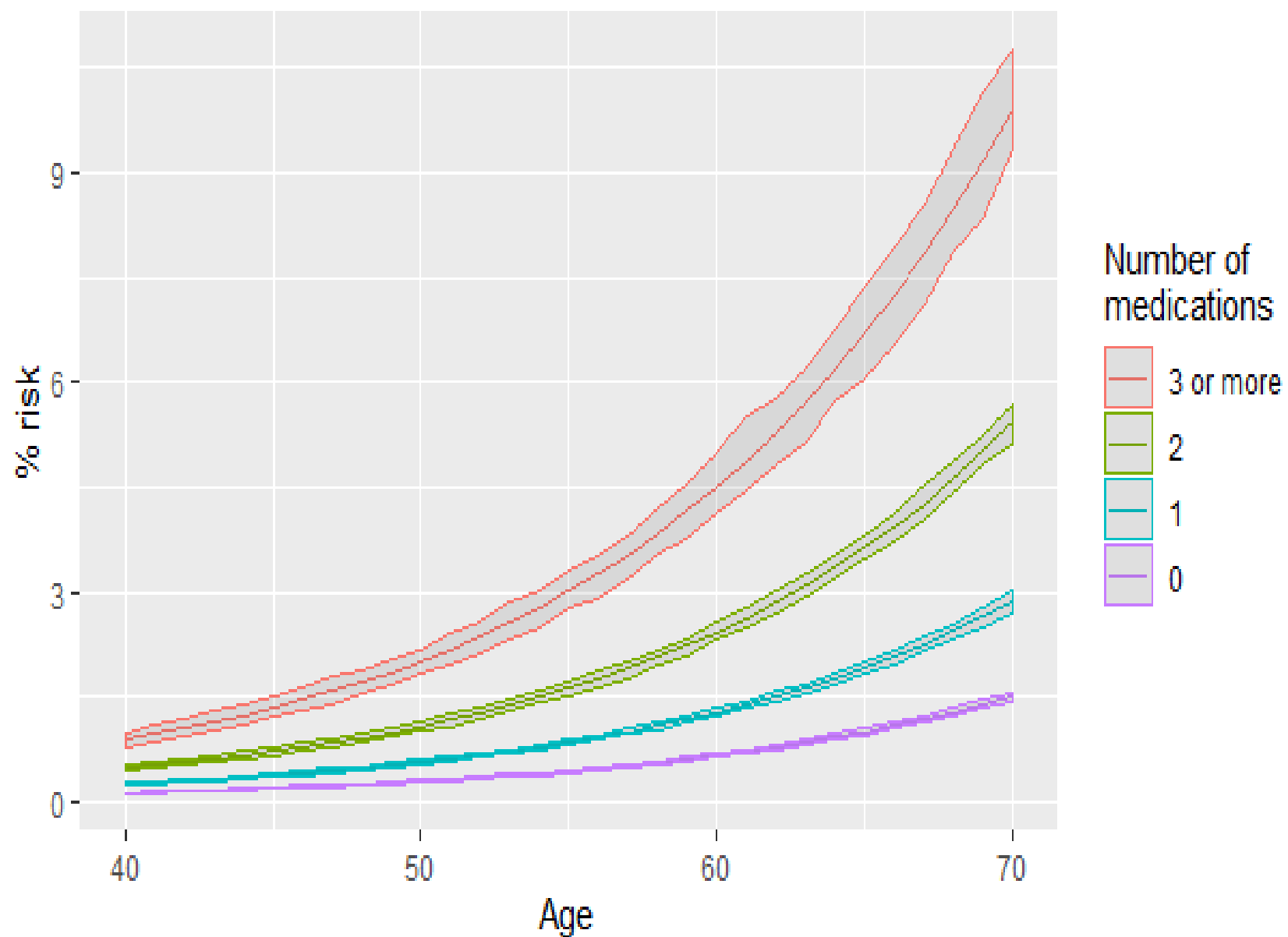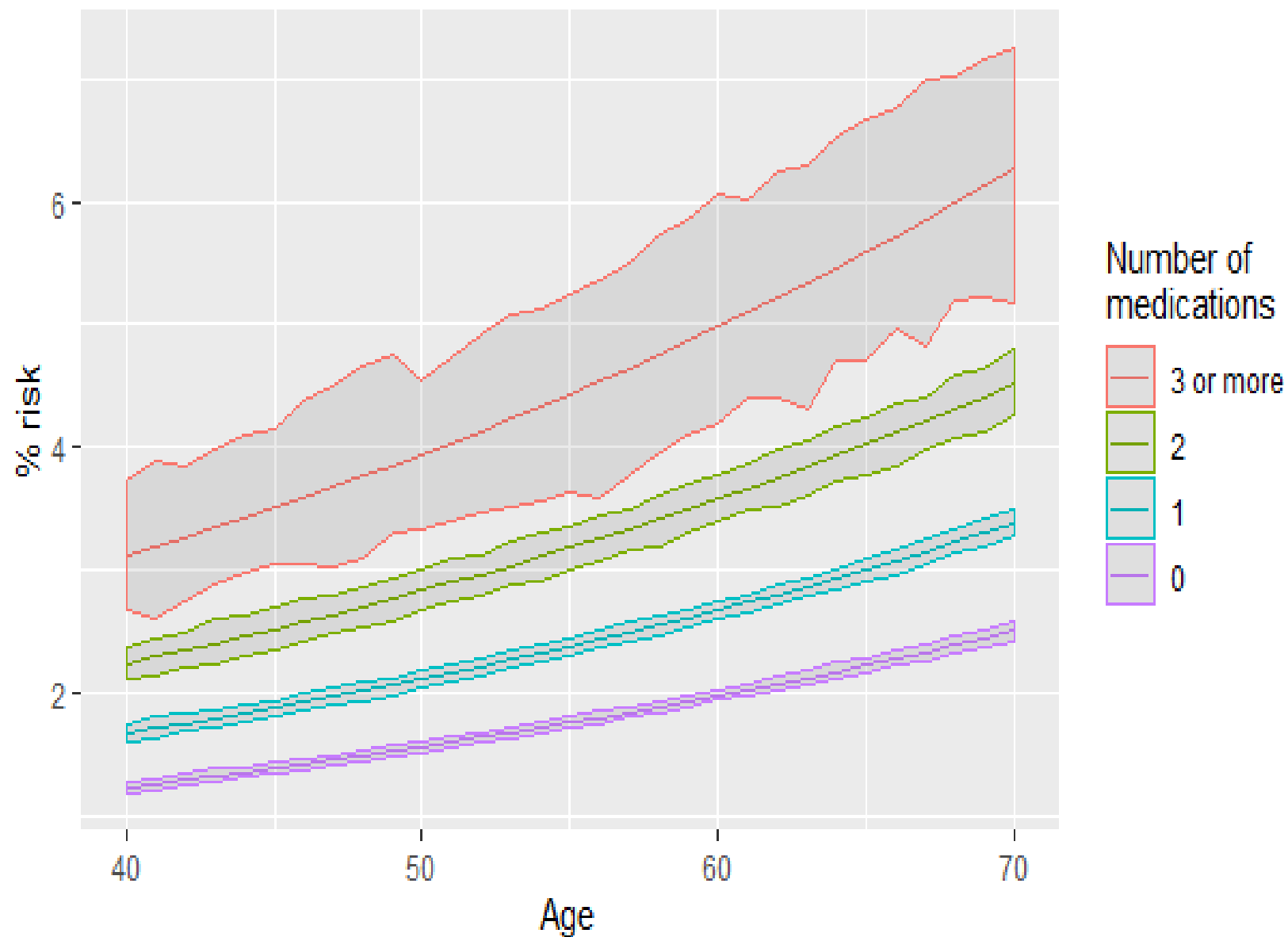
Renal injury: combinations with highest effect sizes
adjusted for age, sex, SES, BMI, smoking, alcohol, and MM count

Drug combination	N taking combination	HR (95% CI)
Aldosterone antiagonist and Loop diuretic	496	2.08 (1.6–2.7)
Aldosterone antiagonist and Angiotensin 2 receptor blocker	257	1.98 (1.38–2.86)
Amiloride and Loop diuretic	625	1.72 (1.36–2.18)
Loop diuretic and Thiazide diuretic	212	1.66 (1.1–2.51)
Loop diuretic and ACE–Inhibitor	2562	1.64 (1.44–1.86)
Amiloride and Angiotensin 2 receptor blocker	144	1.59 (0.95–2.64)
Loop diuretic and Angiotensin 2 receptor blocker	1264	1.58 (1.32–1.88)
NSAID and Loop diuretic	872	1.56 (1.26–1.93)
NSAID and Amiloride	218	1.43 (0.94–2.18)
Aldosterone antiagonist and ACE–Inhibitor	472	1.37 (0.99–1.91)
Amiloride and ACE–Inhibitor	247	1.22 (0.8–1.88)
Angiotensin 2 receptor blocker and ACE–Inhibitor	783	1.13 (0.86–1.48)
NSAID and Angiotensin 2 receptor blocker	2947	1.08 (0.93–1.25)
Amiloride and Thiazide diuretic	343	1.04 (0.68–1.58)
NSAID and ACE–Inhibitor	6372	1 (0.9–1.12)
NSAID and Thiazide diuretic	5224	0.96 (0.86–1.09)
Thiazide diuretic and ACE–Inhibitor	12859	0.95 (0.88–1.03)

Hazard Ratio

0 1 2 3 4 5 6 7

We Need Minimally Disruptive Medicine

Courtesy of BMJ 29 august 2009 Vol 339. May, Montori and Mair. We need Minimally Disruptive Medicine.

EDITORIALS

Thinking about the burden of treatment

Should it be regarded as an indicator of the quality of care?

Frances S Mair *professor of primary care research*[1], Carl R May *professor of healthcare innovation*[2]

[1]Institute of Health and Wellbeing, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow G12 9LX, UK; [2]NIHR CLAHRC, Faculty of Health Sciences, University of Southampton, UK

Illness burden =

the "work" that

patients and

their families do

to understand

and "live with"

a chronic illness
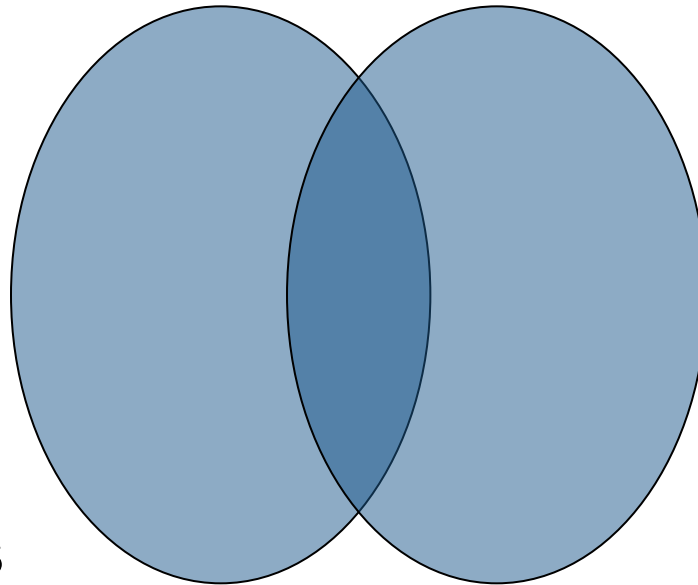
Treatment burden =

self-care

practices that

patients must

perform to

manage

their treatments

and their

interactions

with HPs[1]

What is Treatment Burden?

Learning about treatments and their consequences

- **Gaining an understanding of the illness, investigations, and treatments.**
- **Knowing when to seek help.**

Adhering to treatments and lifestyle changes

- **Attending appointments and taking medications.**
- **Enacting lifestyle changes**
- **Overcoming barriers such as accessibility to healthcare and poor continuity of care.**
- **Integrating treatments into social circumstances. Includes financial efforts.**

THE PATIENT

Engaging with others

- **Gaining support, advice, reassurance relating to treatments**
- **Using organisational skills for transport, prescriptions etc.**

Monitoring the treatments

- **Altering management routines.**
- **Appraising treatments and medical advice.**

Gallacher K, May CR, Montori VM, Mair FS. Understanding patients' experiences of treatment burden in CHF using NPT. Annals of Family Medicine. 2011

Effective treatments

+

Good treatment adherence

=

Optimum treatment outcomes

Patient education and access to information → **Improved patient knowledge** | **Decreased treatment burden** ← Patient centred care delivered by health services

Gallacher K, May CR, Montori V, Mair FS. Treatment Burden in Multimorbidity. In ABC of Multimorbidity 2014

To sum up:

"Aye I feel it's for the institution, its not for the patient, everything is geared for smooth running, that means it's from the hospital point of view and not the patients view, right or wrong, what do you think?" ID04

Treatment burden arises as a consequence of:

Healthcare workload   or   Care deficiencies

Need to reduce Burden of Treatment – SIMPLE IS BEAUTIFUL

- **Encourage Coordination in Clinical Practice**
- **Improve Communication**
- **Acknowledge Comorbidity in Clinical Evidence**
- **Prioritise from the Patient Perspective TAKING INTO ACCOUNT CAPACITY ISSUES.............**

Coping Threshold

1.Gallacher K, May CR, Montori V, Mair FS.Treatment Burden in Multimorbidity. In ABC of Multimorbidity.2014
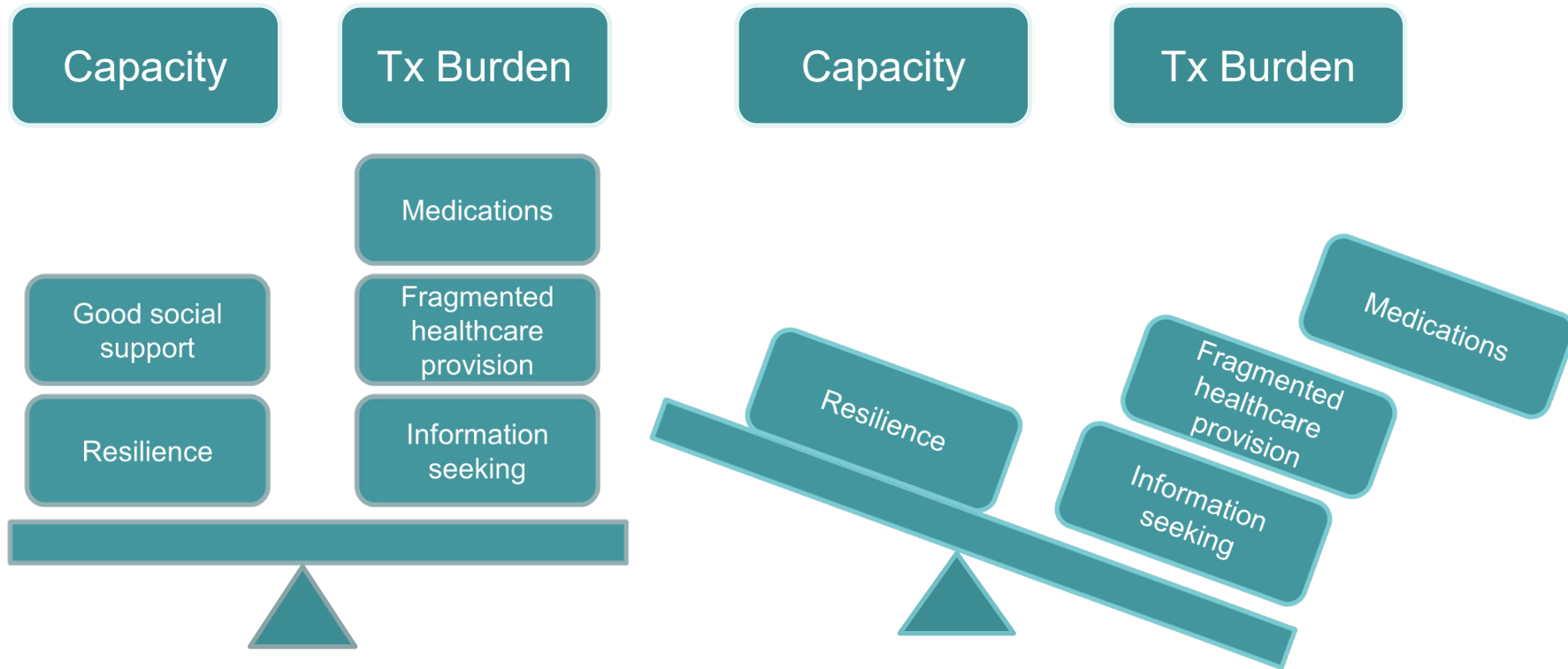
Cumulative complexity: a functional, patient-centered model of patient complexity can improve research and practice

Nathan D. Shippee, Nilay D. Shah, Carl R. May, Frances S. Mair, Victor M. Montori

Debate | Open Access | Open Peer Review

Rethinking the patient: using Burden of Treatment Theory to understand the changing dynamics of illness

Carl R May ✉, David T Eton, Kasey Boehmer, Katie Gallacher, Katherine Hunt, Sara MacDonald, Frances S Mair, Christine M May, Victor M Montori, Alison Richardson, Anne E Rogers and Nathan Shippee

◷ Open Peer Review reports

Fig. 1

1 — As social and clinical complicating factors accumulate, they add to patient workload demands, reduce patient capacity, or both in various ways.

2 — If patient workload expands and capacity dwindles, this creates an imbalance, as the patient passes his/her individual tipping point in one sphere of life or another and becomes overburdened, incapable of carrying out all the required tasks

3 — This imbalance disrupts patterns of access, utilization, and the routine of self-care, influencing how patients make sense of, participate in, achieve, and monitor personal health outcomes—and leading to unplanned prioritization and unaddressed demands.

4 — Workload-capacity imbalances may also persist and strengthen over time, as demands create stress, fatigue begets forgetfulness, and unfinished work piles up, leading to even further challenges and overburden.

Terms and Conditions

Patient workload of demands
Examples:
Job, Family, Self-care, Testing, Scheduling/attending appointments, Transportation, Paperwork

Attributes of workload demands:
Number, Difficulty, Fit

Burden of treatment   (*g*)

Patient capacity
Examples:
Physical/mental functioning, Pain, Symptoms, Fatigue, Finances, Literacy, Social support

Attributes of capacity factors:
Amount, Controllability, Extensiveness

Burden of illness   (*h*)

Access, Utilization, Self-care

Outcomes

a *b* *c* *d* *e* *f*

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VIA VERITAS VITA
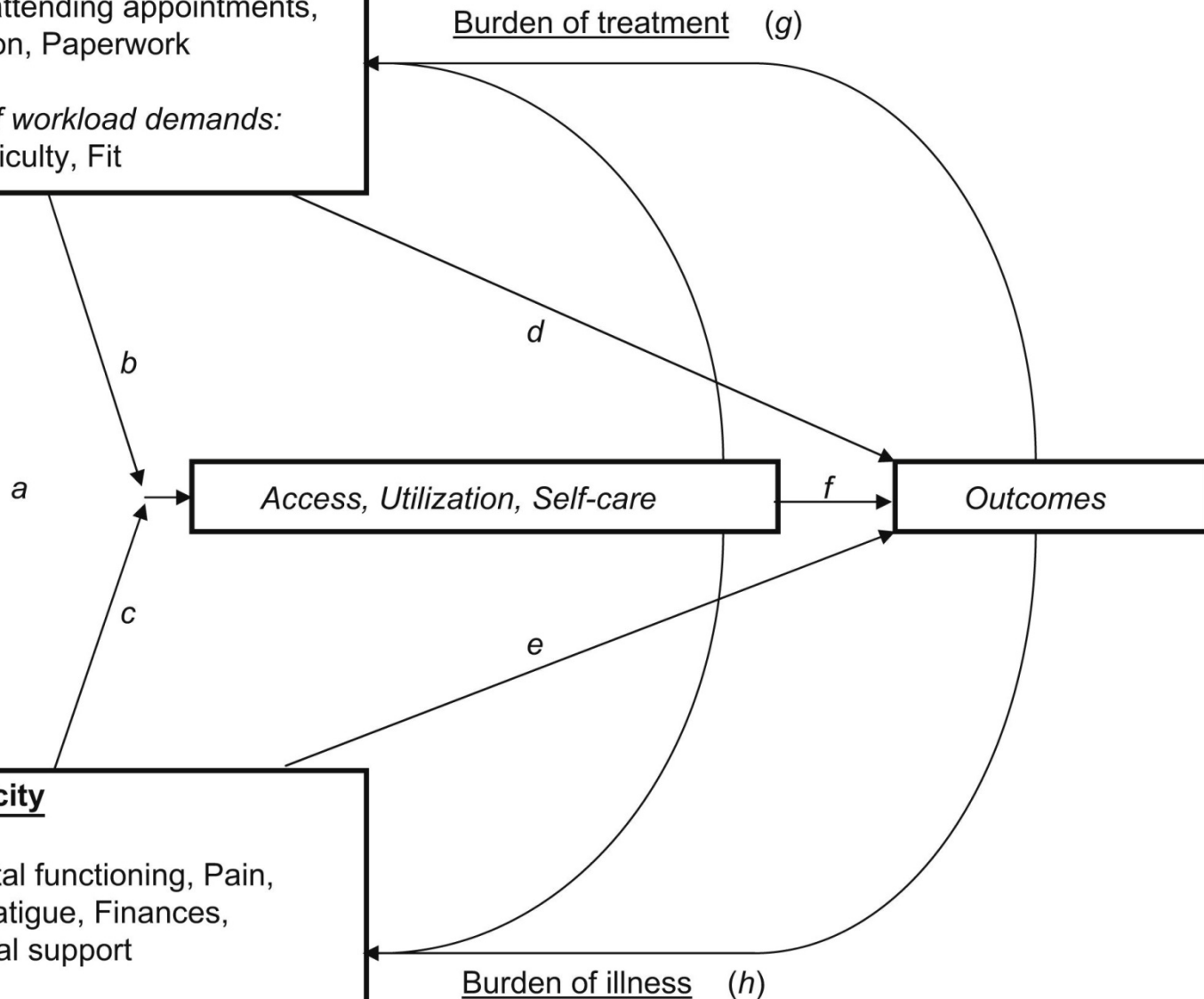
Personal Health Conditions

Polymyalgia Rheumatica
Diabetes
Atrial Fibrillation
Heart Failure
Hypertension
Coronary Artery Disease
Peripheral Vascular Disease
Carotid Artery Disease
Osteoporosis

Self – Management Work

- Arrange to get medications each month
- Take 10 Different Medications at different times of the day
- Endure side effects
- Attend clinics
- Undergo Investigations
- Increase physical activity
- Change Diet etc etc………

Other Illnesses He Has to Manage

Mother has dementia

Father has cognitive impairment, AF and frequent blackouts

Older brother with severe COPD, learning disabilities, poor mobility

Lifeworld work

Daughter aged 8yrs
Having fun?

Any Support?

Yes – a very supportive wife

Capacity

Six factors affected capacity and these were influential on the patient experience:

Personal attributes and skills	Support network	Life workload
Physical and cognitive abilities	Financial status	Environment

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Patience and persistence

Time

Energy

Negotiation & interpersonal

skills

Problem solving

Resilience

Health Literacy

Ability to prioritise and

juggle commitments
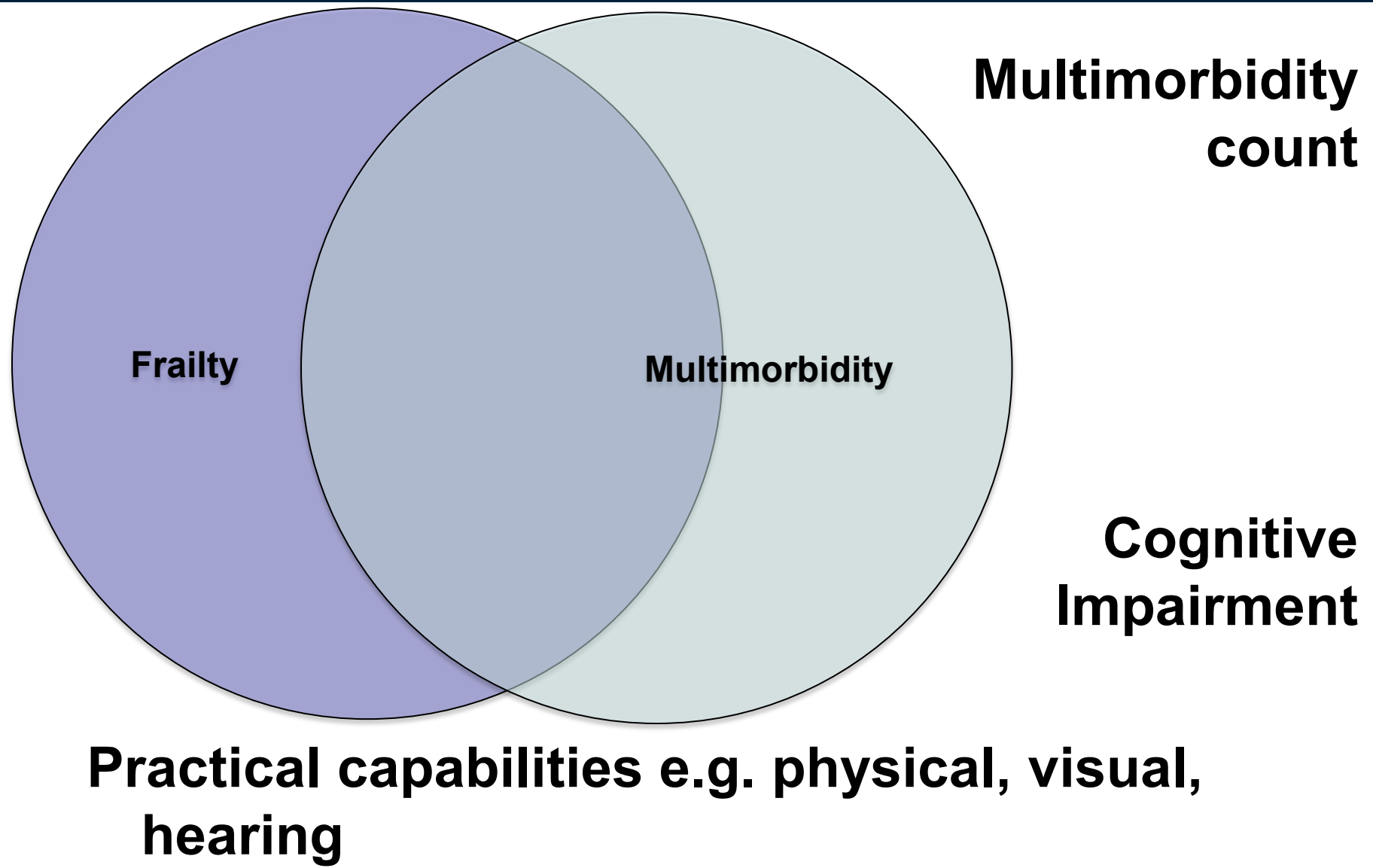
Frailty Phenotype

- *Weight loss*
- *Weakness*
- *Slow gait speed*
- *Low physical activity*
- *Exhaustion*

- **1-2: Pre-frail**
- **≥3: Frail**

Frailty Index

- *Cumulative count of age-associated deficits*

- *Calculated as a proportion of the total*

Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, **Mair FS.** Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493,737 UK Biobank participants. Lancet Public Health 2018;3(7):PE323-E332.

Recruitment:
503,640 participants

Frailty Phenotype:
493,737 with complete data (98%)
- Weight loss
- Grip strength
- Slow walking pace*
- Low physical activity
- Exhaustion

Not frail
n=291,839 (59.1%)

0 frailty indicators

Pre-frail
n=185,360 (37.5%)

1-2 frailty indicators

Frail
n=16,538 (3.3%)

≥3 frailty indicators

Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, **Mair FS.** Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493,737 UK Biobank participants. Lancet Public Health 2018;3(7):PE323-E332.

Prevalence of Frailty and Pre-frailty categorised by number of LTCs
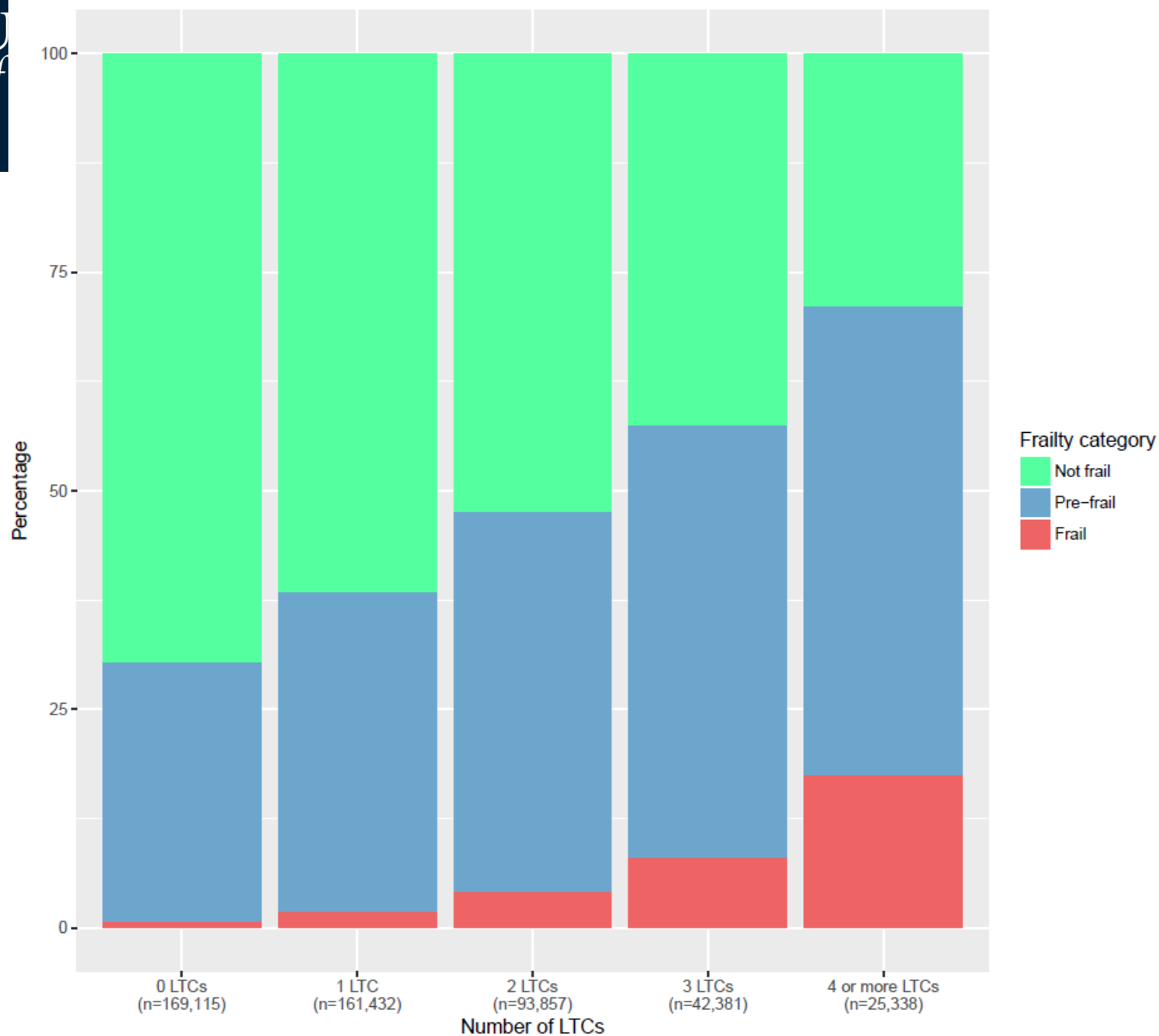

Frailty category
- Not frail
- Pre-frail
- Frail

Hazard ratios of all-cause mortality for frailty status stratified by age and sex, adjusted for socioeconomic status, BMI, smoking, alcohol frequency and multimorbidity count

Age Category	Sex	Frailty Category	Total	No. of deaths	Lower	HR	Upper	
37–45 years	Male	Not frail	18107	115		(ref)		
		Pre-frail	10163	110	1.04	1.36	1.79	
		Frail	478	20	1.58	2.7	4.64	
	Female	Not frail	20205	106		(ref)		
		Pre-Frail	12910	78	0.64	0.87	1.19	
		Frail	903	16	0.74	1.42	2.7	
45–55 years	Male	Not frail	39092	510		(ref)		
		Pre-frail	21194	553	1.33	1.51	1.71	
		Frail	1441	116	1.9	2.41	3.04	
	Female	Not frail	46818	404		(ref)		
		Pre-frail	30692	417	1.11	1.28	1.48	
		Frail	2714	99	1.85	2.38	3.06	
55–65 years	Male	Not frail	58000	1856		(ref)		
		Pre-frail	32363	1788	1.31	1.4	1.5	
		Frail	2777	455	2.25	2.52	2.84	
	Female	Not frail	65433	1210		(ref)		
		Pre-frail	44372	1288	1.26	1.37	1.49	
		Frail	4201	255	1.89	2.2	2.55	
65–73 years	Male	Not frail	19354	1236		(ref)		
		Pre-frail	12600	1365	1.34	1.45	1.57	
		Frail	1043	257	2.09	2.42	2.8	
	Female	Not frail	18793	600		(ref)		
		Pre-frail	14700	767	1.34	1.5	1.68	
		Frail	1583	180	2.1	2.53	3.04	

Hazard Ratio

Hanlon P et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493,737 UK Biobank participants. Lancet Public Health 2018;3(7):PE323-E332.
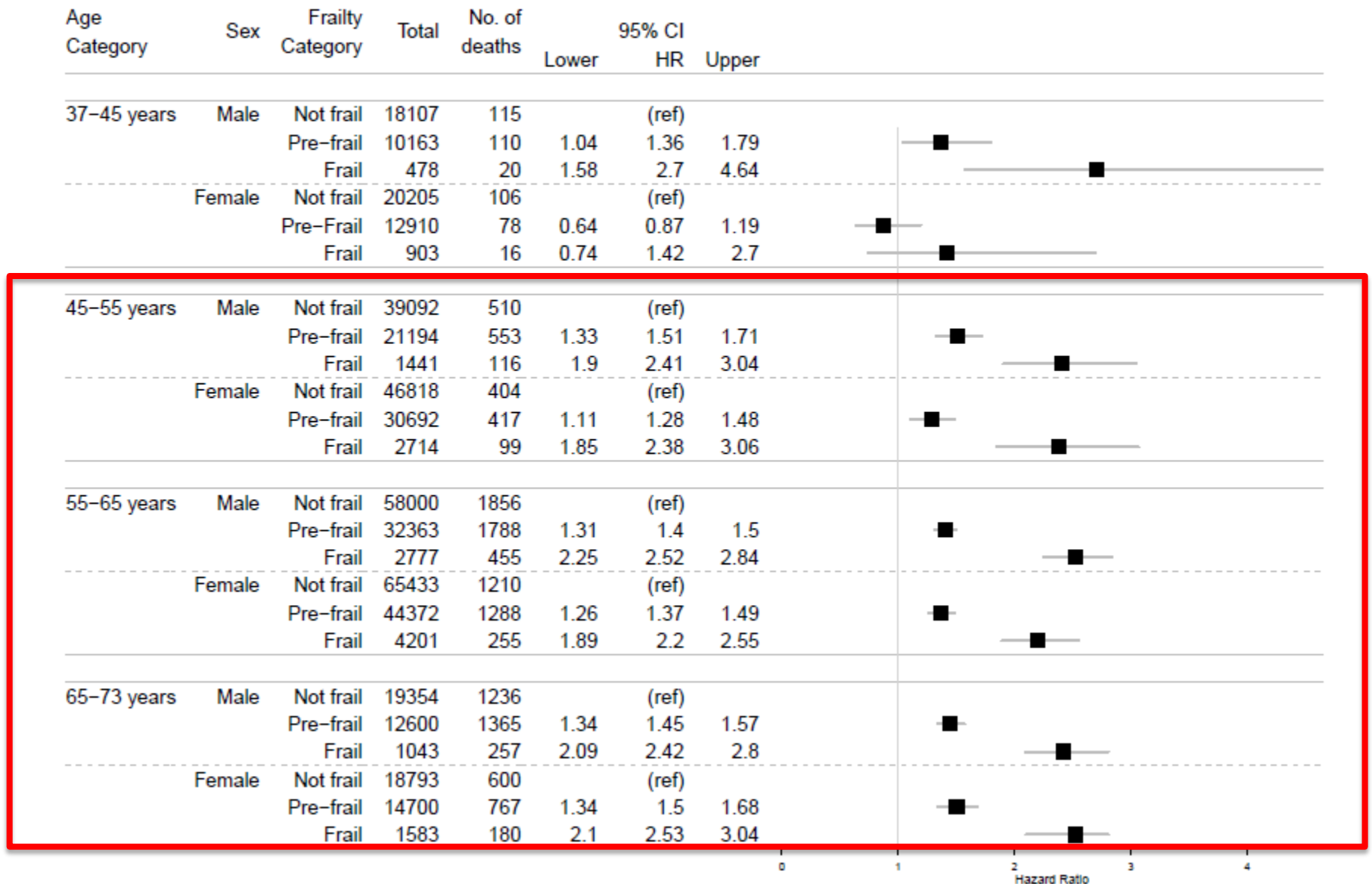
- Friends and family that give practical and emotional support such as information gathering, medications and transport to appointments.
- Volunteers / charities.
- Support groups and other people with similar problems.
- Employment that provides a support network.

- **Financial struggles e.g. loss of income, delay in benefits.**

- **Ability to pay for own mobility aids, adaptations, private healthcare or home care.**

- **Ability to pay for taxis to get to appointments**

Environment

Geographical location e.g. distance from hospital and transport links.

• Home environment e.g. stairs, access to house.

• Availability of aids or gadgets

Life Workload

- **Co-morbidities.**

- **Employment.**

- **Dependants e.g. spouse, children.**

Life Workload – self-management workload is only part of the workload in a person's life!

Preventing 30-Day Hospital Readmissions

A Systematic Review and Meta-analysis of Randomized Trials

Aaron L. Leppin, MD[1]; Michael R. Gionfriddo, PharmD[1,2]; Maya Kessler, MD[1,3]; et al

≫ Author Affiliations | Article Information

Multimorbidity
Why We Need A Precision Medicine Approach

Our focus should be on developing approaches that are better *tailored* to patients' needs (based on genetic, environmental, lifestyle and *capacity* factors) as well as their personal goals.

A one size fits all approach is unlikely to work……….

University of Glasgow

The most dangerous phrase in the language is "we've always done it this way."

Rear Admiral Grace Hopper (1906-1992)

RISK STRATIFICATION IN MULTIMORBIDITY

This is not a homogenous population

Two simple questions from the HCP may suffice:

1. *Can you really do what I am asking you to do?*

2. *Do you think what I am asking you to do is the right thing for you?*

Mair FS, May CR: Thinking about the burden of treatment, vol. 349; 2014

THANK YOU

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And thanks to Dr B Jani, K Gallacher, P Hanlon, and D Blane some of whose slides I've borrowed!