

The association of painful and non-painful morbidities with frailty: a cross sectional analysis of a cohort of community dwelling older people.

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- **Additional Figure 1. IMH&W Questionnaire medical condition checklist.**

**Has a doctor told you that you have any of these medical conditions or problems?
If yes, please place a tick in the boxes provided.**

- | | |
|--|---|
| <input type="checkbox"/> Angina | <input type="checkbox"/> Heart attack |
| <input type="checkbox"/> Arthritis | <input type="checkbox"/> Heart failure |
| <input type="checkbox"/> Asthma | <input type="checkbox"/> Hypertension |
| <input type="checkbox"/> Back or spine problems | <input type="checkbox"/> Kidney disease |
| <input type="checkbox"/> Cancer (not minor skin cancers) | <input type="checkbox"/> Lung disease |
| <input type="checkbox"/> Dementia | <input type="checkbox"/> Osteoarthritis |
| <input type="checkbox"/> Diabetes mellitus | <input type="checkbox"/> Osteoporosis |
| <input type="checkbox"/> Fibromyalgia | <input type="checkbox"/> Rheumatoid arthritis |
| <input type="checkbox"/> Gout | <input type="checkbox"/> Stroke |

Others (please specify any conditions not listed above)

Medicines including pain killers

Please write down the names of any medications, including any pain killers, that you use. They can be prescriptions or bought over the counter.

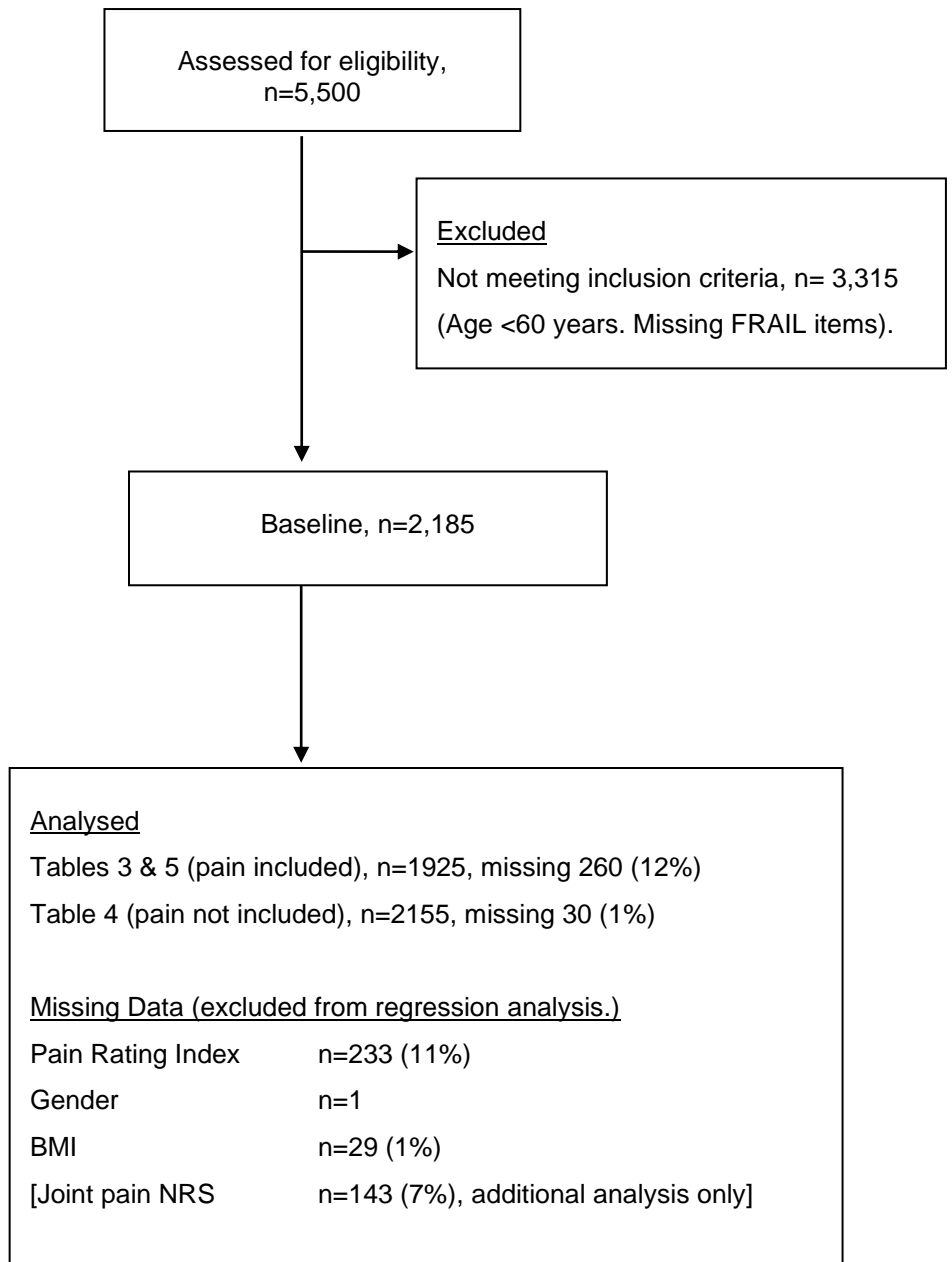
Names of medications

- Additional Figure 2. IMH&W Flow Diagram with missing data details.

IMH&W Database

Baseline

Analysis



- **Additional Table 1. Illness criteria for classification of morbidity free text.**

Illness condition	Illness inclusion criteria
Diabetes	Include type 1 or 2 diabetes on medication; exclude if pre-diabetic or controlled by diet alone
Cerebrovascular disease	Include stroke or TIA; cavernous angiomas multiple brain, brain aneurysm, brain haemorrhage.
Hypertension	Hypertension or high blood pressure
Angina	Angina also include those who had coronary artery bypass graft, and those initially admitted with unstable angina. Include those who report insertion of stents and any heart bypass.
Congestive heart failure	Includes heart failure and exertional or paroxysmal nocturnal dyspnoea.
Myocardial infarction	Include if any heart attack old or new, includes cardiac arrest.
Osteoarthritis, gout	osteoarthritis and gout and arthritis
RA + connective tissue disease	Include all inflammatory arthritis, including ankylosing spondylitis, psoriatic arthritis, RA, and inflammatory systemic conditions such as polymyalgia rheumatica, systemic lupus erythematosus, lupus, polymyositis, seronegative arthritis.
Asthma	Include any form of possible reversible airways obstruction, whether or not there is additional fixed obstruction or other lung pulmonary deficits this means that a patient reporting to have only COPD who is prescribed one of these will also be classified as having asthma
Lung disease	Include any non-reversible-airway limitation. Chronic obstructive pulmonary disease (COPD), acquired respiratory distress syndrome (ARDS), emphysema, pulmonary embolism, and thromboembolic pulmonary hypertension or permanent lung impairment such as resection.
Renal disease	Include patients on dialysis, those who had a transplant, and those with uraemia.
Cancer	Include all cancers, tumours or mention of chemotherapy/ radiotherapy or other cancer treatment <u>regardless</u> of when it occurred. Exclude if minor skin cancer.

Note: Osteoarthritis and Rheumatoid arthritis categories were collapsed into one called arthritis.

- **Additional Table 2. Medications indicating specific illnesses.**

- **Angina**

Glyceryl trinitrate:
 1-glyceryl nasal spray
 2-gtn spray (mouth spray)
 3-gtn tablets
 4-nitromin spray
 5-nitrolingual pump spray
 Ranolazine
 Nicorandil
 Isorbide mononitrate
 Isorbide dinitrate
 Tardisc xl
 Monomil xl
 Isotard xl

- **Asthma**

Drugs in the class selective beta2-agonists (short-acting)
 Salbutamol:
 Salamol easi-breathe cfc-free inhaler Ventolin
 100micrograms/dose evohaler
 Drugs in the class inhaled corticosteroids:
 Beclometasone dipropionate
 Qvar easi-breathe inhaler
 Clenil modulite inhaler
 Budesonide with formoterol
 Formoterol fumate
 Symbicort 100/6 turbohaler
 Beclometason with formoterol
 Fostair nexthaler® 200/6
 Fluticasone with salmeterol
 Airflusal
 Seretide evohaler
 Beclomethasone dipropionate
 Becotide 50 inhaler
 Budesonide
 Pulmicort turbohaler
 Fluticasone with salmeterol
 Salmeterol
 Seretide evohaler
 Seretide 250 accuhaler
 Sirdupla inhaler
 Terbutaline sulfate

Others:
 Uniphyllin continus
 Tiotropium
 Acclidinium bromide with formoterol

Acclidinium bromide
 Glycopyrronium with indacaterol

Nucala inhaler
 Mepolizumab
 Trimbrow inhaler

- **Osteoarthritis, gout**

Colchicine
 Alluprinol
 Febuxostat

- **RA + connective tissue disease***

*Put in a conditional argument (rituximab if not lymphoma), all anti-tnfs if not ulcerative colitis/ Crohn's

Drugs in the class tumour necrosis factor alpha (tnf-a) inhibitors:

Etanercept
 Benepalil solution for injection pre-filled syringes
 Enbrel solution for injection pre-filled myclic pens
 Erelzsolution for injection pre-filled syringes

Drugs in the class disease-modifying anti-rheumatic:

Leflunomide tablets
 Drugs in the class t-cell activation inhibitors:
 Abatacept
 Orencia solution for injection pre-filled syringes

Drugs in the class interleukin inhibitors:

Tocilizumab
 Adalimumab
 Benepali
 Betamethasonevalerat
 Hycophenolate
 Hydroxychloroquine
 Levo humira
 Metoject
 Nivestim
 Methrotexate
 Sulphasalazine
 Leflunomide

All anti-tnfs (unless psoriasis or inflammatory bowel disease, rituximab, tocilizumab)

Infliximab
 Cyclophosphamide

- **Diabetes**

Alogliptin
Basaglar insulin
Bolamyn SR
Dapagliflozin
Dulaglutide
Empagliflozin
Forxiga
Gliclazide
Gliclazide
Glimepiride
Glucophage
Humulin
Insulin
Januvia
Jardiance
Levemir insulin
Levo linagliptin
Linagliptin
Liraglutide
Metabet
Metformin
Novomix
Pioglitazone
Sitagliptin
Sukkarto
Synjardy
Toujeo
Trajenta
Victoza
Vipidia
Zicron

- **Hypertension**

Calcium-channel blockers:
Lacidipine
Lercanidipine hydrochloride
Securon SR tablets
Drugs in the class non-diuretic thiazide:
Indapamide
Drugs in the class antihypertensives, centrally acting:
Moxonidine

- **Lung disease**

drugs in the class mucolytics
Carbocisteine
1-Mucodyne Capsules
2-Carbocisteine capsules

- **Congestive heart failure**

Eplerenone

- **Renal disease**

Lanthanum
Fosrenal

- **Cancer**

Anastrozole
Tamoxifen
Bicalutamide
Oxaliplatin
Imatinib
Hydroxycarbamide
Capecitamine
Ruxolitinib

- **Ulcer disease**

*Put in a conditional argument (Include *azole or ranitidine if not taking NSAIDS or concomitant systemic glucocorticoid steroid.

Drugs in the class proton pump inhibitors:
Lansoprazole
Omeprazole
Pantoprazole
Rabeprazole sodium

Pariet gastro-resistant tablets [k4]
Rabeprazole gastro-resistant tablets [k4]
Ranitidine
Famotidine

- **Osteoporosis**

*Put in a conditional argument: If prednisolone AND Zoledronic acid Or Alendronic acid or Ibandronic acid, then do not code as osteoporosis

Zoledronic acid
Alendronic acid
Ibandronic acid
Raloxifene hydrochloride
Denosumab:
Denosumab 60/1ml
Denosumab (Prolia)

- **Dementia**

Donepezil
Memantine

- **AIDS**

Efavirenz
Atripla

- **Anxiety & Panic Disorders**

Diazepam
Nitrazepam tablets
Lorazepam

- **Depression**

Depefex XL capsules
Citalopram tablets
Cipramil
Imipramine
Lithium
Lofepramine
Mirtazapine
Phenelzine
Reboxetin

- **Neurological**

Dopamine precursors drugs:
Co-careldopa
Co-careldopa tablets
Sinemet tablets
Co-beneldopa (ingredients: levodopa and benserazide):
Co-beneldopa capsules
Madopar tablets
Dopamine receptor agonists:
Acute drug-induced dystonic reactions
Repinex XL tablets
Pramipexole modified-release tablets
rotigotine patches
Antimuscarinics drugs:
Trihexyphenidyl hydrochloride
Trihexyphenidyl 2mg tablets
Procyclidine 5mg tablets
Drugs in the class monoamine-oxidase b inhibitors
Rasagiline
Rasagiline tablets
Azilect tablets
Catechol-o-methyltransferase inhibitors class
drugs
Entacapone tablets
Other:
Ongentys hard capsules
Stanek tablets (levodopa with carbidopa and entacapone)
Amantadine hydrochloride tablets

- **Visual impairment**

(Includes glaucoma irrespective of visual impairment)

Drugs in the class antimuscarinics:

Cyclopentolate hydrochloride (Mydrilate)
Minims cyclopentolate hydrochloride eye drops

Drugs in the class prostamides:

Bimatoprost with timolol (eyzeetan, Ganfort)
Bimatoprost eye drops (Lumigan, Eyreida)

Drugs in the class prostaglandins and analogues:

Latanoprost (Medizol, Monopost, Xalatan, Xelpros)
Travoprost (Bondulc, Travatan, Izba)

Timolol 5mg/ml eye drops

Drugs in the class beta blocking agents, non-selective:

Timolol maleate (azarga, cosopt, timoptic, betimol, tiopex)

- **No specific drug for the condition**

- Congestive heart failure
- Degenerative disc disease
- Myocardial infarction
- Cerebrovascular disease
- Peripheral vascular disease
- Liver disease
- Hearing impairment
- Hemiplegia
- Diabetes end with end organ damage (requires additional comorbidities of retinopathy, neuropathy, or nephropathy to be present)

- **Additional Table 3. Morbidity count by checklist and augmentation (n=6,342)**

Morbidity	Painful Yes/No	Check-list ¹ n	Free text ² n	Medications ³ n	Total n, (%)
Arthritis	Yes	1447	21	9	1477 (68)
Hypertension	No	779	42	35	856 (39)
Degenerative disc disease	Yes	767	24	0	791 (36)
Upper gastro-intestinal	Yes	0	26	658	684 (31)
Asthma	No	325	7	81	413 (19)
Diabetes without complications	No	349	12	25	386 (18)
Osteoporosis	Yes	218	4	29	247 (11)
Cancer	Yes	201	30	6	237 (11)
Angina	Yes	197	14	17	228 (10)
Lung disease	No	139	38	8	185 (8)
Myocardial Infarction	Yes	150	0	0	150 (7)
Stroke	No	126	19	0	145 (7)
Kidney disease	No	116	10	0	124 (6)
Depression	Yes	0	23	81	104 (5)
Visual impairment	No	0	34	57	91 (4)
Chronic Heart Failure	Yes	60	2	1	63 (3)
Neurological	No	0	35	21	56 (3)
Anxiety	No	0	18	22	40 (2)
Lower Gastro-intestinal	Yes	0	29	0	29 (1)
Hearing impairment	No	0	12	0	12 (0.5)
Diabetes with complications	Yes	0	12	0	12 (0.5)
Dementia	No	9	0	0	9 (0.4)
Liver disease	Yes	0	7	0	7 (0.3)
Peripheral vascular disease	Yes	0	6	0	6 (0.3)
Hemiplegia	No	0	1	0	1 (<0.1)
AIDS	No	0	1	0	1 (<0.1)
Subtotal illnesses in FRAIL (11)		3,889	196	182	4,264
Subtotal illnesses not in FRAIL (15)		994	220	868	2,078
Total morbidities identified		4,883	413	1,050	6,342

Abbreviations: AIDS – Acquired immune deficiency syndrome. Items in bold are included in FRAIL, non-FRAIL illnesses are extra morbidities from Charlson and Functional Comorbidity Indices.

Diabetes is classified as painful if the participant reports complications such as neuropathy (Charcot foot), and retinopathy.

1 - morbidity appeared in checklist. This included all FRAIL illnesses plus degenerative disc disease, osteoporosis, and dementia. 2 - morbidity appeared in free text only. 3 - morbidity is inferred from medication only.

Note: there is an order of precedence to columns, the morbidity is counted as present in the following order 1) checklist; 2) free text; 3) medication; and counted once even though it may be originally reported in all three ways.

1159 (53%) of participants reported free text morbidities and 2088 (96%) reported medications.

- **Additional Table 4. Bivariate associations between morbidity count and covariables.**

<i>Variable</i>	<i>'Any' morbidity</i>	<i>Bivariate association β Coef. (95% CI)</i>	<i>Painful morbidity</i>	<i>Bivariate association β Coef. (95% CI)</i>	<i>Non-painful morbidity</i>	<i>Bivariate β Coef. (95% CI)</i>
<i>Sex:</i>						
<i>Male,</i>	3 (2-4)	Ref	2 (1-2)	Ref	1 (1-1)	Ref
<i>Female</i>	3 (2-4)	0.14 (0.03, 0.29), p=0.045	2 (1-3)	0.17 (0.07, 0.28), p=0.001	1 (0-2)	-0.03 (-0.11, 0.05), p=0.455
<i>Age (years)</i>	73 (69-79) *	0.01 (-0.001, 0.02), p=0.064	73 (69-79) *	0.01 (0.001, 0.02), p=0.02	73 (69-79) *	0.001 (-0.005, 0.007), p=0.746
<i>BMI Classes#</i>						
<i>Underweight</i>	3 (1-4)	0.17 (-0.44, 0.78), p=0.582	2 (1-3)	0.25 (-0.21, 0.71), p=0.289	1 (0-1)	-0.09 (-0.44, 0.26), p=0.616
<i>Normal</i>	2 (1-4)	Ref	2 (1-3)	Ref	1 (0-1)	Ref
<i>Pre-obese</i>	3 (2-4)	0.20 (0.03, 0.37), p=0.021	2 (1-3)	0.13 (-0.003, 0.26), p=0.055	1 (0-2)	0.07 (-0.03, 0.17), p=0.134
<i>Obese</i>	3 (2-4)	0.52 (0.34, 0.71), p<0.001	2 (1-3)	0.27 (0.13, 0.41), p<0.001	1 (1-2)	0.26 (0.15, 0.36), p<0.001

*Median age of participants with ≥1 morbidity count. Data are from n=2,155 participants

Abbreviations: BMI – Body Mass Index; β Coef. –beta coefficient; CI – 95% confidence intervals; Ref - reference group. #WHO classification for BMI (kg/m²), underweight <18.5, normal 18.5-24.9, pre-obese 25-29.9 and >30 obese.

- **Additional Table 5. Associations of frailty with standardised NRS pain and other characteristics.**

Factor	Interval/category	Frailty
		aOR (95%CI)
NRS pain	Standardised NRS pain	3.32 (2.79, 3.95), p<0.001
Painful comorbidities	Standardised count	1.37 (1.20, 1.56), p<0.001
Non-painful comorbidities	Standardised count	1.39 (1.24, 1.58), p<0.001
Sex	Male	Ref
	Female	1.36 (1.04, 1.76), p<0.024
Age	Years	1.03 (1.01, 1.05), p=0.001
BMI Class [#]	Underweight	3.49 (1.34, 9.09), p=0.011
	Normal	Ref
	Pre-obese	1.43 (1.01, 2.01), p=0.041
	Obese	2.15 (1.53, 3.02), p<0.001
Pseudo r ²		0.2323

The outcome measure is binary frailty without morbidity (mFRAIL), defined as mFRAIL score >2. The model is frailty with standardised painful and non-painful comorbidities adjusted for standardised pain severity, age, sex, and BMI class. Data are from n=2,015 participants. Standardized coefficients represent the change in the dependent variable's standard deviation associated with a one-standard-deviation increase in the predictor variable, they permit comparison of variable with different scales. Abbreviations: NRS – numerical rating score; BMI – Body Mass Index; aOR –adjusted odds ratio; CI – 95% confidence intervals; Ref - reference group. NA - Not Applicable [#]WHO classification for BMI (kg/m²), underweight <18.5, normal 18.5-24.9, pre-obese 25-29.9 and >30 obese.